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Original Research

A comprehensive overview by region of condoms, natural family planning, and spermicide as a contraceptive method among men aged 13–54 years attending contraceptive services in England

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ABSTRACT

Objectives: This study aimed to (1) provide a comprehensive overview of contraceptive methods self-reported by men in England, over 5 years, focusing on condoms in comparison to any male method; and (2) explore condom as a contraceptive method by region and ethnicity.
Study design: Data were from the Sexual and Reproductive Health Services (Contraception) England census data set from 2014/15 to 2018/19. Once missing data were removed, this left a total of 365,292 men. Two binomial logistic regression models were performed. Model 1 examined ethnicity, region, and time on condom as a method of contraception; and Model 2 examined ethnicity, region, and time by any male contraceptive. Descriptive statistics were run for natural family planning and spermicide.
Results: Model 1 revealed a significant model, χ^2 (15) = 30,976, $P < 0.001$, and predicted that condoms as a method decreased in London with a greater decrease in Midlands. London saw the lowest rate of decline among the non-White ethnic group, whereas North and South regions increased probability over time. The North started at a higher probability and the South at the lowest. Model 2 also revealed a significant model, χ^2 (15) = 32,472, $P < 0.001$, with a similar pattern to Model 1. Contingency tables showed natural family planning and spermicide were the least reported methods and decreased over time.
Conclusions: As any male contraceptive method appears to be decreasing in both models, reproductive health promotion is required. This study has implications for commissioning funds and for identifying regional areas of further investigation.

Introduction

A rich history of men and family planning as part of the global agenda and how this relates to the United Kingdom have already been documented.[1] While the United Kingdom has yet to report successful interventions, several low- and middle-income countries have already reported success engaging men. For example, research in Malawi suggests that increased communication among couples is mediated by an increase in knowledge and a decrease in male opposition within the couple; this is described as an essential part of the intervention's success.[2] Despite the United Kingdom having a history of providing aid for family planning to low- and middle-income countries for targeted programming, albeit this aid has recently been cut,[3] the United Kingdom has invested very little funding into research on their own men's family planning practices, including men's use of condoms for contraception, natural family planning, or spermicide as a method of contraception, leaving little understanding of men and contraception. There is now a public health movement beginning in the United Kingdom for men to 'responsibly ejaculate', or in other words take primary responsibility for contraception, for which there are currently barriers.[4] The literature suggests there is a need to further understand men's choice of contraception to be effective with increasing uptake and overcoming barriers to primary responsibility. However, before we can begin to overcome barriers, we must start with more effective data collection techniques and advanced analysis in published reports to guide decision-making. For a more in-depth review of the literature, see Supplemental Materials.

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Aims and exploration

This study objective was to build upon the research of Pearson[5] and Pearson and Clarke[6] using the same source of national data sets to understand condoms, natural family planning, and spermicide as a contraceptive method of men, by region, in England, over 5 years (from 2014 to 2019). The data sets available from the National Health System (NHS) clinics have some identified limitations by Pearson and Pearson and Clarke, for example, the data set lacked complete demographic information on men such as age (although age was recorded for women). Furthermore, the data were unavailable on men who attend for family planning purposes as part of a couple because the patient in a couple was recorded to be the woman partner. However, some limited information was provided regarding the ethnic background of men; again little is currently known about how ethnic background informs contraceptive method reported among men in the United Kingdom. Therefore, the second objective of this study was to then explore ethnicity and contraceptive as a method by men in England. It is to the authors' knowledge the first study to begin to understand condom as a method by region over time. It is also the first study to look at natural family planning and spermicide as a method of contraception by men in England.

Method

The study was a secondary analysis of data from the NHS Contraceptive Services-England, Community contraceptive services; therefore, according to the University Ethics Committee, this study was exempt from ethical approval as the data are in the public domain. The primary focus of the data is contraceptive care, and the variable for condoms is labeled by NHS Digital as 'contraceptive method' and implies that the data collected is for family planning purposes. Therefore, it is assumed that the data collected is on condoms for contraceptive purposes. The census is run on a yearly basis from April 1 to March 31 each year and is considered the most comprehensive sexual and reproductive service information resource for the United Kingdom.[7] The non-disclosive data set census used for this study included 2014/2015,[8] 2015/2016,[9] 2016/2017,[10] 2017/2018,[11] and 2018/2019.[12] The cutoff year was 2019, as these data were collected before the COVID-19 pandemic, which has affected those men who use contraceptive clinics[13] and would not make for a meaningful comparison at this stage. A total of 997,665 men participated in the national census from 2014 to 2019. The data points are entered by the service provider, which includes national, regional, and local authorities.[8,14] Previous research suggests this is predominantly nurse practitioners in the United Kingdom.[15]

Data set characteristics

The female participants were removed from the data set using an excel macro to ensure only male responses were used. Similar to Pearson[4] and Pearson and Clarke,[5] there was only one classification value for males ("H Male - all ages"), and all observations matching this value comprised the overall dataset ($N = 997{,}665$). A robust sample was an essential part of the inclusion criteria, and the sample consists of data only from the regions of England (North, Midlands, London, and South; for a map of these regions, see Office for National Statistics ONS Geography[16]). The rationale for excluding responses outside of England is that there was not enough data collected over the 5 years on participants from Northern Ireland ($n = 12$), Scotland ($n = 45$), and Wales ($n = 923$) to warrant inclusion in the analyses. However, while limited to England, participants did not have to be British nationals to be included as participants; foreign nationals could present at services and were recorded as part of the data set (although nationality was not recorded). The remaining men's contraceptive method was either not recorded or they were using no contraceptive at all (potentially reliant on female methods), but exactly how many men fell into these subgroups was not clear within the data set. Once missing data on contraceptive method was removed from the data set, there was a total of 365,292 men's data left to analyze. With speculation that some of the 632,373 excluded, with missing data, may have been using the service for sexual health not contraception; however without better data collection methods, this could not be confirmed. Method as a variable meant the patient reported what their method of contraception was to the clinician. To create the contraceptive method variable, the main method, secondary method, and third method were combined into one variable to measure any method of contraception. It did not mean that the method of contraception was given to the participant or used by them in practice.[15] Therefore, this data set then looked at self-reported methods of contraception, not contraceptive use. Each year's data were initially combined into a singular data set, with filtering then occurring for each year's data to provide a view of self-reported contraceptive methods over time.

Analytic techniques

Two binomial logistic regression models were performed. The first model examined the effect of ethnicity, region, and time on condom as a method of contraception. The second model examined the effect of ethnicity, region, and time on any contraceptive as a method in comparison to no contraceptive method. All *P* values reported were two tailed. Furthermore, two contingency tables were performed to understand both natural family planning (not defined in the data set) by ethnicity, region, and time, as well as for spermicide by ethnicity, region, and time. R studio was used to analyze the data. All statistical analyses were conducted using packages in the R statistical environment version 3.5.0.[17] "Packages" in the R statistical environment refers to additional modules within R that allow specific analyses to be conducted. All the data were prepared using the R-package *dplyr*.[18]

Results

Sociodemographics

The number of males per year were 114,027; 85,997; 67,889; 52,593; and 44,786; from 2014 to 2019. This shows a steady decrease from 2014 to 2019, with the number of men attending contraceptive services reduced by more than half. In the overall data set, 258,868 were White and 106,424 were non-White. The responses for the ethnic group not known/stated were filtered from the data set because of the lack of clarity whether this was missing data or the participant refused to answer the question. For any method of contraception, overall, 299,007 men reported condom as a main method of contraceptive, 2,684 reported natural family planning, 159 reported spermicide, and 63,442 men did not report a main contraceptive method. Overall, 76.6% ($n = 279{,}702$) of men were recorded as using the clinic as their main contact, 74.2% ($n = 271, 194$) were contacting the clinic for the first time, 54.7% of men attended a primary healthcare center ($n = 199, 944$), with the majority (58%) choosing to maintain their current contraceptive method ($n = 211{,}869$). It is acknowledged that 70.9% ($n = 236{,}455$) of men received both contraception and sexual health advice, suggesting they may choose condoms for dual protection (contraception and sexually transmitted infections [STIs]). However, whether the sexual health advice was sought by the men or

whether condoms were chosen for dual protection or for non-contraceptive use cannot be distinguished in the data collected. While 74.2% of men in this study reported that it was their first contact for their contraceptive method, 28.5% of men reported that it was not their first contact and they were maintaining their current contraceptive method. Patient identification numbers are used for every visit to ensure accurate reporting, such as ensuring multiple visits are accurately recorded, but these identification numbers are not shared as part of the data set for confidentiality reasons.[8,15] The researcher therefore chose to include men with first and second contacts for contraceptive method, as it could not be determined when the men first accessed the service, although this may bias the data set. The frequency and percentages for the overall data set by demographic category can be found in Table 1.

Model 1: Ethnicity, region, year, and condom as a method

The model used simultaneous forced entry of the variables and dummy coding of the ethnicity and region variable, with those of White ethnicity and the North region treated as the reference values, respectively. This resulted in a significant model, $\chi^2(15) = 30{,}976$; $P < 0.001$ (see Table 2 for parameter estimates, standard errors, and *P* values).

The model revealed that when compared with those in the North region, condom as a method for those of White ethnicity in the South region had a significantly lower log-odds of method at year 0 (2014–2015). Those of White ethnicity in the London region had significantly higher log-odds and those of White ethnicity in the Midlands region had no significant difference compared with those of White ethnicity in the North region. Furthermore, those of non-White ethnicity had a higher log-odds of using condom as a method at year 0 when compared with those of non-White ethnicity in the North region. The log-odds of condom as a method for those of non-White ethnicity at year 0 were lower in the South and London regions but higher in the Midlands region in comparison to those of non-White ethnicity in the Midlands (see Table 2 for parameter estimates, standard errors, and *P* values).

The model also revealed that the log-odds of condom as a method increased over time for those of White ethnicity in the North region. This increase was of a larger magnitude in the South region, but there was a decrease over time in log-odds of the method in the Midlands and London regions. Those of non-White ethnicity in the North region had no significant difference compared with those of White ethnicity in the North region in log-odds of condom as a method over time. Compared with the log-odds of condom as a method of those of non-White ethnicity in the North region, there was an increase in log-odds over time for those of non-White ethnicity in the London region. However, there was no significant difference in log-odds of condom as a method for those of non-White ethnicity over time in the Midlands and South regions when compared with the log-odds of the method for non-White ethnicities in the North.

Overall, the model shows that the predicted probability of condom as a method of contraception for non-White and White ethnicities decreased in the London and Midlands regions over time, and this decrease was at a greater rate in the Midlands region. The rate of decrease over time was slower for non-White ethnicities in the London region. The North and South regions had an increase in predicted probability of condom as a method over time, but the North started as a high predicted probability of the method and the absolute change is not large in magnitude. In contrast, the South started with lowest predicted probability of condom as a method than all other regions but had the highest rate of increase. White ethnicities had a lower predicted probability of the method across all time points, for all regions. Fig. 1 shows a graph of predicted probability of condom as the method of contraception over time for White and non-White ethnic groups for all regions.

Table 1
Sociodemographic characteristics of participants.

Demographic characteristics	Number of participants	Percentage (%)
Aged 13–59 years		
Male, all ages	365,292	100%
Ethnicity		
White	258,868	70.9%
Non-White	106,424	39.1%
Main contact		
Yes	279,702	76.6%
No	85,590	23.4%
First contact		
Yes	271,194	74.2%
No	94,098	25.8%
Location type		
Primary care health centers	199,944	54.7%
Other locations	156,484	42.8%
Other educational	7,103	1.9%
Home	1,614	0.4%
Street or public place	144	0%
Prisons	3	0%
Premises	0	0%
Open space	0	0%
Unspecified	0	0%
Contraceptive method status		
Maintain	211,869	58%
New	87,345	23.9%
Precontraception	63,387	17.4%
Change	2,961	0.7%
Consultation/contraception advice only	0	0%
Contraceptive main method		
Condom (male)	299,007	81.9%
Natural family planning	2,684	0.7%
Spermicides	159	0%
Contraception other method 1		
No other method identified	362,399	99.2%
Condom (male)	2,837	0.8%
Natural family planning	36	0.0%
Spermicides	9	0%
Contraception other method 2		
No other method identified	365,249	100%
Condom (male)	43	0%
Natural family planning	0	0%
Spermicides	0	0%
Emergency contraception		
No	365,292	100%
Yes	0	0%
Postcoital contraceptive method 1		
No	365,292	100%
Yes	0	0%
Postcoital contraceptive method 2		
No	365,292	100%
Yes	0	0%
Sexual and reproductive care activity		
Sexual health advice	236,455	70.9%
None	128,837	29.1%
Year		
2014/2015	114,027	31.2%
2015/2016	85,997	31.2%
2016/2017	67,889	18.6%
2017/2018	52,593	14.1%
2018/2019	44,786	12.3%

Model 2: Ethnicity, region, year, and any contraceptive

The model used simultaneous forced entry of the variables and dummy coding of the ethnicity and region variable, with those of White ethnicity and the North region treated as the reference values, respectively. This resulted in a significant model, χ^2

Table 2
Parameter estimates, standard errors (SE), and *P* values for condom as a method model.

Predictors	Est. (*SE*)	*P*
(Intercept)	1.815 (0.013)	–
Ethnicity	0.599 (0.040)	<0.001***
MID	−0.012 (0.021)	0.562
SOU	−1.698 (0.018)	<0.001***
LON	0.227 (0.031)	<0.001***
Year	0.110 (0.007)	<0.001***
Ethnicity*MID	0.476 (0.057)	<0.001***
Ethnicity*SOU	−0.239 (0.052)	<0.001***
Ethnicity*LON	−0.358 (0.056)	<0.001***
MID*Year	−0.519 (0.010)	<0.001***
SOU*Year	0.385 (0.011)	<0.001***
LON*Year	−0.321 (0.015)	<0.001***
Ethnicity*Year	−0.035 (0.019)	0.059
Ethnicity*Year*MID	−0.027 (0.024)	0.259
Ethnicity*Year*SOU	0.009 (0.031)	0.760
Ethnicity*Year*LON	0.183 (0.026)	<0.001***

***$P < 0.001$.
MID = Midlands; SOU = South; LON = London. The North region treated as the reference value.

(15) = 32,472, $P < 0.001$ (Table 3 provides parameter estimates, standard errors, and *P* values).

The model revealed that when compared with the North region, any contraceptive as a method for those of White ethnicity in the London region and Midlands had a higher log-odds of any method at year 0 (2014–2015), the South had a significantly lower log-odds of any method. Furthermore, those of non-White ethnicity had a higher log-odds of any method as main method at year 0 compared with those of non-White ethnicity in the North region. The log-odds of any method for those of non-White ethnicity at year 0 were lower in the South and London regions, but higher in the Midlands region, in comparison to those of non-White ethnicity in the Midlands.

The model also revealed that the log-odds of any method increased over time for those of White ethnicity in the North region. This increase was of a larger magnitude in the South region, but there was decrease over time in log-odds of the method in the Midlands and London regions. Those of non-White ethnicity in the North region had no significant difference compared with those of White ethnicity in the North region in log-odds of any contraceptive method over time. Compared with the log-odds of any contraceptive method of those of non-White ethnicity in the North region, there was a decrease in log-odds over time for those of non-White ethnicity in the London region and an increase in log-odds of the method over time for those of non-White ethnicity in the South region. However, there was no significant difference in log-odds of contraceptive method for those of non-White ethnicity over time in the Midlands region when compared with the log-odds of contraceptive method for non-White ethnicities in the North.

Overall, the self-report of any contraceptive method model shows a similar pattern to that for condom as a method of contraception. The predicted probability of any contraceptive as a method of contraception for non-White and White ethnicities decreased in the London and Midlands regions over time, and this decrease was at a greater rate in the Midlands region. The rate of decrease over time was slower for non-White ethnicities in the London region. The North and South regions had an increase in predicted probability of any contraceptive method over time, but the North started as a high predicted probability of a contraceptive method and the absolute change is not large in magnitude. In contrast, the South started with lowest predicted probability of any contraceptive method than all other regions but had the highest

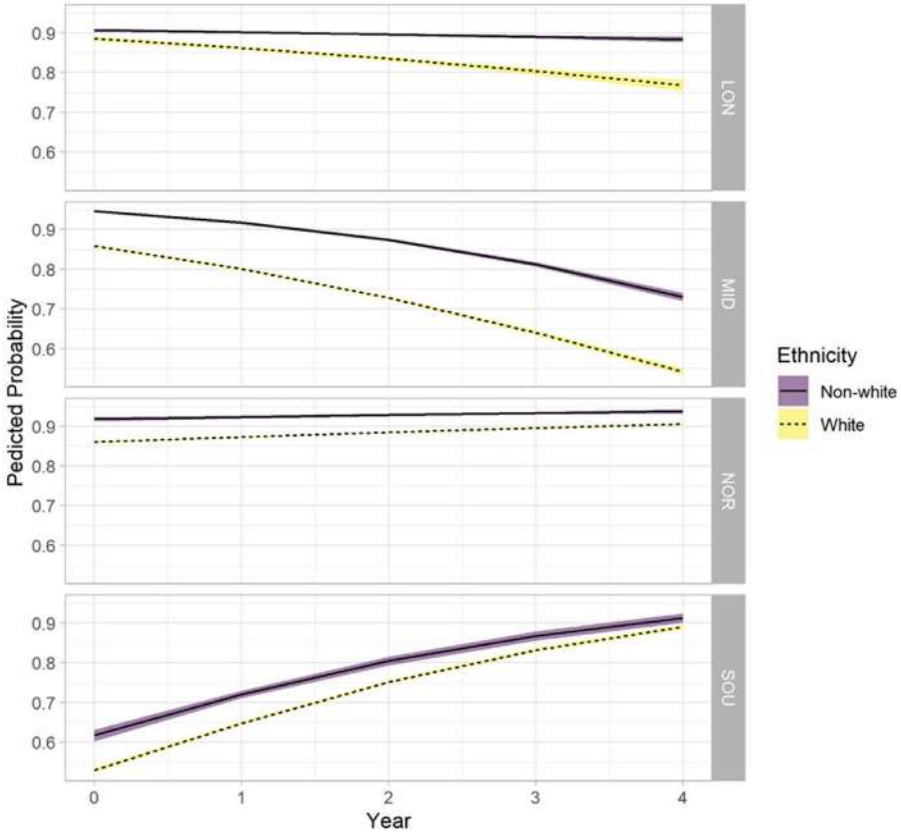

Fig. 1. A graph of the change in probability of condom as method per unit time for White and non-White ethnicities in each region. LON = London, MID = Midlands, NOR = North, SOU = South.

Table 3
Parameter estimates, standard errors (SE), and *P* values for any contraceptive method model.

Predictors	Est. (*SE*)	*P*
(Intercept)	1.841 (0.013)	–
Ethnicity	0.648 (0.042)	<0.001***
MID	−0.0132 (0.022)	<0.001***
SOU	−1.727 (0.018)	<0.001***
LON	0.299 (0.032)	<0.001***
Year	0.121 (0.007)	<0.001***
Ethnicity*MID	0.671 (0.061)	<0.001***
Ethnicity*SOU	−0.284 (0.053)	<0.001***
Ethnicity*LON	−0.459 (0.057)	<0.001***
MID*Year	−0.565 (0.010)	<0.001***
SOU*Year	0.393 (0.011)	<0.001***
LON*Year	−0.347 (0.015)	<0.001***
Ethnicity*Year	−0.052 (0.019)	0.006**
Ethnicity*Year*MID	−0.072 (0.025)	0.004**
Ethnicity*Year*SOU	0.015 (0.031)	0.619
Ethnicity*Year*LON	0.221 (0.026)	<0.001***

**$P < 0.01$, ***$P < 0.001$.
MID = Midlands; SOU = South; LON = London. The North region treated as the reference value.

rate of increase. White ethnicities had a lower predicted probability of any contraceptive method across all time points, for all regions. However, in the South and North regions, the probabilities appear to be on a converging path. Fig. 2 shows a graph of predicted probability of any contraceptive as a method of contraception over time for White and non-White ethnicities, for all regions.

For Contingency Table Natural Family Planning (year, region, ethnicity) and Contingency Table Spermicide (year, region, ethnicity), see Supplemental Material.

Discussion

Principal findings

In summary, the results from our study show that the Midlands of England have the lowest rates of condom as a main method of contraception, followed by men in London. The North and South of England showed slight increases in condoms and other male contraceptives. Irrespective of year, the White ethnic group self-report condoms as a method of contraception less than the non-White ethnic group. For the White ethnic group, the odds of self-reporting condoms as a contraceptive method decreased yearly in the Midlands and London regions, but the North and South regions increased yearly. Comparatively, the overall pattern was almost identical in the non-White ethnic group, although at higher odds of condoms as a contraceptive method across all regions at all time points. However, a key difference between ethnicities was seen in the London region where the White ethnic group decreased over time at a significantly greater rate. Model 2 predicted the self-report of any male contraceptive method and showed a similar pattern to Model 1, where any male method was decreasing and uptake was less among men who identified as White than men who did not identify as White. Any male contraceptive method included condoms, natural family planning, and spermicide. A comparison was run to understand if the decrease in condoms could be explained by an increase in other male methods. The results suggest that the decrease in condoms cannot be explained by an increase in any male method. Furthermore, the White ethnic group did not self-report any form of male method at a higher rate than the non-White ethnic group.

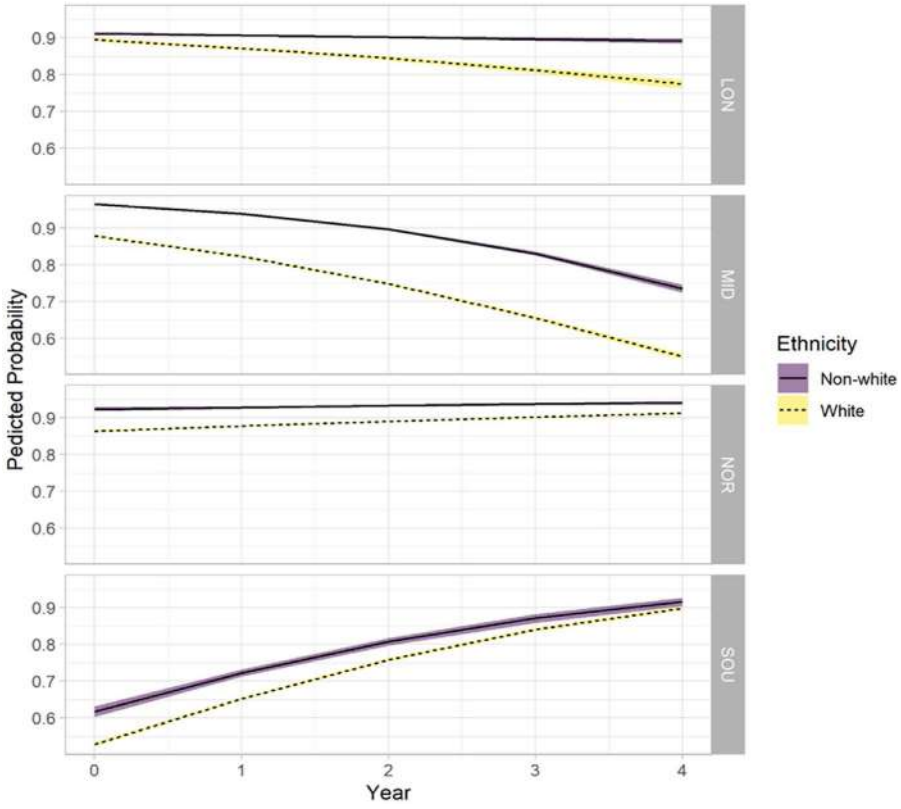

Fig. 2. A graph of the change in probability of any contraceptive as a method per unit time for White and non-White ethnicities in each region. LON = London, MID = Midlands, NOR = North, SOU = South.

Methodological implications of ethnicity as a variable

Ethnicity is an irrational variable; in the data set, it has been oversimplified and service users are limited to choose from three categories, 'White', 'non-White' and 'other/unknown'. This creates a binary other, 'White' vs 'non-White'. This approach is an essentialist view of ethnic background that problematically stereotypes groups as having one true identity that is biological driven.[19] Instead, research suggests that the option should be provided to service users to self-identify, as well as providing the ability to give non-standard responses for the complexity of the variable to be explored and new constructions of ethnic categories to emerge without stigmatization and discrimination.[20] Furthermore, by taking a homogenous approach to the 'White' ethnic group, this ignores other groups that face disadvantage such as White Irish individuals residing in England.[21] While ethnicity is commonly characterized in a problematic way of race, by using skin color, the relationship between ethnocultural group and sexual behavior is important when developing health-based interventions.[22] For example, research on Black Caribbean and Black African heterosexual men show differences in health care utilization and prognosis for sexual health and STIs.[23] Individuals from mixed racial backgrounds also have differences in sexual health behaviors; for example, risk taking among heterosexual sexual health clinic service users was highest among Black/mixed Caribbean heterosexual men, with this group being most likely to test positive for STIs.[24] These studies show how further ethnic categorization within a subgroup such as Black and mixed ethnic backgrounds could be beneficial to better understand how culture informs condoms for reproductive purposes. They suggest that for the purpose of interventions, both social and cultural identities cannot be isolated from the public health approach.[25] Overall, there is a need to provide a more precise understanding of ethnic identity for the purpose of data collection.[26] Owing to the barriers with ethnic grouping, very little can be generalized from the data set, but the model does show that ethnicity and condoms as a method for contraception are a point requiring further enquiry.

Research implications

What the above critical lens suggests is this study's regional information would be helpful not only to target certain regions for interventions but also to tailor the interventions to each region differently. Historically and currently, there is no published record of an intervention around improving the use of condoms by men for contraceptive purposes in England. Any larger intervention or randomized control trial should focus on clinics from all four regions to account for variations in condoms as a method of contraception or focus on the Midlands to understand why condoms are reported less for contraception in this region to aim to improve condom uptake over time. For a discussion of natural family planning and spermicide as well as recommendations for the NHS, see Supplemental Materials.

Strengths and limitations

The strength of this study is it provides the first insight into research on men who live in England's self-reported method of contraception for condoms, natural family planning, and spermicide. Future research is also needed on male contraceptive methods because this census data was unable to capture use, only self-reports of a method. Both the models on condoms and any contraceptive were significant at the 0.001 level, suggesting the models are a good fit. The limitations of the study included that the data were not collected by the research team; therefore, there was little that could be done to influence the variables available for analysis. Furthermore, although the focus is stated by NHS Digital to be primarily on contraceptive care, and the variable is labeled as such in all data sets, the three types of men using this service (contraceptive, sexual health, both) cannot be determined. Dividing the three data points in future data collection is important before any causation can be determined, as it would be advantageous, even in this data set, to know whether when separated if the three groups decreased or increased their choice of contraceptives respectively to better inform targeted services and programs. In addition, NHS Digital should add variables to the data on sexual and reproductive care activity to include divisions between 'sexual health advice sought' and 'sexual health advice provided'. This division could be a quality check for if men were using condoms for contraception, sexual health, or both purposes, which cannot be determined or quality checked in the census currently. Also, in this study, a comparison was run to see if the decrease in condoms could be accounted for by other male contraceptive methods increasing. In the future, to address the issue in this study of causation, it would be key to have a balanced sample of men using each of the male methods for an in-depth comparison. With a more extensive set of sociodemographic variables for men, greater understanding can be applied, including possible explanations and implications for clinicians and policymakers. For further limitations, see the NHS data quality statements publicly available online by following the citations for the data sets. For example, the data lack representation where a male patient contacts an outpatient clinic, a General Practice, a community pharmacist, or a retail setting reporting condoms as a contraceptive method. Including both men who made first contact for their method of contraception and men for whom it was not their first contact, that they were maintaining their method, did not influence the trends of the regression models in this study but could have biased the results. This was because the sample of men maintaining was too small to change the analysis outcome or to make a meaningful comparison, but it could have implications in a larger data set, and seeking a balanced data set is important for making conclusions and comparisons in the future research. The data set was limited in reporting patient identification methods, and the NHS Digital should devise a system to reduce duplicate data points in the data sets and to allow for longitudinal analysis. Finally, if the individual is <13 or >54 years, their data are also not included, which is problematic as they may have a method of contraception at this age.

Conclusion

In all, this is the first study to take a comprehensive overview of several contraceptive methods, including condoms, natural family planning, and spermicide, all male methods. The results from the regression models predict which regions and which ethnic groups are more likely to report condoms as a method of contraception and which groups report any male contraceptive method. These models are helpful to begin to explore differences between regions to inform commissioning and determined that the decrease in condoms is not explained by an increase of any male method. Several important targeted approaches toward data collection have been suggested to improve our understanding of men's contraceptive methods in England, with health promotion and policy makers requiring more evidence-based research to inform messages, commissioning, and policies when aiming to engage men in family planning behaviors.

Author statements

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Ethical approval

Ethical approval was not required as the data sets were available in the public domain, the data on men has not been previously analyzed.

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This project has no funding to report.

Competing interests

The authors report no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.023.

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Original Research

Association between low fluoride exposure and children's intelligence: a meta-analysis relevant to community water fluoridation

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ABSTRACT

Objectives: Previous meta-analyses have mainly focused on studies conducted in endemic fluorosis areas with relatively high fluoride concentrations. These are impoverished rural communities in China, India, and Iran, and the findings cannot be generalised to developed countries. Therefore, we investigated the association between fluoride concentrations relevant to community water fluoridation and children's cognition measured with IQ scores by synthesising effect sizes reported in observational studies.
Methods: A previous meta-analysis and the National Toxicology Program database that included a search of multiple databases and the authors' search of PubMed, Google Scholar, and Mendeley provided the data. Cross-sectional and cohort studies examining the association between fluoride and children's cognition and intelligence scores were selected. Two reviewers abstracted data using standard procedures. We performed three meta-analyses to synthesise the effects using the random effects models.
Results: Eight studies of standardized mean difference in IQ scores from non-endemic fluorosis areas found no statistically significant difference between recommended and lower levels of fluoride (standardized mean difference = 0.07; 95% confidence interval: −0.02, 0.17; I^2 = 0%), and no significant fluctuation in IQ scores across the differences in fluoride concentrations by non-linear modeling with restricted cubic spline (P = 0.21). Meta-analyses of children's and maternal spot urinary fluoride associated pooled regression coefficients ($Beta_{children}$ = 0.16; 95% confidence interval: −0.40, 0.73; P = 0.57; I^2 = 0%, $Beta_{maternal}$ = −0.92; 95% CI: −3.29, 1.46; P = 0.45; I^2 = 72%) were not statistically significant. Further regression analysis by standardizing absolute mean IQ scores from lower fluoride areas did not show a relationship between F concentration and IQ scores (Model Likelihood-ratio test: P-value = 0.34.)
Conclusions: These meta-analyses show that fluoride exposure relevant to community water fluoridation is not associated with lower IQ scores in children. However, the reported association observed at higher fluoride levels in endemic areas requires further investigation.

Introduction

It is well established that fluoride in drinking water has a beneficial effect at lower concentrations in the prevention of tooth decay and detrimental effects on human health at higher concentrations, where it raises the risk for enamel and skeletal fluorosis. Fluoride is added to drinking water worldwide in the 0.5–1.1 mg/l range to prevent tooth decay.[1,2] The US Public Health Service now recommends 0.7 mg/l F for community water fluoridation (CWF).[3] The US Environmental Protection Agency has set the maximum contaminant level of fluoride in drinking water at 4 mg/l to protect against dental and skeletal effects.[4] The World Health Organization (WHO) guideline value for fluoride in drinking water is 1.5 mg/l.[5] Because CWF reaches more than 207 million Americans, its benefits and safety are continually assessed and debated.[6,7] The National Toxicology Program (NTP) asked the National Academies of

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Sciences, Engineering, and Medicine (NASEM) to review draft monographs that assessed the neurodevelopmental hazard associated with fluoride exposure.[8,9] A NASEM committee found the NTP draft monograph fell short of providing a clear and convincing argument that supported its assessment that fluoride is a presumed neurodevelopmental hazard.[10] This appraisal aligns with several other systematic and narrative reviews of the effect of fluoride on neurodevelopmental and cognitive outcomes.[11–17]

Four published meta-analyses of fluoride and neurodevelopmental hazard in humans from mostly endemic fluorosis areas compared the mean IQ scores or odds between higher and lower fluoride exposure groups.[17–20] Duan et al.[20] conducted a meta-analysis of standardised mean difference (SMD) in IQ scores between higher water fluoride communities (mean F = 3.7 mg/l) and normal fluoride communities (mean F = 0.6 mg/l). The summary results indicated high water fluoride exposure was associated with lower intelligence levels (SMD: −0.52; 95% CI: −0.62 to −0.42; $P < 0.001$). However, the dose–response meta-analysis revealed a non-linear relationship with both relative and absolute fluoride doses such that very high fluoride concentrations (5.2 ± 1.1 mg/l F) in water were associated with higher intelligence levels than medium fluoride concentrations (3.1 ± 0.9 mg/l F). The authors cited the lack of socio-economic status data as a limitation that might have affected the relationship between water fluoride intake and intelligence scores. NASEM, in its review of the NTP monograph, recommended that NTP 'emphasize that much of the evidence presented comes from studies that involve relatively high fluoride concentrations and that the monograph cannot be used to draw conclusions regarding low fluoride exposure concentrations (<1.5 mg/l), including those typically associated with drinking water fluoridation.'[10] This highlights a need to assess the association between fluoride exposure relevant to levels observed in communities with CWF and children's intelligence scores. Therefore, the authors posed the following question (Supplementary Table A): *Does fluoride exposure recommended for caries prevention decrease children's cognition and IQ scores?* We assessed fluoride exposure in three ways: 1) an ecological measure based on place of residence; and using fluoride concentration from 2) child; and 3) maternal urine samples. We identify the limitations of the present studies and offer recommendations for future research.

Methods

Search strategy

We started with 26 studies identified by Duan et al.[20] for relevant published articles through November 2016. We then cross-checked the literature search conducted in May 2020 by NTP as part of the report titled Draft NTP Monograph on the Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects to add additional studies.[8] NTP identified 46 studies for the SMD meta-analysis and six studies for the urinary F-IQ meta-analysis. In addition, the authors updated the search using PubMed, Mendeley, and Google Scholar to identify English-language documents published between May 2020 and December 2021. Keywords included combinations of 'fluoride' or 'fluoridation' and 'neurodevelopment' or 'cognition' or 'intelligence' or 'IQ.'

Study selection criteria

Studies were included if they met the following criteria: (1) the exposure variable included water or urinary F; (2) outcomes included information to calculate the SMD and/or regression coefficient for the change in cognition and IQ scores; (3) the study design was an observational study; (4) the article was available in English; and (5) the population was children aged 1–18 years.

Studies were excluded if they met any of the following criteria for assessing the effect at low F levels: (1) studies conducted in endemic fluorosis areas where the higher exposure was greater than 1.5 mg/l F; (2) the exposure variable was other than water or urinary F; and (3) overlapping publications from the same study. We excluded studies that used dental fluorosis as exposure as they were from endemic fluorosis areas (including from coal), or presented IQ outcome and dental fluorosis measurements in a different format than other studies, which made it challenging to synthesise the results.

When multiple publications analysed the same subjects, we included only the article with the largest number of participants. Two authors reviewed each potentially eligible study, and a consensus approach resolved disagreements. We excluded studies where the description of subject recruitment, exposure assessment, and the outcome was not provided.

Data extraction

Two authors abstracted data from the eligible studies using a standard form. For the SMD analysis, the following information was extracted: authors, publication year, study type, age range, fluoride exposure (range and mean), outcome measure, number of children in higher and lower exposure groups, mean IQ, and standard deviation. Where the standard error (SE) was unavailable, we used the method recommended by the Cochrane Handbook for converting confidence intervals and *P* values to SE.[22]

The following information was extracted for the urinary fluoride analysis: authors, publication year, study type, urinary fluoride exposure range, outcome measure, and covariates. In addition, the beta coefficient data for every 0.5 mg/l increase in urinary F and its SE from the multiple regression equation was abstracted for the two analyses.

Data synthesis

SMD in IQ scores

For this meta-analysis, eight studies from non-endemic areas with fluoride exposure in drinking water below ~1.5 mg/l F were available (Table 1).[21–28] These studies provided fluoride concentrations, mean IQ scores, sample size, and standard deviation for calculating the pooled effect size. In addition, upon request, Ibarluzea et al.[25] provided the same data for their study. The characteristics of the studies included in the meta-analysis are shown in Table 2 and Supplementary Table B.

Urinary fluoride and IQ

Two separate analyses were done using children's urinary fluoride (CUF) and maternal urinary fluoride (MUF) to juxtapose studies with similar exposure measures. Three publications each provided CUF- and MUF-associated regression coefficients.[24,25,27,29,30] For the CUF meta-analysis, multiple publications from a study conducted by Yu et al.[30] in Tianjin, China, were excluded. That study provided a regression coefficient for exposure in the 0.01–1.6 mg/l F range. For the MUF meta-analysis, the author included the General Cognitive Index coefficient from the study by Bashash et al..[24] For the Ibarluzea et al.[25] publication, we chose the MUFcr (mg/g) at week 12 associated coefficient, as it was combined for boys and girls.

Table 1
Characteristics of the studies included in the standardized mean difference (SMD) meta-analysis of fluoride and children's IQ scores.

Study Year	Country	Age (years)	Number of subjects	Exposure assessment	Higher level F exposure (mg/l); (range or midpoint)	Lower level F exposure (mg/l) (range or midpoint)	Intelligence assessment test	Reported outcome	Medline Indexed Journal	RoB study quality
An JA 1992	China	7–16	242	Water	4.85 (2.1–7.6)	0.8	Wechsler Intelligence	IQ; IQ by age group; IQ distribution	No	- -
Xu YL 1994	China	8–14	129	Water Urine	1.8 0.8	0.8 0.38	Binet Simon	IQ; IQ distribution	No	- -
Li XS 1995	China	8–13	907	Urine	2.69	1.02	Chinese standardized Raven	IQ; IQ by gender and age; IQ distribution	No	- -
Zhao LB 1996	China	7–14	320	Water	4.12	0.91	Chinese standardized Raven	IQ; IQ by age, gender and education; IQ distribution	No	- -
Wang G 2008	China	4–7	230	Water	4.8 (0.58–8.6)	0.79 (<1.0)	Wechsler Intelligence	IQ by type; IQ less than 90; IQ by head circumference	No	- -
Yao L 1996	China	8–12	536	Water	11 2.0	1.0 1.0	Chinese standardized Raven	IQ; IQ by TSH level; IQ distribution	No	- -
Yao L, Yang S 1997	China	7–12	497	Water	2	0.4	Chinese standardized Raven	IQ; IQ by age	No	- -
Zhang JW 1998	China	4–10	103	Water	0.8	0.58	Japan IQ	IQ; IQ by age	No	- -
Lu Y 2008	China	10–12	118	Water Urine	3.15 4.99	0.37 1.43	Chinese standardized Raven	IQ; IQ distribution	No	- -
Hong FG 2008	China	8–14	117	Water	2.9	0.75	Chinese standardized Raven	IQ; IQ distribution; IQ by education level	No	- -
Wang XH 2001	China	8–12	60	Water	2.97	0.5	Chinese standardized Raven	IQ; IQ distribution	No	- -
Xiang Q 2003	China	8–13	512 290	Water Urine	2.47 (0.57–4.5) 0.75 3.47	0.36 (0.18–0.76) 0.36 1.11	Chinese standardized Raven	IQ; IQ by age, gender and education; IQ distribution	No	–
Seraj B 2006	Iran	N/A	126	Water	2.5	0.4	Raven	IQ	No	- -
Wang ZH 2006	China	8–12	368	Water Urine	5.54 5.5	0.73 1.51	Chinese standardized Raven	IQ; IQ distribution	No	- -
Fan ZX 2007	China	7–14	79	Water Urine	3.15 2.89	1.03 1.78	Chinese standardized Raven	IQ; IQ distribution	No	- -
Wang SX 2007	China	8–12	449	Water Urine	8.3 (3.8–11.5) 5.1	0.5 (0.2–1.1) 1.5	Chinese standardized Raven	IQ; IQ distribution	Yes	- -
Chen YX 2008	China	7–14	640	Water	4.55	0.89	Chinese standardized Raven	IQ; IQ by age; IQ distribution by gender	No	- -
Pourelami 2011	Iran	7–9	120	Water	2.38	0.41	Raven's Progressive Matrices Intelligence	IQ; IQ distribution; IQ in gender	No	- -
Eswar P 2011	India	12–14	133	Water	2.45	0.29	Raven (Standard Progressive Matrices)	IQ; IQ distribution	No	- -
Trivedi MH 2012	India	N/A	84	Water Urine	2.3 2.69	0.84 0.42	Raven (Standard Progressive Matrices)	IQ; IQ distribution; IQ by gender	No	- -
Seraj B 2012	Iran	6–11	293	Water	5.2 (1.1)	0.8 (0.3)	Raven's Color Progressive Matrices	IQ; IQ distribution; IQ by gender	No	- -
Karimzade 2014	Iran	9–12	39	Water	3.94	0.25	The Iranian version of the Raymond B Cattell	IQ; IQ distribution	No	- -
Sebastian 2015	India	10–12	405	Water	2 1.2	0.4 0.4	Raven's Colored Progressive Matrices	IQ; IQ distribution	Yes	- -

(*continued on next page*)

Table 1 (*continued*)

Study Year	Country	Age (years)	Number of subjects	Exposure assessment	Higher level F exposure (mg/l); (range or midpoint)	Lower level F exposure (mg/l) (range or midpoint)	Intelligence assessment test	Reported outcome	Medline Indexed Journal	RoB study quality
Broadbent 2015	New Zealand	7–13	990	Water	0.7–1.0	0.0–0.3	Wechsler Intelligence Scale for Children-Revised	IQ	Yes	+
Bashash M 2017	Mexico	6–12	189	Urine	≥0.80 75th percentile = 1.01	<0.80 25th percentile = 0.54	Wechsler Abbreviated Scale of Intelligence	IQ	Yes	–
Yu X 2018	China	7–13	2380	Water Urine	2.0 1.37	0.5 0.41	Combined Raven's for Rural China	IQ; IQ distribution	Yes	–
Green R 2019	Canada	3–4	400 369	Water Urine	0.59 0.69	0.13 0.40	Wechsler Primary and Preschool Scale of Intelligence-III	IQ; IQ by gender	Yes	–
Ibarluzea J 2021	Spain	4.4 ± 0.1	247	Water	0.8	0.1	McCarthy Scales of Children's Abilities (MSCA)	IQ	Yes	+

Risk of Bias (RoB) rating:+, probably low risk of bias; –, probably high risk of bias; --, definitely high risk of bias.
Except for Broadbent 2015, Yu 2018, and Ibarluzea 2021, all studies are based on non-probability sampling. Broadbent 2015 and Ibarluzea 2021 are population-based birth cohort studies. Green 2019 and Bashash 2017 are cohort studies based on non-probability sampling. All others are cross-sectional studies.

Risk of bias and quality assessment

Two authors assessed the risk of bias and study quality reported in the previous systematic reviews. We adapted the Office of Health Assessment and Translation Risk of Bias rating tool[31] and included seven questions relevant to cohort and cross-sectional studies. The risk of bias assessment is presented in Supplementary Fig. A.[8] This assessment is consistent with other reviews.[15–17]

Statistical analysis

We performed three meta-analyses: (1) SMD in IQ scores between children in higher fluoride non-endemic areas (less than ~1.5 mg/l F in drinking water or its equivalent exposure; World Health Organization guideline value) and lower fluoride exposure groups based on studies that used group-level exposure; (2) a meta-analysis of the effect (beta regression coefficient) of 0.5 mg/l F increase in urinary fluoride on IQ scores based on studies that used CUF; and (3) a similar meta-analysis using MUF. We used the Cochrane Review Manager (RevMan)[32] and the R Language.

The random effects models were used for calculating the pooled SMD in unadjusted IQ scores and the urinary fluoride-IQ meta-analysis. The non-linear relationship between fluoride exposure and SMD in IQ scores was modeled by restricted cubic splines with three knots at 10th, 50th, and 90th percentiles. The model was weighted by the precision of SMD in IQ score. The 95% confidence interval band was generated. The Likelihood-ratio test was used to assess the goodness of fit of splines.

Results

Overall, 28 studies (31 comparisons) were available for the SMD analysis.[21–23,25,26,28,33–55] Two overlapping publications from the Duan meta-analysis[56,57] and one publication with unusually low IQ scores were excluded.[52] Five new studies were added.[24,25,27,28,30] Of these 28 studies, 23 and 8 provided data from endemic and non-endemic areas, respectively (Fig. 1).[21–28]

Fig. 2 shows that the pooled SMD effect size of 0.07 (95% CI: −0.02, 0.17), favoring higher F, was not statistically significant ($P = 0.14$) in non-endemic areas. Furthermore, there was no observed heterogeneity ($I^2 = 0\%$; $P = 0.64$). This estimate contrasts with an effect size of −0.46 (95% CI: −0.58, −0.35) with substantial heterogeneity ($I^2 = 81\%$; $P < 0.001$) for studies from endemic areas. A 95% prediction interval for the true outcomes is −0.95 to 0.02, which suggests that SMD values are possible on both sides of the null in future studies.

The relationship between F concentration in water or urine and IQ was explored. A meta-analysis of non-linear regression with restricted cubic spline for SMD showed that population fluoride concentration exposure differential between recommended F level and lower areas was not associated with SMD (Supplementary Fig. B). The summarised estimates of linear and non-linear terms from the restricted cubic spline are 0.0959 ($P = 0.59$; 95% CI −0.2498, 0.4416) and 0.1960 ($P = 0.77$; 95% CI −1.1338, 1.5257), and the overall model fitting resulted in a P-value of 0.21 with Wald test. Further regression analysis with restricted cubic spline by standardising the 36 absolute mean IQ scores from lower fluoride areas (28 studies) did not show a relationship between F concentration and IQ scores (model Likelihood-ratio test: P-value = 0.34; Supplementary Fig. C).

Fig. 3A shows that the change in pooled IQ score of 0.16 points (95% CI: −0.40, 0.73) for every 0.5 mg/l increase in children's urinary F was not statistically significant ($P = 0.57$). There was no observed heterogeneity ($I^2 = 0\%$; $P = 0.43$).

Table 2
Characteristics of the studies of urinary fluoride and children's IQ scores (regression coefficient) meta-analysis at lower fluoride levels.

Publication	Year	Study location	Age	N	Fluoride exposure	Fluoride range	Regression coefficient (95% CI)/unit	Outcome measure	Covariates
ELEMENT Study from Mexico									
Thomas D ELEMENT Study (Thesis)	2014	Mexico	6–15	550	Urine Contemporaneous	0.123–2.812 mg/l.	Beta for CUF/1 mg/l F 1.32; $P = 0.33$ **Boys 3.81; $P = 0.05$** Girls −1.57; $P = 0.39$	Wechsler Abbreviated Scale of Intelligence	Sex, maternal age, marital status, maternal education, family possessions, cohort, mother's WASI score
			1–3	431	Maternal urinary F	0.110–3.439 mg/l	Beta for MUF/1 mg/l F −0.631; $P = 0.391$	Mental Development Index (MDI), a subscale of the Bayley Scales of Infant Development-II (BSID-II) test	Maternal age, education, marital status, pregnancy smoking status, child's sex, and child's age Breastfeeding not included.
				194	Maternal plasma F	0.00350–0.07700 mg/l	−0.0031; $P = 0.650$		
Bashash et al. ELEMENT Study	2017	Mexico	6–12	189	Contemporaneous specific gravity −adjusted Urinary F	Mean 0.84 Range 0.18–2.8 mg/l	Beta for CUF/0.5 mg/l F −0.89 (−2.63, 0.85) −0.77 (−2.53, 0.99), adjusted for MUFcr	Wechsler Abbreviated Scale of Intelligence measured at the time of urine collection in children	Age; sex; weight at birth; parity; gestational age; maternal characteristics (smoking history, marital status, age at delivery, IQ), cohort.
				211	Maternal urine	Mean 0.89 mg/l Range 0.23–2.14 mg/l F	Beta for MUF/0.5 mg/l F **−2.50 (−4.12, −0.59)** 'non-linear relation, with no clear association between IQ scores and values below approximately 0.8 mg/l' −1.73 (−3.75, 0.29) adjusted for CUF − non-linear relation	McCarthy Scales of Children's Abilities −General Cognitive Index (GCI)	Breastfeeding not included.
			4	287	Maternal urine	Mean 0.90 mg/l Range 0.23–2.36 mg/l F	Beta for MUF/0.5 mg/l F **−3.15 (−5.42, −0.87)**		
Tianjin, China									
Yu et al.	2018	China	7–13	2380	Urine Contemporaneous	0.01–1.6 mg/l urinary F. 1.60–2.50 mg/l urinary F 2.50–5.54 mg/l urinary F	Beta for CUF/0.5 mg/l F 0.36 (−0.29, 1.01) **−2.67 (−4.67, −0.68)** −0.84 (−2.18, 0.50)	Combined Raven's Test for Rural China	Age; sex; maternal education; paternal education; low birth weight Breastfeeding not included
MIREC Study from six cities in Canada									
Green et al.	2019	Canada	3–4	512	Maternal urine	Maternal urinary F level 0.06–2.44 mg/l; MUF mean and SD 0.40 (0.27) and 0.69 (0.42)	Beta for MUF/1 mg/l F All −1.95 (−5.19 to 1.28)/**Boys −4.49 (−8.38 to −0.60)** Girls 2.40 (−2.53 to 7.33)	Wechsler Primary and Preschool Scale of Intelligence-III	Adjusted for city, HOME score, maternal education, race/ethnicity, and child −sex interaction. City included. Second-hand smoke excluded. Breastfeeding excluded
Till et al.	2020	Canada	3–4	350	Maternal urinary F used for adjustment	Mean Fluoridated Breast fed 0.70 (0.39)	Water Fl (mg/l) adjusted for MUF Model	Wechsler Preschool and Primary Scale of	Water fluoride concentration model. Adjusted for maternal

(*continued on next page*)

Table 2 (*continued*)

Publication	Year	Study location	Age	N	Fluoride exposure	Fluoride range	Regression coefficient (95% CI)/unit	Outcome measure	Covariates
						Formula fed 0.64 (0.37) Non-fluoridated Breast fed 0.42 (0.28) Formula fed 0.38 (0.27)	Beta for MUF/0.5 mg/l F: −1.08 (−1.54, 0.47) −0.54 (−3.04, 0.90) [without two extreme IQ outliers] Fluoride intake from formula Model Beta for MUF/0.5 mg/l F: −1.50 (−3.41, 0.43) −1.49 (−3.37, 0.39) [without two extreme IQ outliers]	Intelligence-III (WPPSI-III)	education, maternal race, child's age at IQ testing, child's sex, HOME total score, and second-hand smoke status in the child's house. City excluded. Second-hand smoke included Breastfeeding duration used to calculate fluoride intake.
Farmus et al.	2021	Canada	3–4	434	Children's urine adjusted for specific gravity $n = 434$	Urinary F Mean 0.51 mg/l F (0.39) Range 0.05–2.89 mg/l F.	Beta for CUF/0.5 mg/l F All 0.23 (−1.75, 1.29) Boys 0.09 (−2.10, 2.28) Girls −0.52 (−2.62, 1.58)	Wechsler Preschool and Primary Scale of Intelligence-III (WPPSI-III)	Covariates include maternal education, maternal race, total HOME score, age at urine sampling, and prenatal second-hand smoke.
					Maternal urinary F adjusted for specific gravity $n = 526$	Mean 0.53 mg/l (0.37) Range 0.06–2.48 mg/l F	Beta for MUF/0.5 mg/l F All −1.71 (−3.17, −0.24) **Boys −2.48** **(−4.30, −0.66)** Girls −0.31 (−2.76, 2.14)		City excluded. Second-hand smoke included. Breastfeeding duration used to calculate fluoride intake.
Gipuzkoa, Spain Ibarluzea et al.	2021	Spain	4.4	248	Maternal urinary fluoride adjusted for creatinine	MUFcr (mg/g) at pregnancy Mean 0.64 (SD = 0.38) Range 0.15–1.91 MUFcr (mg/g) at week 12 Mean 0.55 (SD = 0.40) Range 0.05–2.36 MUFcr (mg/g) at week 32 Mean 0.73 (SD = 0.48) Range 0.13–3.07	Beta for MUF/1 mg/l F Boys **15.4 (6.32, 24.48)** Girls −0.19 (−7.31, 6.93) All 3.37 (−2.09, 8.83) Boys **11.48 (4.88, 18.08)** Girls −0.54 (−5.97, 4.9)	McCarthy Scales of Children's Abilities (MSCA)	Adjusted by age of the child at the time of the test (only for McCarthy), order of the child (between siblings), nursery at 14 months, breastfeeding, maternal social class, IQ and smoking. Breastfeeding included.

Note: Of 31 coefficients, five negative (two only in boys) and three positive (all in boys) statistically significant coefficients are shown in bold.
TSH, thyroid-stimulating hormone; WAIS, Wechsler Abbreviated Scale of Intelligence.

Fig. 3B shows that the change in pooled General Cognitive Index and IQ scores of −0.92 (95% CI: −3.29, 1.46) was not statistically significant ($P = 0.45$). However, the substantial heterogeneity ($I^2 = 72\%$; $P = 0.03$) implies that significant discrepancies exist among studies, and therefore, the studies are not combinable.

In addition, sensitivity analyses by including and omitting other coefficients or studies each time did not influence the interpretation of the pooled regression coefficient outcome, suggesting that the lack of an effect was credible (Supplementary Table C). The funnel plot suggests symmetry. Neither the rank correlation nor the regression test indicated any funnel plot asymmetry ($P = 0.5653$ and $P = 0.06$, respectively; Supplementary Fig. D).

Discussion

Meta-analyses of fluoride exposure to levels below 1.5 mg/l in water provide consistent evidence for the lack of an adverse effect on IQ. These results are consistent with the zero effect of fluoride on

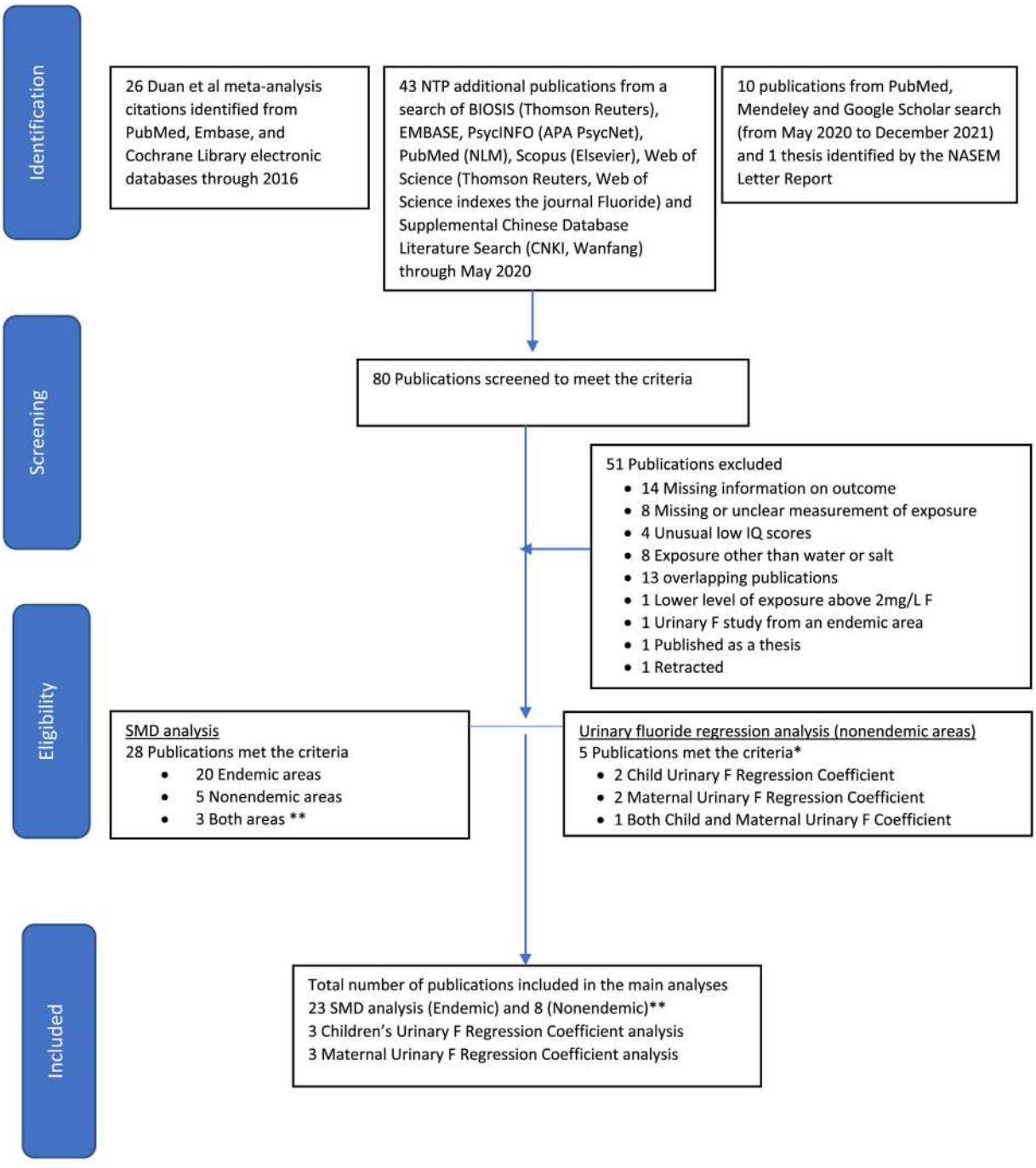

Fig. 1. Flow diagram of the publications selected for meta-analyses. Flowchart of studies identified, screened, excluded and included in the meta-analysis.

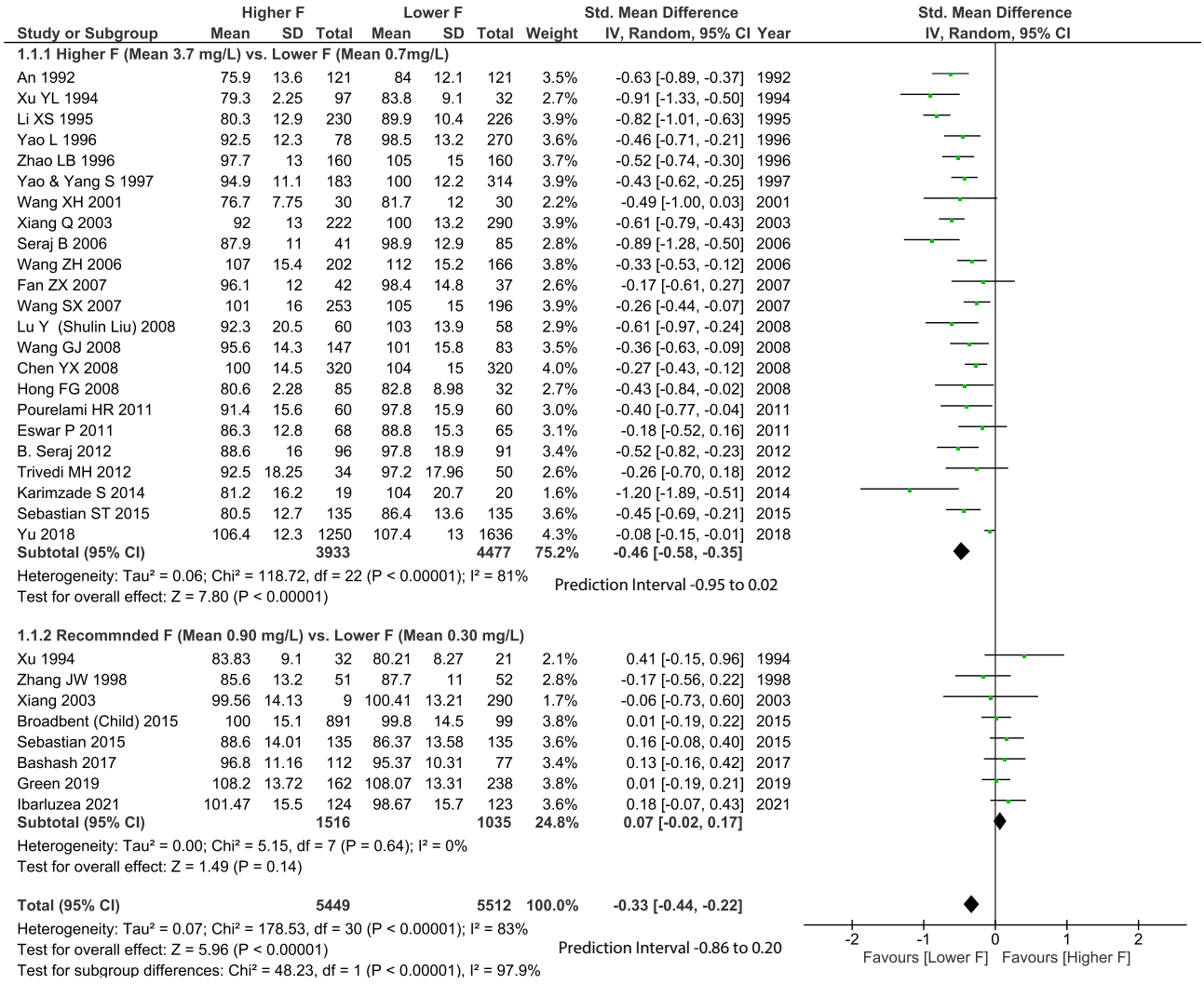

Fig. 2. Random effects analysis of standardized mean difference (SMD) and 95% CI of children's IQ score associated with exposure to higher fluoride. Forest plot of standardized mean difference (SMD) and 95% confidence interval of children's IQ scores according to endemic fluorosis and non-endemic fluorosis study communities. In the endemic areas, the mean F concentration in water or urine for higher and lower exposure groups was ~3.9 mg/l and ~0.7 mg/l, respectively. In the non-endemic areas, the mean F concentration in water or urine for higher and lower exposure groups was ~0.9 mg/l and ~0.3 mg/l, respectively. For each study, squares represent the point estimate, and the horizontal line shows the 95% CIs. Solid diamonds show the pooled estimate. The I^2 and P values for heterogeneity, test for overall effect, respectively, and prediction intervals are shown. The prediction interval reflects the uncertainty we expect in the pooled effect if a new study is included in the meta-analysis.

cognitive ability recently reported by Aggeborn and Ohman,[58] which included 80,000 observations. In addition, a study of school children in Australia showed that exposure to fluoridated water during the first five years of life was not associated with altered measures of child emotional and behavioral development and executive functioning.[59]

SMD analysis comparing higher and lower exposure groups

The meta-analytic finding of no adverse effect at lower F concentrations on IQ scores is not consistent with the meta-analysis of studies at higher F concentrations; thus, these studies should not be combined. Compared with the SMD effect size estimates of −0.45 and −0.52 from higher fluoride areas reported by Duan et al.[20] and Choi et al.,[19] respectively, the SMD effect size at lower F level in this analysis was positive (SMD = 0.07). Several possible explanations exist for the effects observed in studies conducted in endemic fluorosis areas of China, Iran, and India. First, in 23 of 28 studies, the authors did not provide data demonstrating the comparability of higher and lower F groups. These studies were conducted in socio-economically deprived rural areas where access to clean water is a major problem.[36,39,52] Selection bias resulting from non-probability sampling of impoverished population groups, lack of control of confounders and covariates, underestimation of the SE, and unweighted data from complex surveys have distorted the effect.[10] Second, the authors did not explore reverse causality.[10,12,60] Thus, high intelligence may have influenced avoiding fluoride exposure in areas with endemic fluorosis. Third, the exposure dose is much higher in endemic areas than in communities where water is optimally fluoridated. There may be a population threshold effect for IQ similar to severe dental fluorosis in the United States. Several studies have observed non-linear associations and a possible threshold for an IQ effect.[24,30] Fourth, Ioannidis[61] found that effect sizes for many associations, when first discovered and published in the scientific literature, are often inflated and do not reflect the smaller effect sizes reported later. He attributes this to the fact that the 'hallmark of discovery is the performance of exploratory analyses.' Fifth, Egger et al.[62] showed a danger in conducting meta-

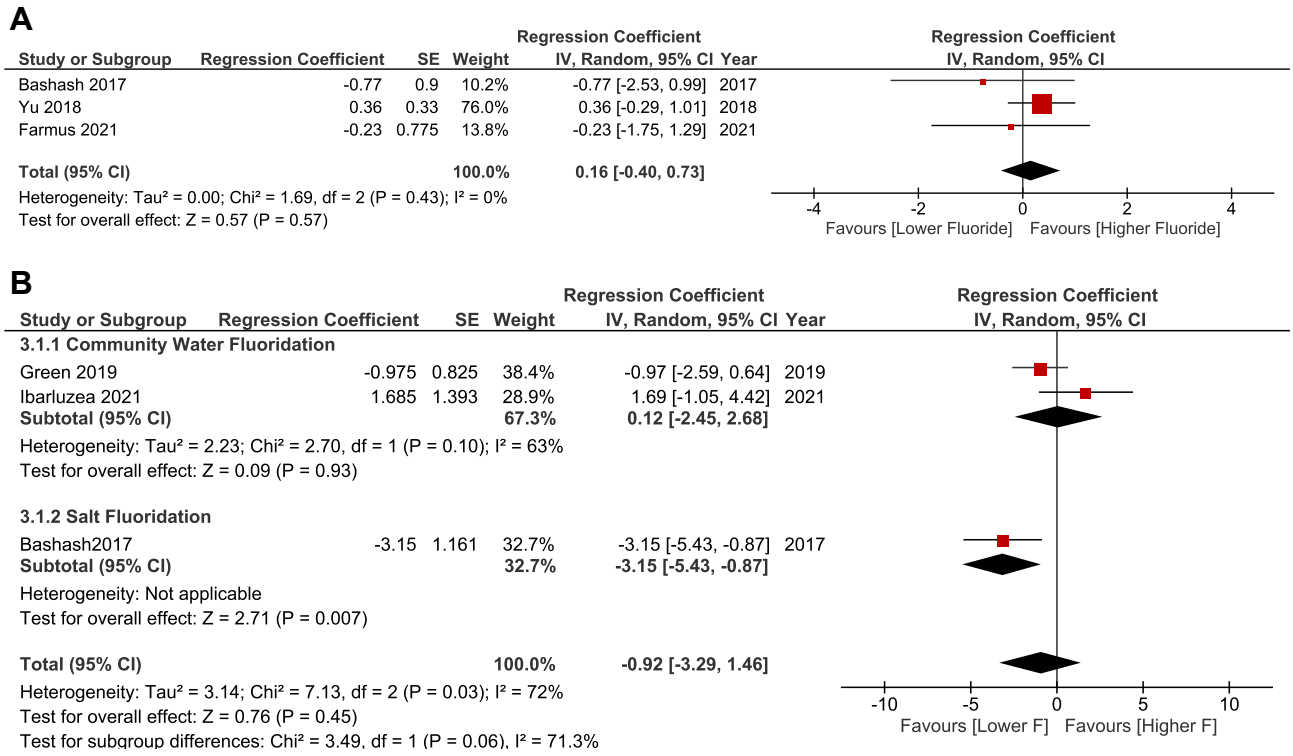

Fig. 3. (A) Random effects analysis of regression coefficients and 95% CI of children's IQ score associated with 0.5 mg/l increase in children's urinary fluoride in non-endemic areas. Forest plot of change in IQ score expressed as regression coefficient for every 0.5 mg/l increase in children's spot urinary fluoride concentrations in non-endemic fluorosis study communities. (B) Random effects analysis of regression coefficients and 95% CI of children's cognition and IQ score associated with 0.5 mg/l increase in maternal urinary fluoride in non-endemic areas. Forest plot of change in IQ score expressed as regression coefficient for every 0.5 mg/l increase in spot MUF concentrations in non-endemic fluorosis study communities according to source of fluoride.

analyses of observational data because they may produce precise but equally spurious results. Thus far, no cogent explanation has emerged for the mechanism of action of fluoride on neurodevelopmental effect.[16] Finally, publication bias is another possible explanation for the effects observed in the previous meta-analyses. The unpublished data showing a beneficial effect of fluoride on IQ in a study by Thomas in Mexico supports the potential for bias.[63]

Meta-analysis of spot CUF as a measure of children's fluoride exposure: postnatal effect

The lack of an adverse effect of fluoride when CUF was used in these studies from non-endemic areas suggests that children's exposure to CWF is not likely to show adverse effects. We selected CUF for the urinary fluoride meta-analysis because it is a direct measure of fluoride exposure to the developing brain. In addition, it likely reflects both prenatal and postnatal exposure if children are lifelong residents of a community.

Meta-analysis of spot MUF as a proxy for fetal fluoride exposure: prenatal effect

Three studies that used MUF as a proxy for fetal fluoride exposure showed inconsistent results characterised by high heterogeneity (Fig. 3B, Supplementary Table B). Ibarluzea et al.[25] could not replicate the previous study findings of prenatal effects. Instead, they found that fluoride exposure during pregnancy increased IQ across all domains among boys. In the Mexico study, Bashash et al.[24] found a threshold effect in older children, whereas Thomas[63] reported that maternal fluoride exposure did not impact children's neurobehavioral development at ages one to three years. A study from China that claimed a prenatal effect (all children had 'normal' intelligence with IQ score >119) was retracted because of methodological issues and misinterpretation of the results.[64] Recently, Farmus et al.[29,65] published a follow-up addendum declaring that exposures during trimesters of pregnancy, infancy, or childhood did not significantly associate with IQ outcomes in their study once the variable city was controlled and adjustments were made for multiple testing.

Salt was the source of fluoride in the Mexico study. Therefore, a high fluoride diet in pregnancy resulting from high salt intake may be confounded by other unhealthy habits.[24,66] However, the most likely explanation for the conflicting and inconsistent results among publications is that spot MUF is not a reliable and valid proxy biomarker of fetal fluoride exposure.[67,68] The limited available data confirm this finding because Thomas et al.[67] reported a weak correlation between MUF and maternal plasma fluoride during the early stage of pregnancy (Spearman correlation coefficient 0.29; $P = 0.004$) and a weak negative correlation in the late stage of pregnancy (Spearman correlation coefficient −0.24; $P = 0.07$) in the ELEMENT cohort. A multiple regression analysis did not show an association between spot MUF and maternal plasma fluoride. Maternal plasma fluoride levels were ~40 times lower than urinary fluoride levels. Gedalia et al.[69,70] found that the fluoride content of the bones, teeth, and cord blood of the fetuses was similar in areas with approximately 1 mg/l of fluoride compared with that of areas with 0.5 mg/l.

Strengths and limitations

We used three different exposure measures, including individual-level measures. This method also allows a direct

comparison of the effect size with the Choi et al.[19] and Duan et al.'s[20] SMD meta-analyses of endemic fluorosis areas. The urinary fluoride meta-analysis takes advantage of adjusted beta regression coefficients derived from individual-level exposures. Although we did not find an adverse effect of lower fluoride levels on IQ in this meta-analysis of SMD, it is important to recognize the limitations of this approach.[71] The SMD analysis methodology is designed for data derived from randomised clinical trials where the treatment and control groups are likely to be similar concerning known and unknown variables. This similarity is unlikely to be the case when applied to observational studies, especially when the mean IQ scores presented are unadjusted for covariates. Furthermore, many studies were cross-sectional analyses based on ecological exposure data using convenience sampling, a feature of the study that renders it to the lowest level in the hierarchy of evidence for assessing causal association. Therefore, we used the standardised IQ scores to determine the fluctuations across fluoride concentrations. However, only four studies reported multiple measurements of fluoride concentration to get an accurate assessment of exposure.

There are also limitations to the meta-analysis of pooling the effects of urinary fluoride studies. Fluoride has a short half-life. Riddell et al.[72] found that urinary fluoride levels varied substantially depending on participant behavior before sampling. Therefore, spot urinary fluoride is not a valid biomarker of long-term exposure.[73] At best, an average total daily fluoride intake may be estimated from the average daily urinary fluoride excretion at a group level.[68]

Future direction for research

These weaknesses in existing evidence and a need for confirmatory studies raise the questions for research institutions of whether to support additional research and, if so, what type. A central issue is whether the fluoride-IQ studies can validly measure long-term exposure to prenatal and postnatal fluoride and relevant confounding variables and covariates to detect a difference of 1 or 2 IQ points, which is also not easy to measure reliably. In addition, it is well known that the findings of secondary data analysis using convenience samples or cross-sectional studies are not as reliable as that of randomised clinical trials and cohort studies in establishing a causal relationship. Huang[74] highlighted the problem of selection bias and convenience sample as major inferential threats in the UK Biobank and other big data repository-based studies where collider stratification and back-door paths among variables become highly likely. Animal studies may be undertaken to assess the effect of fluoride on neurodevelopment; however, the previous high-quality study conducted by NTP researchers did not show an effect at lower fluoride exposure concentrations.[75] The challenges of conducting observational studies to establish a cause-and-effect relationship in non-endemic fluoride areas where the range of exposure is narrow may be insurmountable. A better approach is to conduct interventional studies in endemic fluorosis areas of China, India, and Iran to test the fluoride-IQ hypothesis. These studies would provide an opportunity to assess the outcome of reducing fluoride exposure on purported neurodevelopmental effects.

Conclusions

These meta-analyses show that fluoride exposure at the concentration used in CWF is not associated with lower IQ scores. However, the reported association observed at higher fluoride levels in endemic areas requires further investigation. Uncritical acceptance of fluoride-IQ studies, including non-probability sampling, inadequate attention to accurate measurement of exposure, covariates and outcomes, and inappropriate statistical procedures, has hindered methodological progress. Therefore, the authors urge a more scientifically robust effort to develop valid prenatal and postnatal exposure measures and to use interventional studies to investigate the fluoride-IQ hypothesis in populations with high fluoride (endemic) exposure.

Author statements

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Ethical approval

This study was approved by the California Department of Public Health and did not require institutional review board approval. The findings and conclusions in this report are those of the authors and do not necessarily represent the views or opinions of the California Department of Public Health or the California Health & Human Services Agency.

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Competing interests

J.V.K. is a member of the American Dental Association's National Fluoridation Advisory Committee. He was a reviewer of the National Academies of Sciences, Engineering, and Medicine report *Review of the Revised NTP Monograph on the Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects: A Letter Report (2021)*. S.F.-O. is a member of the American Academy of Pediatrics' Section on Oral Health. She was a co-author of 'Fluoride Use in Caries Prevention in the Primary Care Setting' and 'Review of Safety, Frequency and Intervals of Preventive Fluoride Varnish Application for Children.' She consults for Arcora Foundation on medical–dental integration and has research funding for medical–dental integration from Health Resources Services Administration (HRSA) D88HP37553. She serves on an independent DSMB for a study funded by Colgate.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.011.

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Original Research

Changes in physical activity during the COVID-19 lockdown based on the sociodemographic profile of 5569 students and academic staff of Austrian universities

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ABSTRACT

Objectives: The COVID-19 pandemic and the associated restrictions/lockdowns have influenced the health and lifestyle behaviour of university students and staff, particularly their physical activity (PA) habits. However, the association between the direction of PA changes and sociodemographic characteristics has not been studied. This nationwide study was conducted in Austrian colleges/universities and aimed to identify the magnitude and direction of changes in PA levels during the COVID-19 restrictions and compare participants who had unchanged vs decreased vs increased PA based on sociodemographic characteristics (sex, age, body mass index, study level, living area, nationality and Austrian regions).
Study design: This was a cross-sectional study to measure the association between the explanatory variable and outcome measures.
Methods: A total number of 4528 students (mean age 24.9 years) and 1041 academic staff (mean age 46.4 years) participated in an online survey and provided self-reported data on sociodemographic characteristics and PA change during the pandemic.
Results: A total of 41.3% of students and 37.5% of academic staff reported a decrease in PA level, whereas PA levels increased in 36.3% and 27.9%, respectively. In students, all sociodemographic variables (including sex, age, body mass index, study level, living area, nationality and Austrian regions) were significantly associated with the direction of PA changes ($P < 0.05$). Living area and Austrian region were found to be significant indicators of direction of PA changes in academic staff ($P < 0.05$).
Conclusions: These findings suggest that the inconsistency of previous studies in PA change during the pandemic may at least partly be explained by differences in the sociodemographic characteristics of the participants.

Introduction

Physical activity (PA) is a substantial part of a healthy lifestyle, which includes engagement in sports, physical exercise and movement habits.[1] It has been well documented that regular engagement in PA can be a supplementary or even an independent 'medicine' to control several health problems such as non-communicable diseases[2,3] and the associated risk factors, including obesity.[4] According to the World Health Organization (WHO)[5] and based on conclusions from a systematic review,[6] regular PA is associated with a lower likelihood of adverse COVID-19 outcomes. In this regard, it has been shown that the immunological benefits of regular PA[7] are linked to a protective effect against respiratory infections.[7,8] Therefore, PA is considered an effective strategy in the prevention and management of several diseases associated with COVID-19 (e.g. cardiovascular and metabolic diseases),[9] which are known as predictors of COVID-19 infection,

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severity and mortality.[10] In addition, PA seems to have been an effective strategy at reducing psychological distress during the COVID-19 pandemic social lockdowns.[11]

The COVID-19 pandemic has presented the world with an unprecedented challenge affecting individual and public health. In efforts to control the spread of the disease, social restrictions and lockdowns were frequently implemented by governments, which proved to be highly effective.[12] The restrictions involved social distancing, encouragement to stay at home and avoid unurgent travels and limiting access to public services, including schools and universities, sports facilities and leisure spaces.[12,13] In addition to the unfavourable impacts on education and community life,[14] data show that the COVID-19 pandemic and the associated restrictions have influenced health and lifestyle behaviour, particularly PA habits.[15,16]

Emerging adulthood, commonly defined as the period from the late teens to the mid-20s,[17] is a critical period of life to develop and shape lifestyle habits and the associated health-related consequences.[18,19] University life, which typically links with emerging adulthood, is independently associated with psychological stressors, which can cause further unfavourable health impacts.[20] Data from large-scale studies show that most university students and professors do not meet the existing PA guidelines.[21–23] It seems that the COVID-19 pandemic and restrictions have had a considerable influence on the PA habits of university students and academic staff.[24,25] However, the direction and magnitude of PA changes differ markedly across the available investigations. For instance, previous studies show contradictory results regarding PA changes during the pandemic in the form of a decrease,[26,27] increase[28,29] or no change,[30,31] among university students. Findings from a systematic review indicate that students who met the PA recommendations before the restrictions also met the recommendations during the pandemic.[24] Another study reports while the PA level of university students decreased, their PA behaviour improved during the COVID-19 restrictions.[32] These data, together with the abovementioned inconsistencies in research findings, appear to be associated with differences in sample size and/or the sociodemographic characteristics of participants.[6] Thus, there is a necessity to consider potential moderators of change in PA, and this area remains an open field of research.

Despite the existence of various research reports on university students and their PA change during the COVID-19 pandemic,[26–31] to date, no studies have examined the direction of PA change as an independent variable to test the potential associations with sociodemographic characteristics. Therefore, the present study aimed to identify the magnitude and direction of change in PA levels during the COVID-19 restrictions and compare participants who had unchanged vs decreased vs increased PA to find associations with sociodemographic factors in a large group of Austrian university students and academic staff.

Methods

Study design and sampling

This study is a part of the project Sustainably healthy – From Science 2 Highschool & University, which has been conducted in tertiary education settings with a cross-sectional study design[33] following the original study on secondary schools.[34,35] The boards of college/university deans of all 102 public and private colleges/universities in Austria were directly contacted and received relevant information about the study goals, procedures and instructions. Any individual who was either enrolled as a student or employed as a lecturer, researcher or other academic staff were eligible to participate in the study, which equated to a total population of 376,050 students and 69,310 academic staff. After approval of the study protocol by the ethics board of the associated educational entities, students and academic staff from 52 public and private colleges/universities participated in the present study.

Procedures

Participants received a Web link to take part in an online survey. The associated instructions were included, and participants provided written informed consent to participate in the study. The survey was based on self-reports (LimeSurvey, version 3.25.15) and was provided in German and English languages and separately for students and academic staff. Participants were able to complete the survey within approximately 20 min. Data collection was done from April to July 2021. It is noteworthy to indicate that during the data collection period, a series of restrictions and measures had been implemented in Austria to combat the spread of the COVID-19. The restrictions included mandatory mask-wearing and social distancing between individuals in public indoor spaces, limitations on gatherings, closure of non-essential businesses and a nighttime curfew in some areas. In addition, a majority of university classes were administered online, and classes that required in-person attendance were held in small groups to guarantee the mandated 2-m distance between attendees at all times. Further methodological information is available in the study protocol of the Sustainably healthy – From Science 2 Highschool & University study,[33] which the interested readers are kindly referred to.

Measures and calculations

The standardised questionnaire consisted of questions on sociodemography (nationality: Austrian or international; age; sex: females, males or diverse; living area: urban or rural; federal state: Vienna, Burgenland, Lower Austria, Styria, Carinthia, Upper Austria, Salzburg, Tyrol or Vorarlberg), biometric data (height and body weight), current academic/professional status (including the study level of students: undergraduate level or graduate level) as well as health-related data. To assign participants in the study groups based on PA change during the COVID-19 restrictions, participants were specifically asked to answer a question on their change in PA level during the COVID-19 lockdown with the response options of '*No*', '*Yes, I did less*' or '*Yes, I did more*'. Body mass index (BMI) was calculated using body weight and height values. The WHO cutoff points for BMI were used to assign participants in BMI subgroups, including underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obese (>30.0 kg/m^2).[36,37]

Statistical analysis

Statistical tests were performed using SPSS version 26.0 (SPSS Inc., IBM Corp., Armonk, NY, USA). Exploratory analysis was conducted by descriptive statistics, and data are reported as prevalence (percentage; for nominal data) or mean with standard deviation (M ± SD; for continuous data). Chi-squared tests (χ^2) were conducted to examine differences between the study groups (based on PA change) by sex, weight status, study level, living area, nationality and Austrian region. Analysis of variance (*F* values) was used to examine age differences between the study groups (PA change). When significant differences for multilevel variables were found, post-hoc tests (using Bonferroni adjustment) were also conducted to determine the origin of differences within subgroups. The level of statistical significance was set at $P \leq 0.05$.

Results

A total number of 4528 college/university students (mean age: 24.9 ± 6.3 years) and 1041 academic staff (mean age: 46.4 ± 11.5 years) completed the questionnaire. The final sample size of the present study included 1.2% of student population and 1.5% of eligible academic staff enrolled or employed in Austrian colleges/universities. This response rate successfully met the initial anticipation of 1.0%. Among students, 65.8% were females, and 0.7% reported a diverse gender. Among academic staff, 51.6% were females and 0.2% reported a diverse gender. Classification of participants is displayed in Fig. 1.

While 7.4% of students were underweight (BMI <18.5 kg/m^2), the general prevalence of overweight/obesity was 17.8%, with a higher rate in male students (24.6%) compared with females (14.3%). On the other hand, the prevalence of underweight was higher in female students (9.4%) compared with males (2.9%). The prevalence of overweight/obesity among academic staff was 32.2%, whereas only 2.9% were underweight. Table 1 presents the anthropometric characteristics of the participants based on sex groups.

Across the sample of students, 22.4% of participants reported their PA level had not changed during the COVID-19 restrictions, whereas 41.3% experienced a decrease and 36.3% reported an increase in their PA level. Accordingly, sociodemographic analyses were conducted based on PA change groups: no change in PA, less PA and more PA. A significant sex difference was found between the study subgroups ($P < 0.001$), where female students were more likely to report an increase in PA level during the COVID-19 restrictions compared with male and diverse students ($P < 0.001$); on the other hand, male and diverse participants reported a higher likelihood to decrease their PA level compared with female students ($P < 0.001$). Age significantly differed ($P < 0.001$) between subgroups, where students with increased PA were generally younger than their peers in the two other groups of PA change ($P < 0.001$). Sex-specific analyses, however, showed that this age difference was only present in females ($P < 0.001$). A significant difference between PA change subgroups was also found in BMI categories ($P < 0.001$), with overweight and obese participants being more likely to report a decrease in PA during COVID-19 compared with normal weight or underweight participants ($P < 0.001$). Analysis of the study level showed that undergraduate students were more likely to report an increase in PA during the COVID-19 restrictions than graduate students ($P < 0.001$). Rural participants were more likely to increase their PA level, whereas urban participants were more likely to decrease their PA level ($P < 0.001$). A significantly higher prevalence of participants reporting a decrease in PA level was found among those from eastern Austria (states: Vienna, Burgenland, Lower Austria) compared with centre (states: Styria, Carinthia, Upper Austria) and western Austria (states: Salzburg, Tyrol, Vorarlberg; $P < 0.001$). It was also found that international students had a greater likelihood to decrease PA during the pandemic compared with Austrian students ($P < 0.001$). Further data are presented in Table 2.

Across the sample of academic staff, 34.7% reported no change in PA level during the COVID-19 restrictions, whereas 37.5% and 27.9% reported a decrease and increase in PA level, respectively. Analyses of sociodemographic parameters showed that there were significant differences between the PA change subgroups in 'living area' and 'Austrian region'. Specifically, those who lived in

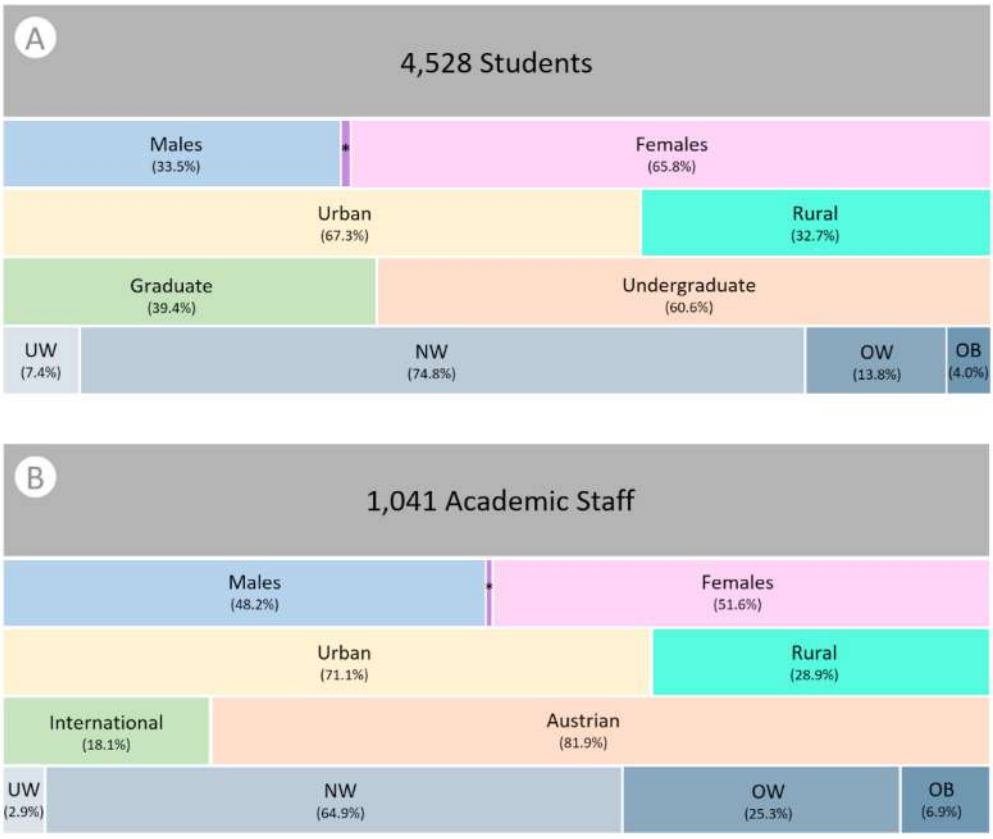

Fig. 1. Classification of students (A) and academic staff (B) based on sociodemographic characteristics. *Diverse population, representing 0.7% and 0.2% of the final sample size for students and academic staff, respectively. UW, underweight; NW, normal weight; OW, overweight; OB, obese.

Table 1
Sex differences in age and anthropometric characteristics.

		Total	Female	Male	Diverse
Study sample	*Students*	4528 (100%)	2981 (65.8%)	1517 (33.5%)	30 (0.7%)
	Academic staff	1041 (100%)	537 (51.6%)	502 (48.2%)	2 (0.2%)
Age (years)	*Students*	24.9 ± 6.3	24.4 ± 6.1	25.7 ± 6.7	27.6 ± 8.2
	Academic staff	46.4 ± 11.5	45.0 ± 10.5	47.9 ± 12.3	47.5 ± 16.3
Body weight (kg)	*Students*	66.9 ± 14.1	61.6 ± 11.0	77.3 ± 13.6	68.3 ± 16.5
	Academic staff	72.9 ± 14.2	65.3 ± 11.5	81.0 ± 12.2	65.4 ± 8.8
Height (cm)	*Students*	171.9 ± 9.2	167.2 ± 6.2	181.2 ± 6.8	168.3 ± 9.7
	Academic staff	173.9 ± 9.0	167.9 ± 6.0	180.3 ± 7.0	169.5 ± 2.1
BMI (kg/m^2)	*Students*	22.6 ± 3.7	22.0 ± 3.6	23.5 ± 3.7	24.0 ± 5.0
	Academic staff	24.0 ± 3.8	23.2 ± 3.9	24.9 ± 3.5	22.8 ± 3.6
Underweight	*Students*	333 (7.4%)	288 (9.4%)	44 (2.9%)	1 (3.3%)
	Academic staff	30 (2.9%)	24 (4.5%)	6 (1.2%)	0
Normal weight	*Students*	3387 (74.8%)	2268 (76.1%)	1099 (72.4%)	20 (66.7%)
	Academic staff	676 (64.9%)	390 (72.6%)	285 (56.8%)	1 (50%)
Overweight	*Students*	627 (13.8%)	312 (10.5%)	310 (20.4%)	5 (16.7%)
	Academic staff	263 (25.3%)	90 (16.8%)	172 (34.3%)	1 (50%)
Obese	*Students*	181 (4.0%)	113 (3.8%)	64 (4.2%)	4 (13.3%)
	Academic staff	72 (6.9%)	33 (6.1%)	39 (7.8%)	0

BMI, body mass index.
Data are presented as mean ± standard deviation or prevalence.

Table 2
Changes in PA of students based on sociodemographic characteristics.

	No change in PA	Less PA	More PA	Statistics
Total participants (n = 4528)	1016 (22.4%)	1868 (41.3%)	1644 (36.3%)	–
Age	25.67 ± 7.55	25.35 ± 6.64	23.77 ± 4.84[a]	$F_{(2)} = 39.136$; $P < 0.001$
Sex				$\chi^2 = 98.539$; $P < 0.001$
Female (n = 2981)	658 (22.1%)	1097 (36.8%)[b]	1226 (41.1%)[b]	
Male (n = 1517)	352 (23.2%)	755 (49.8%)	410 (27.0%)	
Diverse (n = 30)	6 (20.0%)	16 (53.3%)	8 (26.7%)	
BMI				$\chi^2 = 43.346$; $P < 0.001$
Underweight (n = 333)	82 (24.6%)	124 (37.2%)	127 (38.1%)	
Normal weight (n = 3387)	781 (23.1%)	1329 (39.2%)	1277 (37.7%)	
Overweight (n = 627)	124 (19.8%)	320 (51.0%)[c]	183 (29.2%)	
Obese (n = 181)	29 (16.0%)	95 (52.5%)[c]	57 (31.5%)	
Study level				$\chi^2 = 11.952$; $P = 0.003$
Undergraduate (n = 2742)	600 (21.9%)	1092 (39.8%)	1050 (38.3%)[d]	
Graduate (n = 1786)	416 (23.3%)	776 (43.4%)	594 (33.3%)	
Living area				$\chi^2 = 73.406$; $P < 0.001$
Urban (n = 3048)	664 (21.8%)	1385 (45.4%)[e]	999 (32.8%)[e]	
Rural (n = 1480)	352 (23.8%)	483 (32.6%)	645 (43.6%)	
Austrian region				$\chi^2 = 52.355$; $P < 0.001$
West (n = 1114)	274 (24.6%)	407 (36.5%)	433 (38.9%)	
Centre (n = 823)	203 (24.7%)	276 (33.5%)	344 (41.8%)	
East (n = 2591)	539 (20.8%)	1185 (45.7%)[f]	867 (33.5%)	
National/international				$\chi^2 = 13.277$; $P < 0.001$
Austrian (n = 3687)	838 (22.7%)	1475 (40.0%)[g]	1374 (37.3%)	
International (n = 841)	178 (21.2%)	393 (46.7%)	270 (32.1%)	

BMI, body mass index; PA, physical activity.
Statistical methods: Chi-squared (χ^2) and ANOVA (*F* values).
Data are presented as prevalence (number of participants and percentage) or mean ± standard deviation for *age*.
[a] Significant difference with 'Less PA' and 'No change in PA'.
[b] Significant difference with 'Male' and 'Diverse'.
[c] Significant difference with 'Underweight' and 'Normal weight'.
[d] Significant difference with 'Graduate'.
[e] Significant difference with 'Rural'.
[f] Significant difference with 'West' and 'Centre'.
[g] Significant difference with 'International'.

Table 3
Changes in PA of university academic staff based on sociodemographic characteristics.

	No change in PA	Less PA	More PA	Statistics
Total participants (n = 1041)	361 (34.7%)	390 (37.5%)	290 (27.9%)	–
Age	47.20 ± 11.35	46.13 ± 11.55	45.87 ± 11.60	$F_{(2)} = 1.295$; $P = 0.274$
Sex				$\chi^2 = 2.813$; $P = 0.590$
Famale (n = 537)	179 (33.3%)	200 (37.2%)	158 (29.4%)	
Male (n = 502)	182 (36.3%)	189 (37.6%)	131 (26.1%)	
Diverse (n = 2)	0	1 (50.0%)	1 (50.0%)	
BMI				$\chi^2 = 4.771$; $P = 0.574$
Underweight (n = 30)	11 (36.7%)	10 (33.3%)	9 (30.0%)	
Normal weight (n = 676)	244 (36.1%)	239 (35.4%)	193 (28.6%)	
Overweight (n = 263)	82 (31.2%)	111 (42.2%)	70 (26.6%)	
Obese (n = 72)	24 (33.3%)	30 (41.7%)	18 (25.0%)	
Living area				$\chi^2 = 13.996$; $P < 0.001$
Urban (n = 740)	233 (31.5%)[a]	300 (40.5%)[a]	207 (27.6%)	
Rural (n = 301)	128 (42.5%)	90 (29.9%)	83 (27.6%)	
Austrian region				$\chi^2 = 11.855$; $P = 0.018$
West (n = 368)	145 (39.4%)	125 (34.0%)	98 (26.6%)	
Centre (n = 193)	75 (38.9%)	65 (33.7%)	53 (27.5%)	
East (n = 480)	141 (29.4%)	200 (41.7%)[b]	139 (29.0%)	
National/international				$\chi^2 = 0.876$; $P = 0.645$
Austrian (n = 853)	301 (35.3%)	315 (36.9%)	237 (27.8%)	
International (n = 188)	60 (31.9%)	75 (39.9%)	53 (28.2%)	

BMI, body mass index; PA, physical activity.
Statistical methods: Chi-squared (χ^2) and ANOVA (F values).
Data are presented as prevalence (number of participants and percentage) or mean ± standard deviation for Age.
[a] Significant difference with 'Rural'.
[b] Significant difference with 'West' and 'Centre'.

urban areas were more likely to decrease their PA level, whereas rural participants were more likely to maintain their PA level during the COVID-19 pandemic ($P < 0.001$). In addition, participants in the eastern region of Austria were more likely to report a decline in PA during COVID-19 compared with participants living in the west or centre of Austria ($P = 0.018$). No significant difference was found between the study groups in other sociodemographic variables, including age, sex, BMI and nationality ($P > 0.05$). Table 3 presents further data regarding the association between PA changes and different sociodemographic variables in Austrian academic staff.

Discussion

This Austrian nationwide study aimed to examine PA changes during the COVID-19 pandemic in college/university students and academic staff, focusing on potential influences of sociodemographic characteristics on behaviour change. In general, it was shown that (1) the majority of students (77.6%) experienced a change in PA level during the COVID-19 restrictions in form of decrease (41.3%) or increase (36.3%); (2) among academic staff, 37.5% reported a decrease and 27.9% experienced an increase in PA level; (3) analysis of sociodemographic characteristics of students showed that females (compared with male and diverse students), younger (compared with older students), underweight and normal weight (compared with overweight and obese students), undergraduate (compared with graduate students), rural (compared with urban students) and Austrian students (compared with international students) were more likely to report an increase in PA during the restrictions compared to their peers; (4) among academic staff, a significant association between PA change and two sociodemographic parameters (i.e. living area and Austrian region) were observed, where urban (compared with rural participants) and participants from the eastern region of Austria (compared with those who live in centre and west of Austria) reported a greater decrease in PA level during the pandemic.

Consistent with the present findings, another study concluded a range between 50 and 90% of university students changed PA level during the COVID-19 pandemic.[38] However, there has been an inconsistency in the direction of PA changes between studies in terms of decrease,[26,27] increase[28,29] or unchanged.[30,31] Data from a comparable study on German university students show that half of the students indicated a decrease and one-third of students reported an increase in PA level during the pandemic; however, a general decrease in their daily walking time was found.[39] This contradiction may highlight that sedentary time (which is associated with the current sharp increase in usage of online platforms) is not necessarily translated to daily PA levels. In this regard, a study reports that although university students' sedentary behaviour (in terms of daily sitting hours) increased during COVID-19 restrictions, a considerable number of them experienced an increase in PA level.[28] PA changes may also be related to previous PA background because it has been reported that highly active students had a greater change in their PA behaviour before and during the restrictions.[25] Conclusions from a review study indicated that while most investigations on university students reported a decrease in PA level during the pandemic, the intensity of PA seems unrelated to PA change.[24]

In the comparison of study groups, students in the present study showed a slightly greater PA change compared with academic staff (77.6% vs 65.4%). Consistently, another study found that the PA level of university students was more affected by the COVID-19

pandemic compared with the university employees,[25] which may be explained by the steadiness of daily routines in university staff, mostly because of maturity and/or stable life. Previous studies showed that young adults, including university students, are prone to experience many unexpected changes in their life (because of variations in, e.g., academic, social and occupational situations), which may profoundly affect their lifestyle.[18] This is in line with the general fact that environmental or institutional barriers are accountable for 90% of predictors of lifestyle behaviour among university students.[20]

There are contradictory reports in the literature regarding sex differences in PA change following the lockdowns in terms of the predominance of female[25,26,40] or male students[41–43] in the magnitude of change. The present findings show that sex was a significant indicator for direction (not magnitude) of PA change in students but not academic staff, where female students reported a greater likelihood to increase PA and male (as well as diverse) participants had a greater likelihood to decrease PA during the COVID-19 restrictions. Similar results were found in a Spanish study on university students.[44] Consistently, the results from studies on general populations show that increases in PA levels were more commonly reported by females than males, whereas decreases in PA levels were more prevalent in males.[45,46] It has also been reported that being female is associated with the probability of meeting the PA recommendations during the pandemic.[47] A possible explanation may be that females are more likely to be able to adopt their movement habits based on online opportunities/platforms, whereas males may be more dependent on organised club activities that were shut-down during COVID-19 restrictions. Sex differences in health-related motives, particularly the greater health and weight consciousness of females, may also play a significant role in health behaviour, including PA.[48]

In the present study, there was a significant association between the direction of the PA change and age as well as BMI in students (but not academic staff). We observed that students with a greater likelihood to increase PA during COVID-19 restrictions were generally younger than the two other groups (i.e., unchanged and decreased PA). Consistently, it has been shown that being younger than 22 years of age is positively associated with regular engagement in PA during the restrictions.[47] However, data in general populations show that mature adults were significantly more likely to keep and even increase PA levels during the COVID-19 time compared with younger adults.[49] While the prevalence of overweight/obesity in the present study was 17.8% in students and 32.2% in academic staff, overweight/obese students (but not staff) were more likely to decrease their PA during the pandemic compared with the students with BMI <25 kg/m^2. This can be partially justified with previous research, indicating that students who met the PA recommendations before the pandemic were more likely to meet the recommendations during the pandemic.[24] The distribution of weight categories in the present study was in line with the global data,[50] where the majority of both samples had normal weight (74.8% of students and 64.9% of academic staff). However, the low prevalence of obesity/overweight in the sample of students (17.8%) is in accordance with the data from the WHO European Regional Obesity Report 2022, in which the Austrian people present among the lowest rates of overweight and obesity in Europe.[51]

Living environment was also found to be a significant indicator for PA change in the present study. In both groups, university students and academic staff, urban participants were more likely to decrease their PA level compared with rural members. This finding might be explained by the greater severity of COVID-19 restrictions in cities and towns and/or more outdoor opportunities in rural areas for PA. Interestingly, we found that students and academic staff from the eastern parts of Austria were more likely to reduce their PA during COVID-19 compared with participants living in the centre or west of Austria (which is widely encompassed by highlands, including mountains and forests). In this regard, it has been documented that geographical area is a remarkable indicator of the health-related consequences of COVID-19.[52] Another study found that health behaviour of university students during the pandemic varied by the country of residence,[53] which is in line with the present finding where international students were more likely to decrease PA level compared with Austrian students. According to European Observatory on Health Systems and Policies (EOHSP) reports, Austrian adults are among the most physically active in Europe,[54] which is comparable with the previous data indicating that the majority of Austrian university students are physically active.[55] Altogether, these findings suggest that cultural and environmental situations need to be taken into account when interpreting changes in health-related behaviours.

The present study includes some limitations. The cross-sectional study design and the associated self-reported data carry the risk of misreporting, particularly socially desired statements from overreporting (e.g. in PA engagement) and/or underreporting (e.g. in body weight). In addition, there might be confounding factors, including direct and indirect lifestyle parameters, which may potentially influence the findings and the associated interpretations. Another limitation of this study is the use of a self-reported assessment of PA using a single-item question, which may be subject to recall bias and/or social desirability bias. Because of practical considerations, self-reported assessment of PA was the only option for this study. The large sample size of the study may also minimise the likelihood of the abovementioned limitation. Evidence suggests that single-item questionnaires can be considered valid and are consistently used in the social and behavioural sciences, as they may significantly reduce the problems associated with lengthy surveys.[56] Nevertheless, interpretations of the findings should be done with caution. Despite the aforementioned limitations, the nationwide nature of the sample and the large sample size in both groups of students (n = 4528) and academic staff (n = 1041) are considerable strengths of the present study. Research-based evidence in the area of public health provides a basis for health administrations to upgrade and establish policies and guidelines. Particularly, efforts towards understanding of the predictors of health behaviours, including PA patterns during the COVID-19 pandemic are crucial for policymakers at educational settings. Such evidence may ultimately help increase the health status of university students in such an important period of life — called emerging adulthood — which eventually leads to the promotion of public health.

Conclusions

Taking a large sample into account (n = 5569), the present Austrian-wide study is the first to map the association between the direction of PA change during the COVID-19 time and sociodemographic characteristics of college/university students and academic staff. Most students (77.6%) and academic staff (65.4%) experienced a change in PA level (in terms of decrease or increase) following the COVID-19 restrictions. In the sample of students, almost all sociodemographic variables (including sex, age, BMI, study level, living area, nationality and Austrian regions) were significantly associated with the direction of PA change; however, only living area and Austrian region were found to be indicators of increased or decreased PA among academic staff. These findings provide the first explanatory evidence specifying that the inconsistency between data from previous studies may be, at least partially, because of differences in sociodemographic characteristics of university students and staff.

Author statements

Author contributions

K.C.W., together with G.R., W.K. and C.D. contributed to conceptualisation and study design. M.M. and C.D. contributed to methodology, formal analysis and writing original draft preparation. K.C.W., C.D., G.R., D.R.T. and W.K. contributed to critical review and editing. G.W. contributed to technical support. All authors have read and agreed to the published version of the article.

Ethical approval

This study was conducted in accordance with the medical professional codex, the Helsinki Declaration as of 1996, Data Security Laws and good clinical practice guidelines. Informed consent was obtained from all participants involved in the study. Participation in the study was voluntary and could be terminated at any time without providing reason or negative consequences. The study protocol was approved by both the ethics board of the 'Board for Ethical Questions in Science of the University of Innsbruck', Vice Rectorate for Research (Certificate of good standing, 22/2021; 6 April 2021) and the Rectorate of the University College of Teacher Education Tyrol (PHT-HSa-17-Z1.8-5n_4927; 22 March 2021).

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Competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Original Research

Does health insurance solve health care utilization puzzle in Tanzania?

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ABSTRACT

Objectives: The global target of achieving universal health coverage by 2030 is a nightmare in most developing countries. To seek in-depth reasons, this study examines the effects of health insurance on healthcare utilization in Tanzania.
Study design: This study used a non-experimental research design.
Methods: Probit model, negative binomial regression, and instrumental variable Poisson with generalized method of moments were used to solve the healthcare utilization puzzle by the use of Andersen Health Care Utilization Model by using the Tanzania Panel Survey data of 2020/21.
Results: The findings showed that education level, income, age, residence, household size, insurance, and distance from homestead to health facilities are significant policy intervention factors for improving households' healthcare utilization behavior among households in Tanzania.
Conclusion: Prioritize should be made on interventions that ensure the affordability of health services without compromising the quality of services offered and expanding the share of the government budget on health sector.

Introduction

The question of whether health insurance has a role to play in facilitating households' healthcare utilization is highly debatable in most developing countries. The debate is louder in these countries because of poverty, which increases pressure on the households' decision to seek medical services that are accompanied with unfriendly user fees and out-of-pocket expenditures, which have been threatening households' incomes.[4,12,13,17,23,28]

The joint statement by World Bank and World Health Organization in 2017 revealed that nearly half of the global population cannot access basic health services due to several reasons. One of the key reasons suggested by these international organizations was the burden of healthcare costs, which have pushed more than 100 million households into extreme poverty.[13,37] The problem is severe in African countries where <50% of the entire population has access to health services. In addition, health care in Sub-Saharan Africa has remained one of the worst globally, whereas only 42.56% of the population in the sub Saharan Africa (SSA) has access to health services.[9,12,13]

Tanzania, similar to many other sub-Saharan African countries, is worst performing in terms of health outcomes[12] because of poor healthcare utilization and a lack of health insurance. This is evidenced by the basic health indicators for 2020, where the average life expectancy was 66 years, the infant mortality rate per 1000 live births was 34.7, and the maternal death rate per 100,000 live births was 524. Furthermore, 32% of children aged <5 years were stunted (have low height for age), and 58% were anemic. Up to 14% of children aged <5 years were underweight (too thin for their age), whereas 4% were overweight.[12,25]

Another potential threat to Tanzania's health sector is the rapid and uncontrolled population growth; according to the 2012 national census report, there were 45 million people in the country, but the latest 2022 national census indicates an increase of 16 million people just in 10 years.[12,13] While the population is increasing, the trend of healthcare utilization has been decreasing from 71% in 2011/12 to 56% in 2017/18.[18] In line with the global agendas, the government of Tanzania has been increasing its share of expenditure on health care;[13] however, the share is still below that of the Abuja Declaration of at least 15% of the government budget.[12]

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In addition, since independence, several health insurance schemes have been established to lower healthcare costs and increase accessibility to health services for the underprivileged groups in the country. The most famous health insurance schemes are the National Health Insurance Fund (NHIF) and the Community Health Fund (CHF), which are all run by the government.

Despite the establishment of these insurance schemes, households in Tanzania have been reluctant to subscribe to any of these, making it hard for the government to achieve both its development vision on health and global targets. In fact, besides the limited preference for health insurance subscriptions, only one-third of ill people in Tanzania seek medical care services.[32,34] This suggests the existence of health care utilization challenges in the country. The problem gets even bigger as those with health insurance are required to pay extra fees (out-of-pocket expenditure) to get treatments and medications. This indicates that despite most of the public health insurance packages being cheap, they cover treatments for simple diseases (such as fever, malaria, and flu).

Similar problems are experienced in most of the sub-Saharan African countries where the average out-of-pocket expenditure for health care is 30%.[12,13,28,29] To this end, reliance on out-of-pocket expenditure to finance access to health invariably affects quality and is inequitable, thus leading to lower healthcare utilization with only <16.99% of the population in the region being covered with health insurance.[12,28] Therefore, to increase the rate of health insurance subscription and healthcare utilization, more scientific studies are needed from the country level to the regional level.

Nonetheless, most studies made in Tanzania focused on evaluating the performance of health insurance in terms of enrollment, financial management, and sustainability, as well as patients' perceptions toward services offered under specific health insurance schemes, whereas few have tried to examine the impacts of health insurance on lessening out-of-pocket expenditure and toward healthcare utilization. Most of these studies are qualitatively designed and cover small areas with very limited sample sizes (ranging between 100 and 200), which makes them unable to provide strong econometric arguments and analytics on the extent of health insurance adoption and its effects on healthcare utilization. In this regard, the present study bridges these gaps by introducing the Andersen Healthcare Utilization Model in Tanzania's context and assess the Andersen Healthcare Utilization Model dynamics' (i.e. predispose, enable, and need factors) influence toward healthcare utilization. Moreover, methodologically, the study has applied negative binomial regression (NBR) and instrumental variable (IV) Poisson with generalized method of moments (GMM) techniques, which have rarely been applied to increase the accuracy of estimates by controlling the endogeneity problem. Finally, this study has used large data collected countrywide by the Tanzania Bureau of Statistics, which helps in providing results that reflect the entire picture of the country as shown at Fig. 2.

Theoretical foundation and empirical reviews

Theoretically, the study used the *Andersen Healthcare Utilization Model* created by Ronald M. Andersen in 1968.[1–3] The Andersen Healthcare Utilization Model is a conceptual model that demonstrates factors that influence the use of healthcare services. According to the model, three dynamics influence healthcare utilization, including factors that predispose, enable, and need factors, which have been summarized in Fig. 1.

In explaining these dynamic factors that influence the use of health services, Shin et al.[36] examined factors determining children's private health insurance enrollment and children's healthcare utilization in Korea using a logit model. The study found that factors such as children's age, sex, parents' education status, employment status, and household income quality are important determinants for children's enrollment in private health insurance, as they were significantly related to the insurance enrollment. They also found that private health insurance has a significant effect on both outpatient and inpatient costs.

Saeed et al.[22] in Ghana and López-Cevallos and Chi[33] in Ecuador analyzed the effects of health insurance on healthcare utilization. Both studies indicated a significant increase in healthcare utilization when households subscribe to health insurance. In addition, these studies showed that households that tended to renew their health insurance packages early had a higher rate of healthcare utilization compared with those who renew their health insurance lately. Moreover, there was an inverse relationship between healthcare utilization and household economic status.[33]

Abu-Bakari et al.[1] and Osei and Agyemang[20] examined the impacts of health insurance ownership on households' health-seeking behavior in Malaysia and rural Ghana by the use of a logit model and zero truncated Poisson regressions, respectively. Their findings showed that health insurance status has a significant influence on healthcare utilization. People with health insurance status had higher number of healthcare visits compared with those without healthcare insurance. These studies advanced some recommendations that government and policymakers should focus on leveraging health insurance so that it can benefit large number of poor people whose healthcare utilization is compared with those who are well off.

Other studies[7,15,26,35] suggest that age, sex, education, marital status, household size, income, health insurance status, and homestead distance to health facilities had a significant relationship with healthcare utilization. Despite such a significant relationship, these studies represent a different standpoint from Abu-Bakari et al.[1] who found that insurance ownership determines access to health care but does not influence the frequency of use.

Methods

The non-experimental research design was used in this study to analyze secondary data from Tanzania's National Panel Survey (NPS) 2020/21 that were collected by the country's National Bureau of Statistics (NBS) funded by the World Bank and European Union. The NPS is a large-scale survey that includes equal representation of households across regions throughout the country.[18] The choice of the data set is based on the reputation of the NBS in collecting and managing national datasets, which has made this survey to have one of the best response rate of more than 97%. Moreover, the NPS has crucial information concerning health, poverty, and regional economies, which are normally used to monitor the country's progress toward the realization of the Sustainable Development Goals (2030) and Tanzania Development Vision 2025.[28,37] On the other hand, all ethical and data collection arrangements, including the sampling technique, were prepared and implemented by the NBS.[13,18]

Analytical modeling

Analytically, the probit model was used to explain factors influencing household subscription to health insurance in Tanzania, of which insurance subscription was a binary outcome.[8,27,28] Thus, the following equation with the latent response variable and the observable index (exogeneous variable) represents such relationship for the household to subscribe for any of the health insurance schemes in Tanzania.

$$y_i^* = \beta_0 + \beta_1 X + \mu_i \quad \text{where } \mu_i \sim \left(0, \delta^2\right) \tag{1}$$

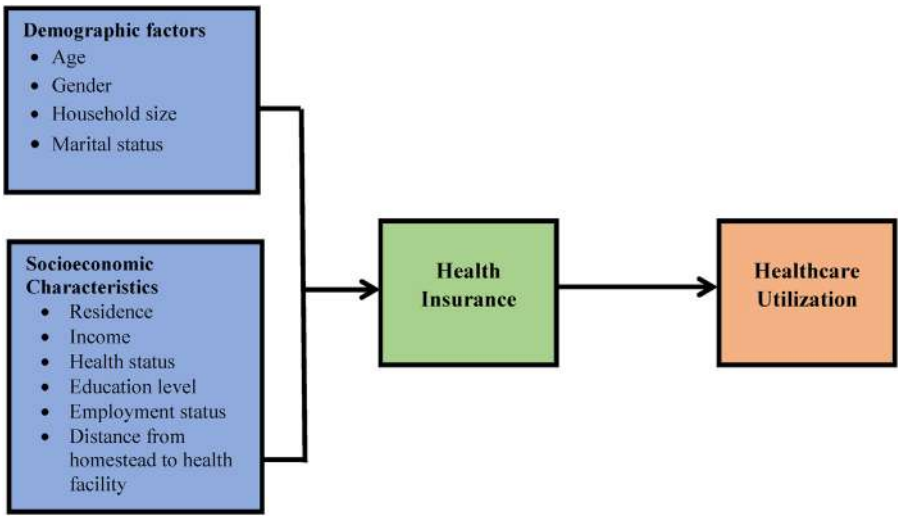

Fig. 1. Conceptual framework (authors' design).

where y_i^* is the dependent variable, which assumes an unobservable utility index, X represents the observable indices, β represents the coefficient of the independent variable, and μ_i is the error term with standard normal distribution.[27] Basing on this function, the probit model will be derived to analyze factors influencing households' decision to subscribe to health insurance.

As y_i^* is unobservable, what we observe is y_i, which takes only two values as explained that one may or may not subscribe to health insurance, thus presented as follows:

$$Health\ insurance = \begin{matrix} 1\ if\ subscribe\ to\ health\ insurance^* > 0 \\ 0\ if\ dont\ subscribe\ to\ health\ insurance^* < 0 \end{matrix} \quad (2)$$

Moreover, the NBR and IV Poisson via GMM were used in estimating the effects of health insurance on healthcare utilization among households in Tanzania. The NBR is similar to the multiple linear regression model with the only difference being the nature of the dependent variable, which in NBR is always considered as Count data.[27,46,48]

Consider an NBR equation with k regressors:

$$\mu_i = \exp(ln(t_i) + \beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_k x_{ki}) \quad (3)$$

Often, $x_1 \equiv 1$ and β_1 …, β_k are unknown parameters. Therefore, using this representation, the fundamental NBR model for an observation i is given as:

$$\Pr(Y = y_i|\mu_i, \alpha) = \frac{\tau(y_i + \alpha^{-1})}{\tau(y_i + 1)\tau(\alpha^{-1})}\left(\frac{\alpha^{-1}}{\alpha^{-1} + \mu_i}\right)^{\alpha^{-1}}\left(\frac{\mu_i}{\alpha^{-1} + \mu_i}\right)^{y_i} \quad (4)$$

where $\mu_i = t_i\mu$ and $\alpha = \frac{1}{v}$.

As a result of the definition of the gamma function, the results below are based on the relationship described below:

$$ln\left(\frac{\tau(y_i + \alpha^{-1})}{\tau(\alpha^{-1})}\right) = \sum_{j=0}^{y_i - 1} \ln\left(j + \alpha^{-1}\right) \quad (5)$$

In addition to that, this study used the IV Poisson regression model, which is an extension of the generalized linear models with the ability to suppress possible endogeneity that arises during estimations.[28,38,41] Generally, Poisson models provide an extension of the linear model in dealing with different types of responses, including the count data; in this study, the number of visits to healthcare facilities was used.[50] Let Y_i be the response variable, and $X_i = (X_{i1,..,}X_{ip})^T$ be the corresponding p dimensional covariates. The Poisson regression model assumes the response variable Y_i is a count and follows a Poisson distribution given by:

$$P(Y_i, \mu_i) = \frac{\mu_i e^{-\mu_i}}{Y_I!} \quad (6)$$

Moreover, the stochastic disturbance term (μ_i) is described as:

$$\mu_i = E(Y_i|x_I) = exp\left(X_i^T\ \beta\right) \quad (7)$$

where $\beta = (\beta_1, \ldots, \beta_p)^T$ is an unknown parameter vector. Using the same argument as in Greenland,[39] the conditional mean specification implicitly defines a regression model.

$$Y_i = exp\left(X_i^T\beta\right) + \varepsilon_i \quad (8)$$

Given that, $E(\varepsilon_i|X_i) = 0$

However, the covariate X_i may be endogenous in many practice disciplines.[38–40] That is, X_i is correlated with ε_i, and $E(\varepsilon_i|X_i) = 0$ does not hold anymore. For such Poisson regression model with endogenous covariates, many articles have considered the estimation for the parameter β when some instrumental variables are available. For example, Windmeijer and Santos Silva[38] proposed a GMM estimation procedure. Mullahy[42] studied the GMM estimation procedure for a class of Poisson regression models with nonlinear instrumental variable strategy. However, the variable selection for such Poisson regression model with endogenous covariates seems to be omitted. Taking this issue into account, we consider the variable selection for the Poisson regression model with endogenous covariates, which has the following structure:

$$\begin{cases} Y_i = exp\left(X_i^T\beta\right) + \varepsilon_i \\ X_i = \varphi Z_i + e_i, i = 1, \ldots, n \end{cases} \quad (9)$$

where $\beta = (\beta_1, \ldots, \beta_p)^T$ is an unknown parameter vector, φ is a $p \times q$ matrix of unknown parameters, Y_i is the response, and ε_i and ei are zero mean model errors. Furthermore, ε_i and e_i are assumed to be

Fig. 2. Map of Tanzania. Source: NBS.[18]

independent of each other. In this model, X_i is a $p\times$ 1 vector of endogenous covariates, and Z_i is a $q \times 1$ vector of instrumental variables. Then, we have $E(\varepsilon_i|X_i) \neq 0$ and $E(\varepsilon_i|Z_i) = 0$. Because of the endogeneity of covariate, classical variable selection methods will give an endogeneity bias and cannot be consistent anymore. The use of instrumental variable adjustment based on smooth-threshold estimating equations (SEE) variable section method for model can provide a way to obtain consistent variable selection procedure.[43–45] The variable selection procedure used in this study has helped to eliminate the unimportant covariates by setting the corresponding coefficients as zeros and can simultaneously give consistent estimators for the non-zero regression coefficients in theory.

The rest of the article is organized as follows. Results section presents the result of the study, where a thorough discussion was made based on the other relevant empirical literature. Conclusion section presents conclusion of the study and explanation of some of the key findings relative to their practical and policy implications, whereas Limitation of the study section presents the limitation of the study, especially on the usage of the secondary data.

Results

The general characteristics of the sample from 9463 households are presented in Tables 1–3. These tables provide information on the household demographic and socio-economic composition for the period of 2020/21.

Findings in Table 1 show that 6675 households equivalent to 70.54% were residing in rural areas, whereas the remaining 2788 equivalent to 29.46% were residing in urban areas. Most of the heads of household were males (72.73%), whereas only 27.27% of households were headed by females. Most households (73.81%) in Tanzania do not have health insurance, whereas only 26.19% of households have healthcare insurance. Furthermore, the findings show that 53.13% of households use healthcare services through various health facilities in the country.

The findings in Table 1 also show that the majority (47.19%) of the heads of household do not have any formal education background; 32.10% have primary education, and 16.67% had completed their primary education. Other 0.35% had some secondary education, whereas 2.89% had completed a secondary education level. The household heads with postsecondary level of education form

Table 1
General characteristics of the sample.

Variable	Attribute	Frequency	Percentage
Residence	Rural	6675	70.54%
	Urban	2788	29.46%
	Total	**9463**	**100.00%**
Sex	Male	6882	72.73%
	Female	2581	27.27%
	Total	**9463**	**100.00%**
Insurance covers	Yes	2478	26.19%
	No	6985	73.81%
	Total	**9463**	**100.00%**
Healthcare utilization	Yes	5028	53.13%
	No	4435	46.87%
	Total	**9463**	**100.00%**
Education level	No schooling	4408	47.19%
	Some primary	2998	32.10%
	Completed primary	1557	16.67%
	Some secondary	33	0.35%
	Completed secondary	270	2.89%
	More than secondary	75	0.80%
	Total	**9463**	**100.00%**
Marital status	Monogamous married	5352	56.60%
	Polygamous married	1059	11.20%
	Living together	410	4.34%
	Separated	478	5.05%
	Divorced	422	4.46%
	Never married	507	5.36%
	Widowed	1228	12.99%
	Total	**9463**	**100.00%**

0.80% of the entire sample. With regard to household marital status dispersion across the sample, 56.60% of heads of household are monogamous and 11.20% are polygamous. Other 4.34% of the sample were found to live together but had not married. Moreover, 5.05% were separated, 4.46% were divorced, and those who never married and widowed form 5.36% and 12.99%, respectively.

The findings in Fig. 3 show that 75.91% of those who are not using healthcare services are males, whereas only 24.095% are females. Moreover, 69.91% of those who use healthcare services are also males, whereas female constitutes 30.09%. The higher proportion of males reflects the fact that most households are led by males in Tanzania.

The findings in Fig. 4 show, on the one hand, that 89.31% of households who do not use healthcare services are not covered by health insurance, whereas 10.69% are covered. On the other hand, most of the households who used the health services (5028 households) across the country (60.15%) have no healthcare insurance, whereas 39.85% have healthcare insurance.

The findings of this study have shown that most households in Tanzania tend to consult medical services when they are ill. However, there are greater variations in healthcare utilization or medical consultation among households with different levels of education. As shown in Table 2, 43.22% of 4435 households that use healthcare services do not have formal education background.

A comparative impression of the findings in Fig. 5 shows that household heads who have completed secondary education and those with postsecondary education have a higher tendency of medical or healthcare utilization compared with their counterparts without formal education.

As presented in Table 3, the average age of head of households under the study was 47.06 years, whereas the head of household with the least age had 13 years and the oldest had 112 years. Furthermore, the average household size across all households was 4.8 members. The household that had few members had only one member, and those with the largest number had 38 members. Moreover, the average household healthcare expenditure was Tshs 423,692, whereas that of out-of-pocket expenditure was Tshs 7970.33. As the average number of healthcare visits per household per month was 10.393, the average healthcare expenditure per visit was Tshs 40,764.593, which is approximately 6.92%[a] of the entire household's average income. This implies that healthcare costs deplete nearly 7% of the household income.

The findings in Fig. 6 show that the majority of heads of household (36.10%) are self-employed in various economic activities. Moreover, 18.54% are unemployed, 18.88% are employed in various private and public organizations, and the retired servants form 7.07%. Those who have never worked anywhere and the unpaid household worker constitute 15.82% and 3.59%, respectively.

Moreover, the findings in Fig. 7 show that Dar es Salaam region *(green-shaded)* is the leading region with a large number of health-insured households (8.86%), followed by the Kilimanjaro region *(yellow-shaded)* with 5.09% of insured households. The least health-insured region was Katavi, with 2.30% of households with healthcare insurance.

Determinants of health insurance among households in Tanzania

Under this section, the probit model was used to capture factors affecting household subscriptions to health insurance. Moreover, various demographic and socio-economic household characteristics were examined to establish whether these characteristics have any effects on the household decision to subscribe to health insurance as presented in Table 4.

The findings in Table 4 have shown that the likelihood of households subscribing to health insurance is lowered significantly by 3.4%, given that such household is in rural areas. Studies (Kitole et al.,[12] Liu and Zhao,[15] Kitole et al.[28] Chen et al.[7]) suggest that such trend is attributed by lower income and low education levels of most rural dwellers.

On the other hand, this study has shown that the more households use health care, the more they are likely to subscribe to health insurances by 33.9% significantly. Such observation implies that people subscribe to health insurance as a means to avoid future uncertainties related to their health statuses and healthcare costs. However, some studies have also argued that health insurance subscription has been related to the increase of moral hazard challenges,[2,7,11,14,17,24] as most of the insured persons increase their attitude toward health risk lifestyle compared with non-insured ones.

Moreover, the findings in Table 4 reveal that having more years of schooling is an added advantage toward the increase of household decision to subscribe to health insurance significantly by 10.9%. This implies that those with higher education are more likely to have health insurance than those with low or no formal education. These findings are similar to studies of Kitole et al.[28] and Tungu et al.[24] but different from that of Andrew[29] who argued that formal education is not only a necessary reason for health insurance subscription but rather the use of awareness rising campaigns and information spread on the importance of insurance across societies.

In addition, an increase in the healthcare costs (health expenditures) and diseases prevalence (sickness) among households increases the likelihood of households to subscribe to health insurance by 16.8% and 41%, respectively. This implies that for households to overcome regular payment for health care and thus minimize healthcare costs due to sickness uncertainties, they are easily opting for health insurance subscriptions. These results are similar to studies of Li et al.[14] and Andrew[29] who argued that since the demand for is derived demand even the cost of health care are subjected to raise because of the necessity of the service in saving

[a] $\frac{\text{Average health care expenditure per visits } (Hv)}{\text{Average household income } (m)} = \frac{40.764.593}{589.335.4} \times 100\% \approx 6.92\%$.

Table 2
Healthcare utilization, level of education.

Health utilization	Level of education						Total
	No schooling	Some primary	Completed primary	Some secondary	Completed secondary	More than secondary	
No	1917 (43.22%)	1492 (33.64%)	690 (15.56%)	70 (1.58%)	206 (4.64%)	60 (1.36%)	4435
Yes	2088 (41.52%)	1532 (30.47%)	913 (18.15%)	135 (2.68%)	269 (5.35%)	91 (1.83%)	5028
Total	**4005**	**3024**	**1603**	**205**	**475**	**151**	**9463**

Table 3
Summary statistics of the household socio-economic characteristics.

Variable	Measurements	Mean	St. deviation	Minimum	Maximum
Age	Age of the head of household in years	47.06584	15.74102	13	112
Household size	Number of people in a household	4.853535	2.910977	1	38
Children under 5 years	Number of children <5 years	0.9406108	1.138971	0	14
Children under 14	Number of children <14 years	2.154391	1.98279	0	23
Adults	Number of adults (18–63 years)	2.699144	1.511055	0	19
Elderly	Number of elderly people (>64 years)	0.2292085	0.5137968	0	5
Food expenditure	Amount of money spent on food	139,102.5	123,241	2300	3,727,345
Total household consumption	Total amount of money spent by household in food and non-food consumption	356,056.3	573,125.1	25,370.42	43,700,000
Out-of-pocket	Amount of money spent out-of-pocket for healthcare services	7970.33	46,666.16	3900	3,440,000
Total health expenditure	Total amount of money spent on healthcare services	423,692.1	1,693,704	5434.524	15,000,000
Distance from homestead to health facility	Distance (in kilometers) from the household to the nearest health facility	5.944309	2.845631	1	38
Income	Monthly income of the household	589,335.4	705,236	38,372.88	12,900,000
Health utilization (number of visits)	Number of times household members visited health facilities in the last year	10.39363	3.568184	0	17

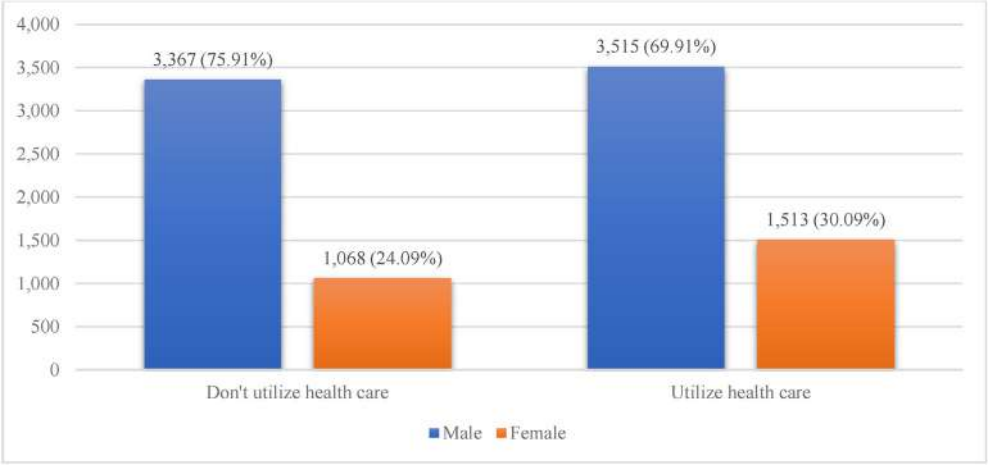

Fig. 3. Healthcare utilization across sex among households in Tanzania.

life, thus in avoiding these costs, which hurt households incomes severely through catastrophic expenditure, then households are forced to subscribe to health insurances. However, studies suggested most households have been easily subscribing to cheap health insurance, whereas only few households manage to buy expensive health insurance.[7,16]

Effects of health insurance on healthcare utilization in Tanzania

The study used both NBR and the IV Poisson via the GMM in examining the effects of health insurance (variable of interest) on healthcare utilization. This is measured by the use of the number of visits that a household went for medical services.

The findings of this study (see Table 5) are in line with Andersen Healthcare Utilization Model,[5] showing that predisposing factors and enabling factors have significant contributions in the change of households' healthcare utilization status.[1,20–24] This study has shown that variables such as education, income, age, residence (location), household size, health insurance, distance from homestead to health facility, and membership to social groups have significant effects on household health care utilization statuses.

Specifically, the study has proven that an increase in the level of education increases healthcare utilization significantly by 9.45% and 13.028% in NBR and IV Poisson GMM, respectively. This justifies that those with higher education have more knowledge of the importance of attending medical care or using healthcare services than those with lower education levels. These results are similar to the study by Caitlin et al.[5] and Erlangga et al.[9] that the more people are educated, the more they are willing to subscribe to health insurance and use healthcare services. This implies that educated

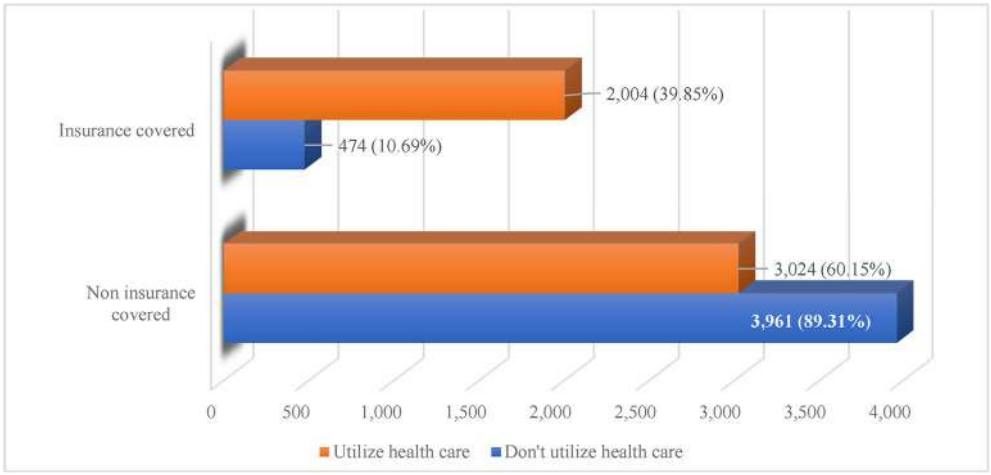

Fig. 4. Distribution of healthcare utilization across health-insured households.

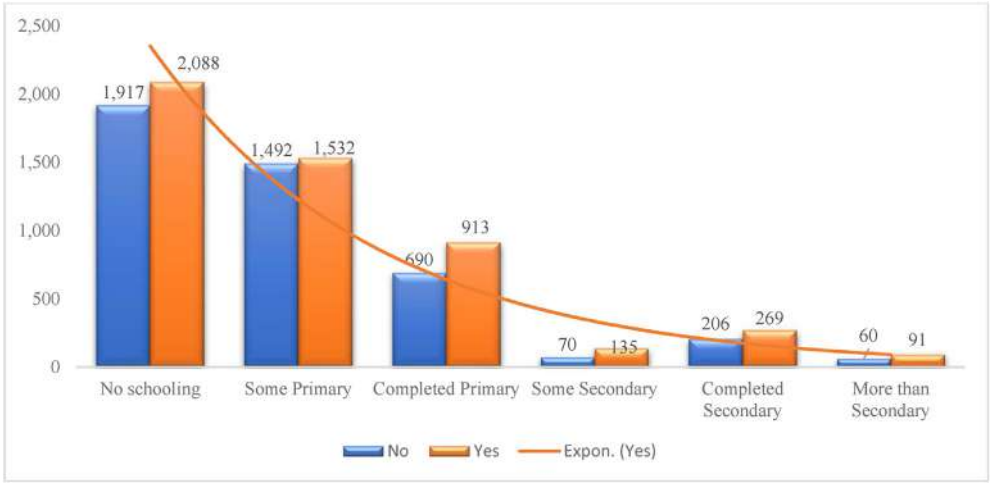

Fig. 5. Health utilization variations among households with different levels of education.

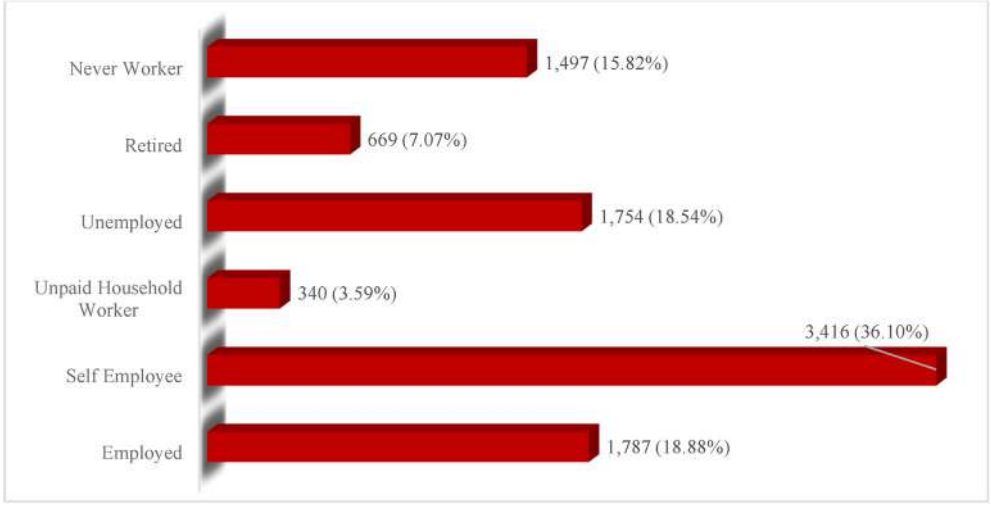

Fig. 6. Distribution of household employment status.

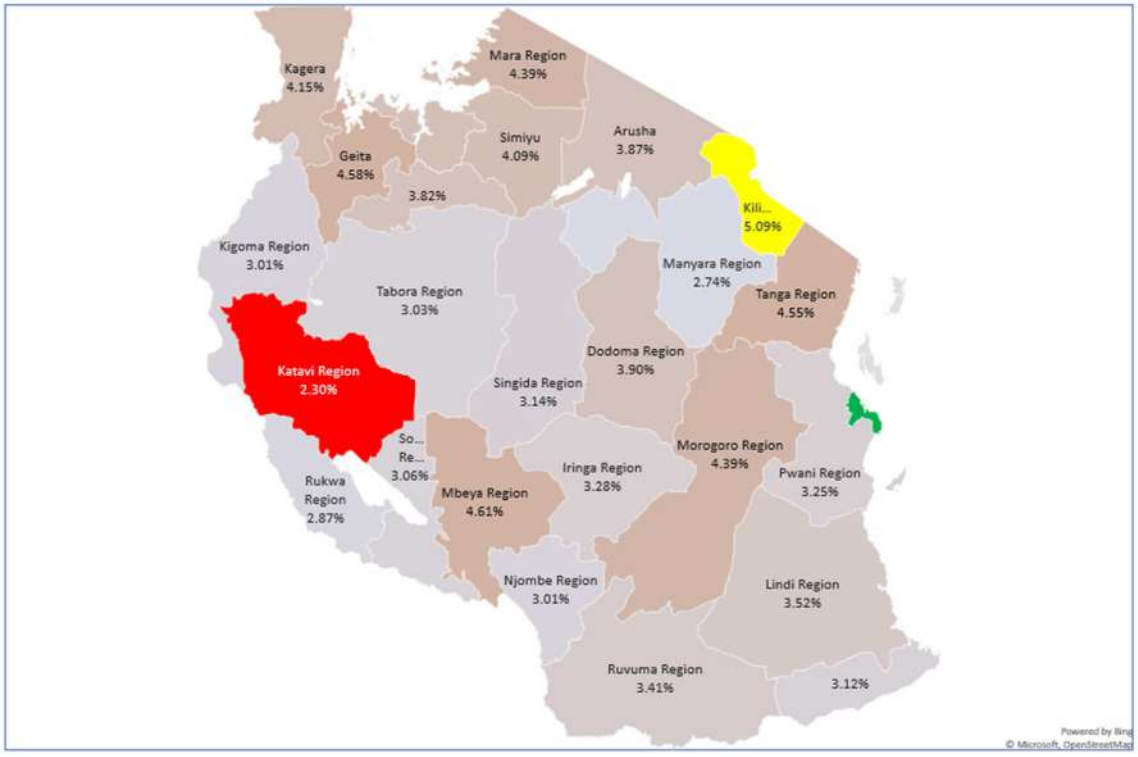

Fig. 7. Distribution of health insurance across households in Tanzania.

persons are keen on taking care of their health compared with uneducated ones. Moreover, John[30] had different findings to the present study and argued that people with a lower level of education suffer from poorer health than the highly educated; hence, their demand for health is higher than those with higher education.

On the other hand, the results have shown that an increase in income increases the household's healthcare utilization significantly by 22.84% and 32.822% under NBR and IV Poisson GMM, respectively. The positive and significant relationship between income and healthcare utilization implies that the more people become well off, the more they are able to use health care even at the highest price. Unlike John,[30] this study argues that the demand for health is higher among higher income groups compared with the lower income groups. These findings are similar to several studies in developing countries, which suggest that the more households' income increases, the more these households are likely to subscribe to health insurance. This further implies that such households are likely to attend healthcare services more frequently than households with lower incomes.[12,21,22,26]

Table 4
Determinants of households' health insurance covers.

Insurance	Probit coefficient	Marginal effects
Residence (rural)	−0.155** (0.042)	−0.034*** (0.009)
Female	0.103* (0.05)	0.024** (0.001)
Age	0.009* (0.001)	0.012** (0.000)
Marital status (married)	0.101 (0.155)	0.023 (0.192)
Education (years of schooling)	0.082* (0.038)	0.109** (0.019)
Health utilization	0.273** (0.033)	0.339*** (0.007)
Sanitation status (good sanitation)	0.239*** (0.042)	0.261*** (0.012)
Household size	0.079** (0.006)	0.086** (0.001)
Health expenditure	0.114** (0.000)	0.168*** (0.000)
Income	0.125*** (0.007)	0.247*** (0.097)
Agricultural participation	0.033 (0.036)	0.007 (0.068)
Sickness	0.378*** (0.096)	0.410*** (0.003)
Out-of-pocket expenditure	−0.096*** (0.001)	−0.105*** (0.000)
Employment status (employed)	0.199** (0.023)	0.223** (0.012)
Mean dependent variable		0.162
Pseudo r-squared		0.081
Chi-square		680.742
Akaike information criterion		7760.788

***$P < 0.01$, **$P < 0.05$, *$P < 0.1$.
Standard errors in parenthesis.

In addition, the study has found that a year increase in age increases healthcare utilization among households significantly by 12.193% and 23.589% under NBR and IV Poisson GMM, respectively. This implies that the demand for health care increases as one gets older as the result of the depreciation of human health[29] due to diseases. Moreover, the likelihood of healthcare utilization among rural (remote) areas residents was found to be lower compared with the urban counterparts by 4.384 % in the NBR model and 6.583% in IV Poisson GMM. There is significant evidence that healthcare utilization is lower in most of the rural areas in developing countries compared with urban areas[29–31] because of the inequality in the distribution of healthcare facilities, education, and other important supporting infrastructure, such as roads, which are highly impassable during rainy seasons. These results are similar to those of Okoroh et al.[19] and Bintabara et al.[4] that households that are close to healthcare facilities exhibit frequent visits to these health care compared with the distant ones.

Other variables that had a significant and positive relationship with the healthcare utilizations were household size (12.96% in NBR and 19.805% in IV Poisson GMM) and social group membership (9.567% under NBR). The findings similar to Osei and Agyemang[20] showed that having a large household size increases the likelihood of healthcare utilization significantly. In the same view, Osei and Agyemang[20] households argued that most people's decisions and life is influenced by the acts of other through social gatherings; therefore, the more household members attend social or

Table 5
Effects of health insurance on healthcare utilization.

Number of healthcare visits	Negative binomial regression	IV Poisson GMM
Marital status (married)	0.04179453 (0.0127918)	0.05135635 (0.0036076)
Education (years of schooling)	0.0945071** (0.0008929)	0.1302892*** (0.0120285)
Income	0.22840543** (0.0205215)	0.3282278*** (0.0032481)
Age	0.12193610*** (0.0002807)	0.23589203*** (0.0003763)
Residence (rural)	−0.0438495* (0.0105742)	−0.0658375** (0.0115247)
Household size	0.12960223** (0.0023293)	0.1980596** (0.0038387)
Insurance	0.28590031*** (0.0082950)	0.347053441*** (0.0934620)
Distance from homestead to health facility	−0.18921036** (0.0045321)	
Social group	0.09567241** (0.0001601)	
Instrumented		Insurance
Instrument		Distance from homestead to Health Facility
Observation	7683	7683

***$P < 0.01$, **$P < 0.05$, *$P < 0.1$.
Standard errors in parenthesis.

community gatherings and groups, the more their behaviors and lifestyle change. Andrew[29] added that the healthy life of most people is through imitations of "monkey see, monkey does" engaged and various social groups also had a positively significant relationship with the healthcare utilization. Studies with similar results include those of Matsushima et al.[16] and Erlangga.[10]

Furthermore, this article found that having health insurance increases household healthcare utilization significantly by 28.59% under NBR and 34.705% in IV Poisson GMM, respectively. This implies that having health insurance increases household healthcare utilization. This is attributed by factors such that people with health insurance are normally more flexible to check their health status frequently than those who do not have healthcare insurance and they are more likely to risk compared with those with no health insurance. Andrew[29] and Kitole et al.[28] argued that health insurance has positive effects on healthcare utilization through reduced out-of-pocket payments.

Conclusion

Healthcare utilization is an important aspect of public health improvement and productivity from the household to the national level. Healthcare utilization symbolizes the health system and its ability in delivering health services to the public. This article has found that only 26.19% of 9463 households in Tanzania have healthcare insurance; this leaves the majority (73.81%) without any health insurance coverage. This explains the extent to which households in Tanzania spend a huge amount of money on user fees and other forms of healthcare payments that accelerate healthcare catastrophic spending, which has inverse effects on healthcare utilization.

Moreover, factors such as living in rural areas and distance from homestead to healthcare facility were found to have negative effects on household healthcare utilization. Such findings provide light on the existing policy and intersectoral gaps in most of the developing countries that have similar characteristics in the fragility of healthcare services. Therefore, the government should increase investment in healthcare infrastructure. This may involve the construction of healthcare facilities close to people's residents, especially in rural areas. Such initiatives will not only increase healthcare utilization but also reduce the number of deaths, especially among women who chose to give birth at home or opted for local healers because of the remoteness of health facilities.

In addition, the government should conduct regular health campaigns to advocate for the necessity of making regular healthcare visits, especially among households in rural and urban areas. This should go hand in hand with promoting the use of cheap community health insurance. The article highlights the need for governments to increase investment in health financing by subsidizing important healthcare services and making them accessible through cheap or affordable public health insurance. Subsidization of such important services in public healthcare facilities will promote a household visit to healthcare facilities even if such facilities are located far from their residents.

Furthermore, this study is useful to the entire developing world as it helps policymakers, practitioners, researchers, and international organizations that operate in these developing countries, especially in the health sector to mobilize resources that will facilitate an increase in the healthcare utilization and enhance the realization of the sustainable development goals toward universal health coverage. Thus, based on the findings of this study, areas of intervention toward improving and increasing households' subscription to health insurance are education, lessening the economic burden of out-of-pocket expenditure, and increasing investments in household income-generating activities.

On the other hand, developing countries should lower costs for health insurance premiums that cover broader medical services. Thus, by lowering these premiums, most households in rural and urban areas will be motivated to subscribe to health insurance schemes and hence increases the rate of healthcare utilization. The decision to lower the costs of health insurance premiums and improve healthcare-related infrastructures reflect developing countries' government initiatives to increase healthcare expenditure and abide with both global and regional conventions on the thresholds of gross domestic product (GDP) share on health expenditure.

Limitation of the study

Despite the usefulness of the study in bringing into light major issues concerning the effects of health insurance toward healthcare utilization in Tanzania, the use of secondary data in this study has several limitations, which have to be taken into consideration as a caution. Few to mention, lack of control over data collection as secondary data are collected by someone else or other authorities; thus, researchers had no control over how the data were collected or how variables were measured.[53] Therefore, this scenario can implicate quality as well as accuracy of the data. On the other hand, the problem of the limited scope was experienced, as the secondary data used in this study have failed to address specific research question as most variable that was highly needed to increase insight were not found; hence, the study's results are limited.[51]

In addition, secondary data are always subjected to biasedness, which can be made intentionally or unintentionally during data

collection or management processes. Despite the mitigation measures taken in this study, it is important to note that it is always possible to provide incorrect estimates and information, as data are not reliable because of omission or errors in the original data collection processes or during data processing and analysis.

Other specific limitations based on the result of using panel data in this study include the problems of time-invariant variables, generalizability, and the attrition bias. On the time-invariant variables, panel data are normally limited in its ability to examine effects variables that do not change with time while they have major effects on the outcome variables, example of such variable used in this study is sex of the head of households.[52] On the other hand, as panel data used in this study have been collected from Tanzania's household (specific population) for the period of 2020/21, this limits the generalizability of the findings to other population or context.

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None declared.

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Original Research

Electronic device or regulated tobacco product? Learning from the diffusion of heated tobacco products in Spain

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ABSTRACT

Objectives: Tobacco companies have introduced heated tobacco product (HTP) in many countries and marketed it on the grounds that it is a less harmful alternative to health. However, tobacco companies have been widely criticized for taking advantage of a loophole that allows electronic devices to circumvent regulations limiting tobacco advertising. This work aims to determine whether HTPs respected the rules that regulate tobacco advertising when it was introduced in Spain.
Study design: This is an observational epidemiological study.
Methods: Using monthly time series data from September 2016 to June 2020, we analyzed whether the adoption of HTPs has followed the same behavior patterns as other brands that were introduced under the same conditions of use. The Bass model is used to analyze the diffusion of HTPs, and 30 other traditional cigarette brands introduced under the same conditions as this HTPs.
Results: The adoption of HTPs in Spain has been like that of brands of slim cigarettes that are mistakenly considered to be healthier than traditional cigarettes. The results indicate that the use of HTPs has spread in the same way as additive-free and ultra-slim cigarette brands.
Conclusions: Policymakers should keep in mind that laws should restrict any marketing of tobacco products that promotes positive connotations between tobacco use and being healthy. If manufacturers are allowed to classify a category and/or brand of tobacco products as less harmful to health, the imitation effect is very high, leading to the proliferation of smoking.

Introduction

Tobacco companies have been aggressively promoting heated tobacco product (HTP) cigarettes in Spain since its launch in September 2016. The fundamental motivation for this strong promotion is tobacco companies' stated intention to move toward a world free of smoke and offering 'less harmful alternatives to tobacco."[1,2] Previous literature suggests that tobacco companies have promoted HTPs strongly in jurisdictions where the promotion of the electronic device is regulated differently from heated tobacco.[3] In Spain, tobacco companies have marketed HTPs under different brands. In this context, in Spain, there is a divisive debate on this issue, given that there are strict prohibitions on the marketing of tobacco products (including HTPs), but not on e-cigarettes, vaping products or tobacco heating devices.

Although there is heterogeneity in the marketing restrictions of HTPs, there is a global debate about whether these products reduce the risk that tobacco use causes to health. Some studies suggest that HTPs do not meet sufficient standards to be considered a reduced-risk product.[4] Furthermore, these studies argue that allowing tobacco companies to promote HTPs as a reduced exposure product would amount to a legally sanctioned repeat of the "light and mild" fraud that, for conventional cigarettes, is prohibited by law in some countries.[4] Some works on this topic claim that independent human-based studies indicate that there is a potentially harmful impact on human health of both active and passive smoking with HPT. Notwithstanding, based on the available evidence, HTPs produce lower levels of toxic chemicals by comparison to conventional cigarettes, but they are not without risk.[5–7]

Evidence indicating that exposure to HTP marketing results in increased use of these harmful products has led to concern about marketing restrictions on these products. Along these lines, some

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studies indicate that awareness and the use of HTPs are related to greater dependence on cigarette consumption.[8–11] In addition, evidence indicates that those consumers who use electronic cigarettes are susceptible to consuming HTPs.[12,13] Regarding the age appeal of tobacco companies' HTPs, the literature indicates that the most likely age bracket to share the perception of these products as a healthy alternative to tobacco use is that of young people.[14,15]

In this context of concern about the perception of HTPs by the population, especially young people, there are many articles that suggest that governments should ensure that HTPs are regulated just as tobacco products or addictive substances are and reject tobacco companies' assertions of "harm reduction."[16] Tobacco companies continually develop new product concepts, such as HTPs.[17] This situation is new for governments; HTPs are fundamentally new products because it is the first time that tobacco products have comprised heatable tobacco sticks and a separate electronic device that is marketed independently.[18] Regarding the marketing of heated tobacco sticks, some studies indicate that the prohibition of their promotion on television, on radio or in the press generates adequate results.[19] Although this regulation may seem simple, there is an overlap between heated tobacco sticks and the electronic device itself, which can sometimes weaken smoking control legislation.[20] Thus, some studies indicate that in the countries in which HTPs are marketed, both the electronic device and the heatable tobacco sticks must be regulated to avoid exposing the population to the marketing of these products.[21–23]

Tobacco companies have stated that HTPs are the only alternative on offer to adult smokers wishing to abandon traditional cigarettes.[24] This statement, despite evidence from Japan that it may have some truth,[25] is debatable, given that the market share of HTPs is still exceedingly small in many countries.[26,27] This is also the case in Spain, a country in which, since its introduction in September 2016, HTPs have only managed to reach a market share of 1%. However, a recent article shows how tobacco companies are using the same tactics to promote heated tobacco that it used historically with traditional cigarettes.[28] These actions are based on promotions including financial incentives based on HTPs sales for retailers and industry provision of display cases, among others. In addition, another recent article focused on the analysis of the effect of HTPs' introduction on tobacco companies' cigarette sales in Spain shows that tobacco companies are using HTPs to replace the traditional cigarette, which is generating tax benefits.[29] This could generate a significant increase in the sales of HTPs in Spain. For this reason, continuous surveillance of HTPs through online marketing and points of sale is needed.[30]

Since 2016, tobacco companies have been promoting HTPs in Spain. As Fig. 1 shows, HTPs have not managed to change the structure of the Spanish tobacco market (it barely reaches 1% market share of the total products sold). However, the promotion of HTPs in Spain has generated a lot of controversies. In 2018, a tobacco company sued another for promoting a press advertising campaign of HTPs as an electronic device. The complainant tobacco company considered it proven that the purpose of the campaign was to promote a tobacco product because electronic device can only be used with HTP sticks. The ruling was favorable to complainant tobacco company, mainly arguing that there are few advertisements in which a photograph or any other image of the electronic device does not appear without the HTP sticks incorporated. This study analyzes whether the diffusion of HTPs in Spain has followed the dynamics of other brands of cigarettes introduced or, on the contrary, tobacco companies have managed to spread HTPs more quickly in violation of the regulations that have prohibited tobacco advertising in Spain since 2005. Therefore, to analyze the diffusion of HTPs since its introduction in Spain (September 2016), we use the popular Bass Diffusion Model introduced by Bass (1969). Although the model was proposed many years ago, it continues to be used in analyses that meet some conditions. The model has been improved and modified and is still very useful and applicable to different study areas.[31–33] In our case study, we use non-linear methods, as proposed by Srinivasan and Mason[34] and which have been further developed in the literature. Mahajan et al.[35] indicate three conditions that the analyzed products must meet to be able to analyze their diffusion with the Bass model. These conditions are, first, that the model is designed for product adoption (initial purchases of a new product). Second, the model can be applied to niches within a product category. Third, the products cannot have supply restrictions, that is, difficulties in the distribution systems. We believe the case study about the diffusion of HTPs meets these conditions by the selected and compared products.

To the best of our knowledge, although the Bass model has already been used to explain the spread of cigarettes in Spain,[36] it is the first time that the diffusion of HTPs has been studied. A recent article indicates that the regulation of HTPs in Spain is improvable in several respects, among which are the limitation of advertising and consumption of these products.[37] For this reason, we consider this study relevant to understanding how HTPs proliferate and, thus, to know what aspects and to what extent they should be regulated.

Methodology and data

To compare whether the introduction to the market of HTPs has been different from that of other products, we need a methodology that allows us to understand the differences in the diffusion of the products. In addition, we need to obtain sales data from HTPs as well as from other brands that have entered the market in a similar period.

Therefore, we use one of the most influential models in the history of management science, the Bass model, and data from 31 brands including HTPs that have been introduced in the Spanish market in recent years.

Method

To measure the spread of a product in the market, many methodologies and models have been proposed in the literature. Among the most popular is the Bass Diffusion Model, introduced by Bass.[38] This model is frequently applied to model and predict the

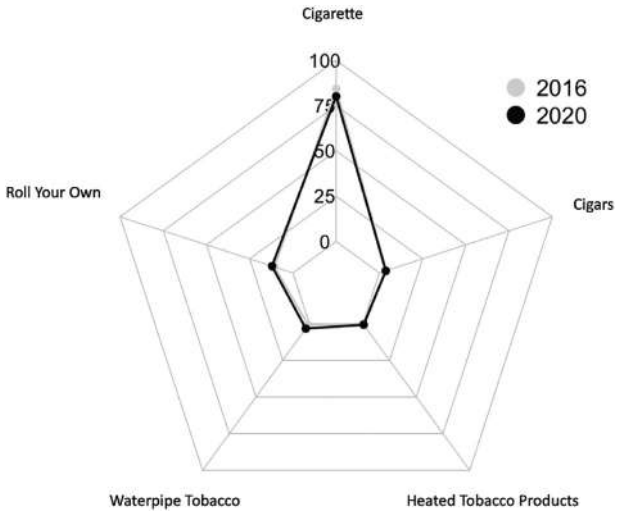

Fig. 1. Composition of the Spanish tobacco market.

diffusion of a product. The basic assumption of the model is that the initial consumer purchase is related to the number of previous buyers. A behavioral rationale for the model is based in terms of innovative and imitative behaviors. Its popularity is probably because it can capture a great variety of diffusion patterns and the interpretation of the parameters of the model is very useful for understanding the diffusion process.[39]

Regarding the many existing alternatives in the literature (see a study by Guidolin and Manfredi[31] for a recent review), we use the non-linear model initially proposed by Srinivasan and Mason,[34] as it is one of the most solid, contrasted, and widely used models in the literature. Future works can extend this model with the inclusion, for example, of explanatory variables.

In line with our abovementioned objective, our empirical application using Bass's diffusion model aims to estimate the following parameters, which, in turn, determine the diffusion of a product.[39,40]

- *P*: interpreted as the innovation parameter or the coefficient of external (mass media) influence. A higher value of this parameter suggests that the product is being adopted by innovation, that is, by independent initiatives of innovative people.
- *q*: the imitation parameter or the coefficient of internal (interpersonal) influence. A higher value of this parameter would imply that the product is being adopted by "word of mouth" or "social contagion."

The parameter m of saturation level (maturity) can also be calculated although its usefulness as a predictive tool allowing us to know the level of sales saturation, a quality that is not useful in our case study because of its limited explanatory value.

Kijek, A. and Kijek, T[41] put forward four proposals to estimate the Bass model. In this work, we follow non-linear methods as first proposed by Srinivasan and Mason,[34] solving the inconsistent estimation that might be achieved by the Ordinary Least Squares (OLS) estimation method.

The basic assumptions of the Bass model start from the distribution function $F(t)$ that represents the adoption in period t and its associated density function $f(t)$. The probability of an individual to adopt for the first time at t, among those who have not yet adopted in the same time, $\frac{f(t)}{1-F(t)}$, is defined as (1):

$$\frac{f(t)}{1-F(t)} = p + q \cdot F(t) \tag{1}$$

where p is the innovation coefficient and q is the imitation coefficient. The coefficients P and q are in the interval (0,1), which imply that $p < q$ and $(p+q) < 1$.

The estimation from the initial equation is made by using the estimation of its solution expressed as an equation in differences of the total sales at time t, $S(t)$, so that $S(t) = m \cdot \frac{dF(t)}{dt}$, being m the maximum number of people who can potentially adopt:

$$\frac{dF(t)}{dt} = p \cdot m + (q-p) \cdot F(t-1) - \frac{q}{m} \cdot F(t-1)^2 \tag{2}$$

The solution for $f(t)$ (3) is reached by solving the equation in differences (2):

$$f(t) = \frac{\left(\frac{p+q}{p}\right)^2 \cdot e^{-(p+q)t}}{\left[1 + \frac{q}{p} \cdot e^{-(p+q)t}\right]^2} \tag{3}$$

The estimation of this solution (3) allows us to directly obtain the parameters p, q, and m, where p, and q determine the density function of the diffusion process of each product.

Data

For this work, we obtain monthly sales data of tobacco products in Spain published by the Trade of Tobacco Commission of Spain (Commissioner for the Tobacco Market) from January 2005 to the present. To protect the privacy of the companies involved, all names of the organizations and brands referenced in this article have been anonymized. The monthly data of HTPs sales are available from its launch on the market in September 2016 until the last period consulted (December 2020), which adds up to a total of 48 months of diffusion of the product.

From the total of available brands that register sales, we select those that satisfy the necessary conditions to apply the Bass model as indicated in a study by Mahajan et al.[35] First, the model is designed for initial purchases (periods of product adoption and not replacement demand). Each of the selected brands has been introduced to the market throughout the period analyzed. Second, the Bass model was developed to analyze the generic demand for a product category, although, in some cases, it may apply to the demand for individual brands or niches within a category. And third, supply restrictions can limit the model, something that does not apply in our case study. In addition to these initial conditions of the model, we must bear in mind that the data collected shows erroneous or null values for those brands which were subject to exceptional situations such as stockouts, miscommunication of sales, or lower sales compared with other brands.

Therefore, we have selected the first 48 months of diffusion of all those brands for which we have data that started their sales within the period of analysis (2005–2020), in total 31 brands, among them HTPs. The brands analyzed include both blonde, black, slim, ultra-slim and additive-free cigarette brands.

Fig. 2 shows the temporal evolution over the first 48 months of sales diffusion of these 31 brands. It can be seen how each brand behaved differently during the market introduction period.

Almost all brands increased their sales in the period analyzed, something logical, as it was an introduction period. However, not all have the same behavior. We found the growth pattern among the 48 brands studied as the main difference. Some brands show linear and constant growth, with HTPs showing the most striking evolution. Other brands suffer from seasonality, such as Brand23 or Brand3.

To observe the temporal dynamics of sales in the analyzed period, we disaggregate the time series of each market by observing its trend (Fig. 1 in supplementary material), its seasonality, and its random movement (Figs. 2 and 3 in supplementary material).

Focusing on Fig. 1 in supplementary material, which analyzes the trend of the sales series for the first 48 months, we can see that for most sales, the trend is growing, although there are brands where the trend has changed or has even remained constant during the period of the study.

Results

To analyze the diffusion of the 31 different brands and tobacco products, we applied the Bass model to each of the brands to obtain the parameter "p" of innovation or coefficient of external influence (mass media) and the parameter "q" of imitation or coefficient of internal (interpersonal) influence. Furthermore, the model allows us to obtain the parameter "m" of the saturation level, although for our case study, this parameter is not relevant because its usefulness is predictive and not explanatory. The results are shown in two

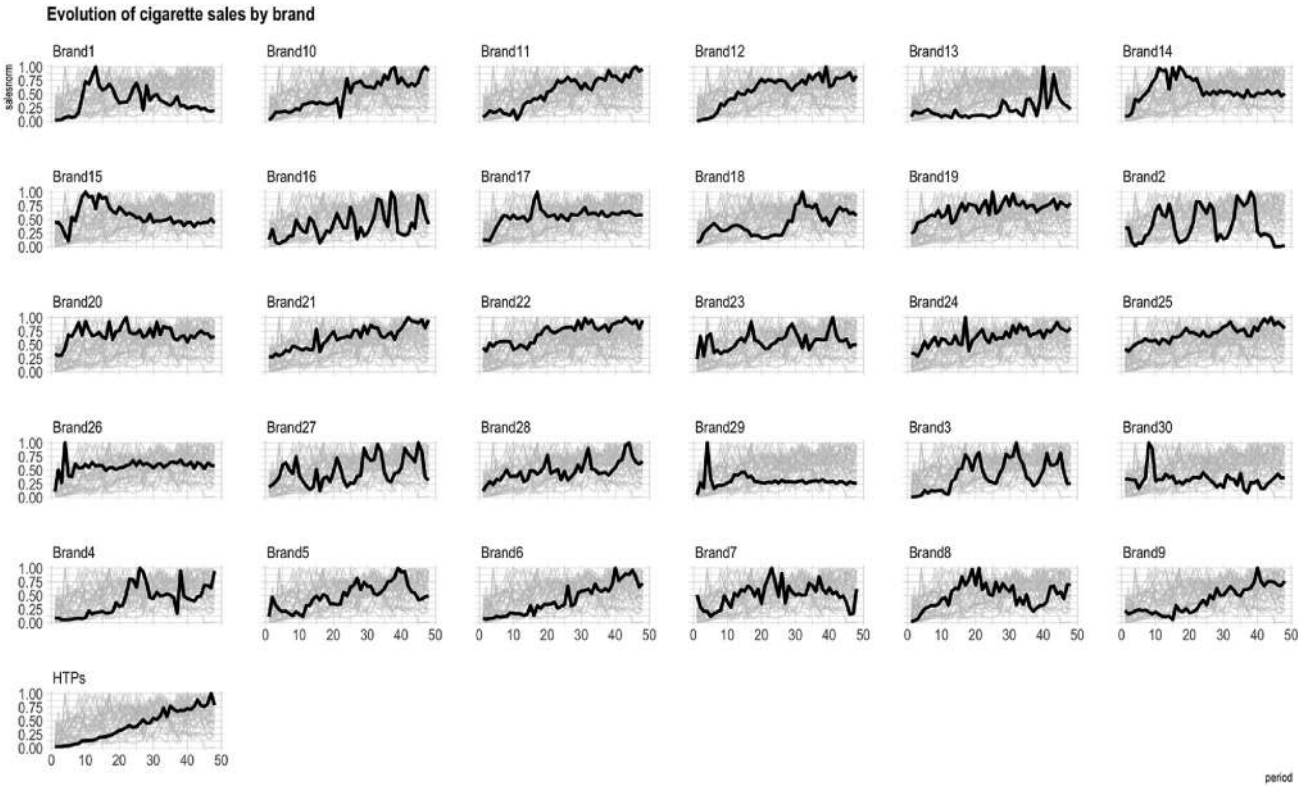

Fig. 2. Evolution of cigarette sales by brand.

ways: Table 1 presents the estimated parameters and Fig. 3 shows a scatterplot that allows us to analyze whether there are groups of brands that behave homogeneously.

Table 1 presents the result of the estimates of the parameters *P*, *q*, and m for the 31 brands. As can be seen, not all brands present significant values of *P*, *q*, and m, so the Bass model is not very useful in explaining the diffusion behavior of these brands. Fortunately, this only occurs in 5 of the 31 brands, so the estimates allow us to obtain useful results for the purposes of our case study.

As can be seen, we find a variety of different coefficients in the 31 brands, which show the first general result. The brands introduced in the market in the period under analysis promote their

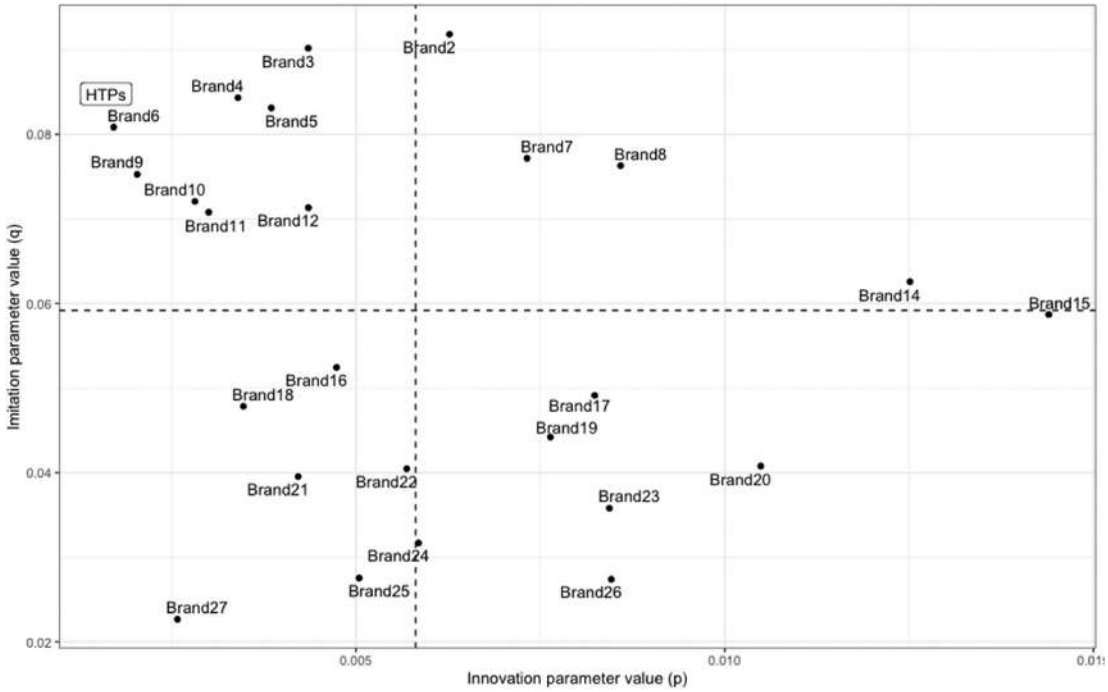

Fig. 3. Scatterplot of innovation and imitation parameters.

Table 1
Diffusion parameters of all brands analyzed.

Brand	*m*	*P*	*q*
Brand1	5761755.19	0.010	0.099
Brand2	5349536.68[a]	0.006[b]	0.092[a]
Brand3	29222665.06[a]	0.004[a]	0.090[a]
HTPs	23529350.78[a]	0.002[a]	0.085[a]
Brand4	7953255.28[a]	0.003[c]	0.084[a]
Brand5	1756757.17[a]	0.004[a]	0.083[a]
Brand6	12711783.82[a]	0.002[a]	0.081[a]
Brand7	1277883.74[a]	0.007[a]	0.077[a]
Brand8	32451449.36[a]	0.009[a]	0.076[a]
Brand9	3343500.34[a]	0.002[a]	0.075[a]
Brand10	12979216.65[a]	0.003[a]	0.072[a]
Brand11	5552708.72[a]	0.003[a]	0.071[a]
Brand12	93327222.03[a]	0.004[a]	0.071[a]
Brand13	1449778.97	0.002[b]	0.070[b]
Brand14	97687518.78[a]	0.013[a]	0.063[a]
Brand15	1282945.69[a]	0.014[a]	0.059[a]
Brand16	10869916.17[c]	0.005[a]	0.052[b]
Brand17	13367558.9[a]	0.008[a]	0.049[a]
Brand18	35896924.04[b]	0.003[c]	0.048[c]
Brand19	105831996.2[a]	0.008[a]	0.044[a]
Brand20	185510837.81[a]	0.010[a]	0.041[a]
Brand21	193569833.49[a]	0.004[a]	0.040[a]
Brand22	50089879.38[a]	0.006[a]	0.040[a]
Brand23	1079742.56[a]	0.008[a]	0.036[c]
Brand24	118733537.23[a]	0.006[a]	0.032[a]
Brand25	276019048.42[a]	0.005[a]	0.028[a]
Brand26	11828954.37[a]	0.008[a]	0.027[c]
Brand27	263562904.8[a]	0.003[a]	0.023[a]
Brand28	245619556.33	0.002	0.022
Brand29	11860491.58	0.012[b]	0.017
Brand30	708564.52	0.013[b]	0.015

[a] Significance at 1%.
[b] Significance at 10%.
[c] Significance at 5%.

products in different ways. As the objective is to compare the diffusion of HTPs with respect to the rest of the brands, Fig. 3 presents a scatterplot of *P* and *q* to compare the position of the diffusion parameter by innovation and by imitation with respect to the rest of the brands.

The different brands can be grouped into four quadrants based on whether the innovation and imitation parameters are above or below the average. Thus, it can be observed how HTPs are in the upper left vertex of the cloud of points of the scatterplot representing them. This means that HTPs are the brand that has been least influenced by innovation and the most influenced by imitation of all the brands analyzed. As you can see, HTPs are in a quadrant that also includes Brand10, Brand6, Brand9, Brand4, and Brand5. The first three brands are super-slim cigarettes, whereas the last two are additive-free cigarettes. Both ultra-slim cigarettes and additive-free cigarettes, such as HTPs, are marketed by manufacturers as a "healthier" way of smoking. This result is consistent with a recent study that analyzes the consumption of slim cigarettes.[42] All the brands, of the 31 analyzed, that are not super-slim or additive-free cigarettes are found outside of the upper left quadrant of the graph, which seems to indicate a clear pattern of the diffusion of brands that are marketed under the premise of “being healthier.” The results seem to indicate that HTPs have not spread differently from other cigarette brands, which were introduced to the market with the “healthier” label.

Conclusions

In recent years, the interest of academics, policymakers, and practitioners in understanding the behavior of the demand for new-generation tobacco products has grown. This interest arises from the need to have evidence of tobacco company compliance with standards in the marketing of these new products, which in some countries are not yet fully regulated. In Spain, as in the rest of the world, tobacco companies have marketed HTPs’ alternative since 2016. Although there is literature that aims to provide evidence on HTPs, very few works focus on tobacco companies’ compliance with regulatory standards in their marketing activity. Furthermore, none of these previous studies have compared the pattern of the demand for HTPs with the demand for traditional cigarettes that were introduced to the market under the same regulatory conditions. In this article, the diffusion of HTPs in the Spanish market has been studied from a novel perspective because of its application to the tobacco market.

In this article, using the Bass model, we reveal that HTPs have spread in a similar way to other cigarette brands that have been introduced in the Spanish market under the same restrictions. Regardless of that, the HTPs demonstrate a lower demand for innovators and a higher demand from those who consume due to the recommendation effect of all those studied. These results seem to suggest that the electronic device advertising campaigns in the press have not had an effect that indicates a breach of the regulations that prevent the promotion of tobacco products in Spain. However, although tobacco companies have not obtained advantages by marketing heated tobacco as an electronic device, it is observed that they have positioned themselves arguing that these products are a healthy alternative to smoking. The results indicate that HTPs have spread in the same way as additive-free and ultra-slim cigarette brands. This diffusion is mainly because of the imitation effect of consumers, who could be thinking that they are imitating a "healthy" way of smoking. Policymakers should keep in mind that laws should include limitations on the marketing of tobacco products under the "healthy" label. If manufacturers are allowed to classify a category and/or brand of tobacco products as less harmful to health, the imitation effect is very high, leading to the proliferation of smoking. Future works can expand our results by incorporating new variables, such as the regional sales distribution or the effect of other substitute products. Different models, such as the generalized Bass model, can be used.

Author statements

Ethical approval

No ethical approval required as the analysis used summary statistics from national agencies, with no individual patient-level data.

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Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.017.

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Original Research

Estimated number of symptomatic Lyme borreliosis cases in Germany in 2021 after adjusting for under-ascertainment

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ABSTRACT

Background: Although nine of 16 federal states in Germany conduct public health surveillance for Lyme borreliosis (LB), the extent of under-ascertainment is unknown.
Objective: As a model for European countries that conduct LB surveillance, we sought to estimate the population-based incidence of symptomatic LB after adjusting for under-ascertainment.
Methods: Estimating seroprevalence-derived under-ascertainment relies on data from seroprevalence studies, public health surveillance, and published literature. The number of symptomatic LB cases in states that conduct LB surveillance was estimated from studies reporting the seroprevalence of antibodies against *Borrelia burgdorferi* sensu lato, the proportion of LB cases that are asymptomatic, and the duration of antibody detection. The number of estimated incident symptomatic LB cases was compared with the number of surveillance-reported LB cases to derive under-ascertainment multipliers. The multipliers were applied to the number of 2021 surveillance-reported LB cases to estimate the population-based incidence of symptomatic LB in Germany.
Results: Adjusting for seroprevalence-based under-ascertainment multipliers, the estimated number of symptomatic LB cases in states that conducted surveillance was 129,870 (408 per 100,000 population) in 2021. As there were 11,051 surveillance-reported cases in 2021 in these states, these data indicate there were 12 symptomatic LB cases for every surveillance-reported LB case.
Conclusions: We demonstrate that symptomatic LB is underdetected in Germany and that this seroprevalence-based approach can be applied elsewhere in Europe where requisite data are available. Nationwide expansion of LB surveillance would further elucidate the true LB disease burden in Germany and could support targeted disease prevention efforts to address the high LB disease burden.

Introduction

Lyme borreliosis (LB), the most common tickborne disease in Europe, is caused by the spirochete *Borrelia burgdorferi* sensu lato (s.l.).[1] LB is endemic in many countries in Europe, including Germany.[2] Clinical manifestations of LB include erythema migrans (EM) and several forms of disseminated disease (e.g. Lyme neuroborreliosis [LNB], Lyme arthritis [LA]).[1] LB diagnosis is based on a complete diagnostic workup that includes medical history, clinical symptoms, objective signs, possible exposure to tick bites, and exclusions of other diseases.[3] Typical EM cases are usually diagnosed clinically and do not require serological testing.[3] The diagnosis of LNB and other manifestations, however, requires laboratory testing.[3] Germany and 27 other countries in Europe conduct public health surveillance for LB.[4] Although many European surveillance systems capture both clinician-reported and laboratory-confirmed LB cases, surveillance systems may fail to detect (i.e. under-ascertain) symptomatic LB cases for a variety of reasons (Figure S1).

Under-ascertainment of symptomatic cases occurs with all infectious diseases in public health surveillance systems. Studies conducted in other countries and for other diseases have used a variety of approaches to estimate the extent of underdetection of symptomatic cases (i.e. estimated the under-ascertainment

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"multipliers" for symptomatic cases) and then have applied the estimated multipliers to the surveillance-reported cases to estimate the population-based incidence of symptomatic cases after adjusting for under-ascertainment.[5,6]

In Germany, one approach for estimating under-ascertainment multipliers compared the number of medically attended LB cases in an outpatient medical insurance claims database, which covered 88% (73 M) of the German population, to the number of public health surveillance–reported LB cases. In this analysis, researchers concluded that for every surveillance-reported LB case, there were six medically attended LB cases.[7] The researchers also estimated that after adjusting for the underdetection, the incidence of medically attended LB cases in the German states that conduct LB surveillance ranges from 113 to 346 per 100,000 population per year. Using a similar approach, an earlier analysis of a smaller nationwide health insurance database (6 M members) estimated an incidence of 261 medically attended LB cases per 100,000 population per year.[8] A key limitation of these studies, however, is that they only include medically attended LB cases and not all symptomatic LB cases seek medical attention.

In contrast to the medical claims–based approach, a seroprevalence-based approach provides a more comprehensive estimate of underdetection of public health surveillance. Although a seroprevalence-based approach for estimating the under-ascertainment multipliers for symptomatic LB has been conducted in Finland,[9] such an approach has not been conducted in Germany. LB surveillance is conducted in nine of 16 federal states in Germany[10]; approximately 42% of the 83.2 M inhabitants in Germany reside in states that conduct LB surveillance. LB surveillance began in six states (Berlin, Brandenburg, Mecklenburg-Vorpommern, Saxony, Saxony-Anhalt, and Thuringia) before 2000, in two states (Rhineland-Palatinate and Saarland) in 2011, and in one state (Bavaria) in 2013. In these nine states, notification of an EM, LNB, or LA case is mandatory for both clinicians and laboratories. LB cases are reported to local public health offices, and data are transferred to state health offices and then to the Robert Koch Institute (RKI), the national public health institute responsible for aggregating and reporting public health surveillance data.

As a model for any country in Europe that conducts public health surveillance for LB, we sought to derive estimates of the seroprevalence-based under-ascertainment multipliers for symptomatic LB cases in the nine German states that conduct LB surveillance. We also sought to estimate the incidence of symptomatic LB in Germany after adjusting for under-ascertainment to more accurately describe the LB disease burden and better inform public health policies.

Methods

Seroprevalence literature search

A systematic literature review of PubMed, EMBASE, and CABI Direct (Global Health) from 2005 to 2020, described elsewhere,[11] was conducted to identify seroprevalence studies in Germany. Two nationally representative seroprevalence studies, both conducted by RKI, were identified. The first was a seroprevalence study[12] conducted during a national health survey of children, with blood samples collected from 12,614 children (age range: 1–17 years) from 2003 to 2006. Samples underwent two-tier testing with enzyme-linked immunosorbent assay (ELISA) (Enzygnost Lyme link VlsE/IgG; Siemens Healthcare Diagnostics GmbH, Eschborn, Germany) and confirmatory line blot. The seroprevalence of detectable immunoglobulin G (IgG) antibodies against *B. burgdorferi* s.l. was reported in two regional stratifications (East vs West and North vs Middle vs South)[12] (Fig. 1). The second seroprevalence study was conducted during a national health survey of adults,[13] with blood samples collected from 6,945 persons (age range: 18–79 years) from 2008 to 2011 and tested by the same two-tier protocol as the child seroprevalence study. Similar to the study in children, the adult study reported seroprevalence of detectable IgG antibodies against *B. burgdorferi* s.l. using the same regional stratifications.[13] For our analysis, we assumed study results represented the seroprevalence in the last full calendar year of sample collection: 2005 for children and 2011 for adults. Given that both studies do not provide state-specific seroprevalence results, we derived under-ascertainment multipliers using the regional stratifications.

Additional literature searches

Three additional literature searches were conducted to identify data inputs for the under-ascertainment multipliers. The first was a PubMed literature search from 1990 to 2021 to derive an estimate of the duration of antibody detection in persons infected with *B. burgdorferi* s.l. The second was a PubMed search conducted from 1997 to 2021 to identify the proportion of persons infected with *B. burgdorferi* s.l. who are asymptomatic. As neither of these two literature searches identified a sufficient number of studies conducted in Germany, the searches were expanded to studies elsewhere in Europe, and a third PubMed literature search was conducted from 1990 to 2021 to determine the *B. burgdorferi* genospecies distribution in Germany. Because the duration of antibody detection and the proportion of infections that are asymptomatic might vary by *B. burgdorferi* genospecies, and genospecies might vary between Germany and other European countries, the results of this last search were compared with the genospecies distributions reported in the previous two PubMed literature searches. This revealed that the genospecies distribution in Germany is similar to the distribution in the studies used to estimate the proportion of infections that are asymptomatic and in the countries represented in the studies used to estimate the duration of antibody detection (Supplement Table 1).[14–17]

Under-ascertainment multiplier derivation process

The number of surveillance-reported LB cases was adjusted for under-ascertainment using seroprevalence-derived multipliers in five steps. First, estimates of the prevalence of LB infection in the general population were identified from the seroprevalence studies. Second, an estimate of the number of incident symptomatic LB cases was derived from the prevalence of LB infections, accounting for the proportion of infections that are asymptomatic and the duration of antibody detection determined from the literature searches. Third, the number of reported LB cases was obtained from national public health surveillance for the period corresponding to when blood samples were collected in the seroprevalence studies. Fourth, the estimated number of symptomatic incident cases was compared to the number of surveillance-reported cases to estimate the under-ascertainment multiplier. Finally, the number of symptomatic LB cases in 2021 was estimated based on the number of surveillance-reported cases in 2021 and the multiplier.

Steps 1–2: Estimation of seroprevalence and incident symptomatic LB cases—Estimates of the prevalence of LB-infected children and adults derived from the seroprevalence studies were converted to estimates of the number of incident symptomatic LB cases using the formula below:

$$\textit{Estimated number of incident symptomatic LB cases} = \frac{\textit{seroprevalence} * \textit{population size} * 50\%\ \textit{asymptomatic}}{10 - \textit{year duration of antibody detection}}$$

In our primary analysis, regional seroprevalence point estimates were used to estimate the number of incident symptomatic cases that occurred in each of the nine states that conduct LB public health surveillance in the last year that the blood samples were collected in each seroprevalence study. We used a 10 year duration of IgG antibody detection; this was the median duration based on the five studies from our literature search.[18–22] There was no apparent difference in the duration of antibody detection for EM vs disseminated LB cases. We excluded asymptomatic cases as persons without symptoms are unlikely to be captured in surveillance data. Our literature search for the proportion of infected persons who are asymptomatic yielded three studies, of which the median proportion was 50%.[23–25]

The number of incident symptomatic cases for children and adults in each of the nine states in the last year that blood samples were collected in each seroprevalence study was estimated from the regional seroprevalence data using the formula presented earlier, and these state-specific estimates were summed to estimate the number of incident symptomatic LB cases across all nine states that conduct LB surveillance.

Step 3: Extraction of surveillance-reported LB cases—Public health surveillance data were retrieved from the RKI website.[26] The number of surveillance-reported LB cases among children and adults in each of the nine states was extracted for 2021 and for the last year that blood samples were collected in each seroprevalence study. For Rhineland-Palatinate and Saarland, which began LB surveillance after the seroprevalence study in children was conducted, and Bavaria, which began LB surveillance after both seroprevalence studies were conducted, the average number of LB cases reported during the first three years of surveillance was used as a proxy for the number of LB cases in the last year that blood samples were collected in each seroprevalence study.

Step 4: Multiplier estimation—The estimated number of incident symptomatic cases in each state in the last year that blood samples were collected in each seroprevalence study was compared with the number of surveillance-reported cases in each state in the same

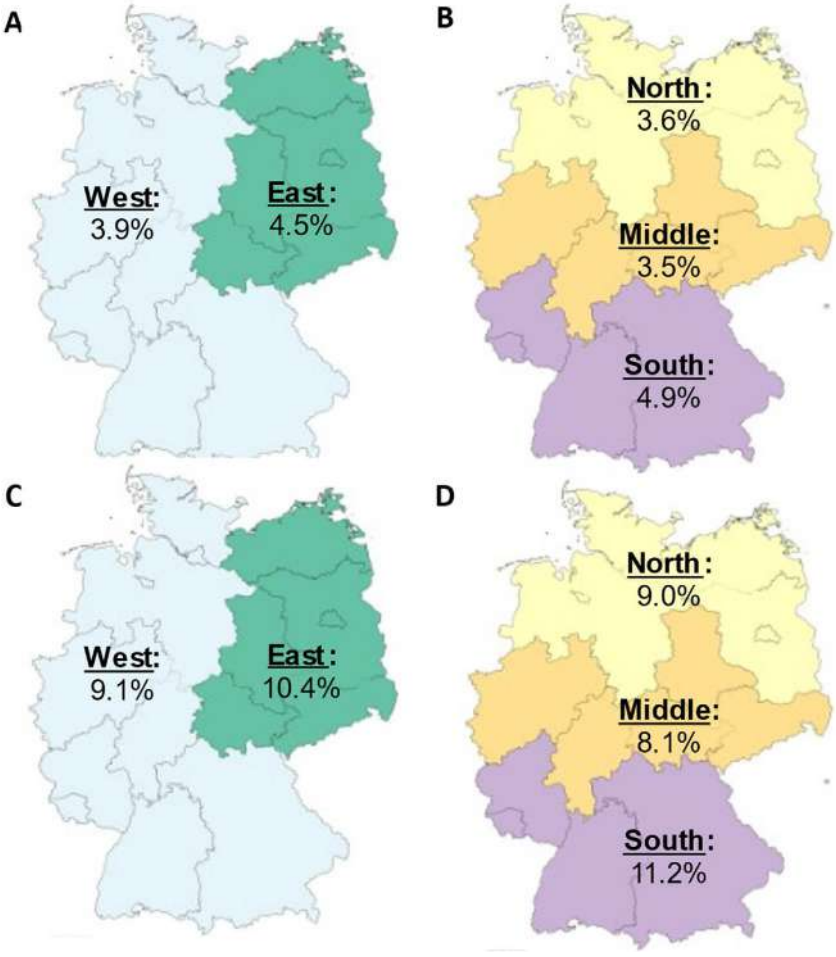

Fig. 1. (**A**) Seroprevalence of IgG antibodies against *B. burgdorferi* from a 2005 national seroprevalence study of children,[12] East vs West regional stratification, Germany, and (**B**) North vs Middle vs South regional stratification, Germany. (**C**) Seroprevalence of IgG antibodies against *B. burgdorferi* from a 2011 national seroprevalence study of adults,[13] East vs West regional stratification, Germany, and (**D**) North vs Middle vs South regional stratification, Germany.

year to derive estimates of state-specific under-ascertainment multiplier. Children and adult multipliers, in addition to an all-age multiplier, were calculated for each state.

Step 5: Estimation of 2021 symptomatic LB incidence—The state-specific multipliers were then applied to the number of surveillance-reported cases in each state in 2021 and summed to estimate the total number, and population-based incidence, of symptomatic LB cases in the nine German states that conduct LB surveillance in 2021. To derive an overall under-ascertainment multiplier, the total estimated number of symptomatic LB cases in these nine states in 2021 was compared with the total number of surveillance-reported cases in these nine states in 2021.

Seroprevalence estimate sensitivity analysis

As estimated 95% confidence intervals for the seroprevalence estimates were also provided, we conducted a sensitivity analysis to evaluate the impact of using the lower bound of the 95% seroprevalence confidence interval in every region on the under-ascertainment multipliers and population-based incidence of symptomatic LB cases in the nine states in 2021. We repeated the analysis using the upper bound of the 95% seroprevalence confidence interval in every region as well.

Duration of antibody detection sensitivity analysis

A sensitivity analysis was conducted to evaluate the impact of using five year and 20 year durations of antibody detection on the under-ascertainment multipliers and population-based incidence of symptomatic LB cases in the nine states in 2021.

Results

In 2021, 11,051 LB cases were reported to RKI (Fig. 2), for an incidence of 34 surveillance-reported LB cases per 100,000 population in the nine states that conduct LB surveillance. Of these surveillance-reported LB cases, 132 cases were missing age and thus are excluded in the age-specific analyses.

Children

For children, regional seroprevalence point estimates ranged from 3.5% to 4.9% (Table 1A).[12] Using an asymptomatic proportion of 50% and a 10 year duration of antibody detection, there were an estimated 11,721–12,202 incident symptomatic LB cases in the nine German states that conduct surveillance for LB in 2005.

State-specific under-ascertainment multipliers in 2005 ranged from three to 29 (Table 2A). When multipliers were applied to the number of surveillance-reported LB cases in 2021 and summed, there were an estimated 11,637–11,940 symptomatic LB cases in children in the nine German states that conduct LB surveillance. When the average number of symptomatic LB cases (11,789) is compared to the number of surveillance-reported LB cases in 2021 (1304), this indicates that the under-ascertainment multiplier of symptomatic LB cases in children in these nine states is nine.

Using the lower (upper) bound of the regional seroprevalence 95% confidence intervals, the estimated number of incident symptomatic cases in 2005 is 9951–10,070 (13,890–14,714), corresponding to an estimated 9832 (14,139) incident symptomatic cases in 2021 and a multiplier of eight (11) (lower bound: Supplement Table 2, Supplement Table 4; upper bound: Supplement Table 3, Supplement Table 5).

In the duration of antibody detection sensitivity analysis, using a five year duration of antibody detection, the state-specific multipliers for children ranged from six to 57 (Supplement Table 8). When these multipliers were applied to the surveillance-reported LB cases in 2021, there were an estimated 23,274–23,881 symptomatic LB cases in children in the nine states in 2021, for a multiplier of 18. Using a 20 year duration of antibody detection, the multipliers ranged from one to 14, and there were an estimated 5818–5970 symptomatic LB cases in children in the nine states in 2021, for a multiplier of symptomatic LB cases of five.

Adults

Regional seroprevalence point estimates of LB ranged from 8.1% to 11.2% for adults (Table 1B).[13] Using an asymptomatic proportion of 50% and a 10 year duration of antibody detection, there were an estimated 128,859–131,024 incident symptomatic LB cases among adults in the nine German states that conduct LB surveillance in 2011.

State-specific multipliers ranged from five to 22 (Table 2B). When these under-ascertainment multipliers were applied to the number of surveillance-reported LB cases in 2021 and summed, there were an estimated 117,040–119,122 symptomatic LB cases among adults in the nine states that conduct LB surveillance. When the average number of symptomatic LB cases (118,081) is compared with the number of surveillance-reported LB cases in these nine states in 2021 (9615), the under-ascertainment multiplier of symptomatic LB cases among adults is 12.

Using the lower (upper) bound of the regional seroprevalence 95% confidence intervals, the estimated number of incident symptomatic cases in 2005 is 108,568–109,143 (151,867–157,150), corresponding to an estimated 98,534 (140,846) incident symptomatic cases in 2021 and a multiplier of 10 (15) (lower bound: Supplement Table 2, Supplement Table 4; upper bound: Supplement Table 3, Supplement Table 5).

In the duration of antibody detection sensitivity analysis, using a five year duration of antibody detection, the state-specific multipliers for adults ranged from 10 to 44 (Supplement Table 9). When these multipliers were applied to the number of surveillance-reported LB cases in 2021, this resulted in an estimated 234,080–238,244 symptomatic LB cases among adults in the nine states for a multiplier of 25. Using a 20 year duration of antibody detection, the state-specific multipliers ranged from three to 11, and there were an estimated 58,520–59,561 symptomatic LB cases among adults in the nine states in 2021, for a multiplier of symptomatic LB cases of six.

All ages

There were an estimated 128,980–130,758 symptomatic LB cases among all ages in the nine states that conduct LB surveillance in 2021 (Table 3). When the average number of symptomatic LB cases (129,870) is compared with the number of surveillance-reported LB cases in 2021 (10,919), the under-ascertainment multiplier in these nine states is 12. This results in a population-based incidence of 408 LB cases per 100,000 population in these nine states in 2021.

Using the lower (upper) bound of the regional seroprevalence 95% confidence intervals, the average estimated number of incident symptomatic cases in 2021 among all ages is 108,365 (154,984), corresponding to a population-based incidence of 340 (487) incident symptomatic cases per 100,000 population in these nine states in 2021 (lower bound: Supplement Table 6; upper bound: Supplement Table 7).

In the duration of antibody detection sensitivity analysis, using a five year duration of antibody detection, there were an estimated

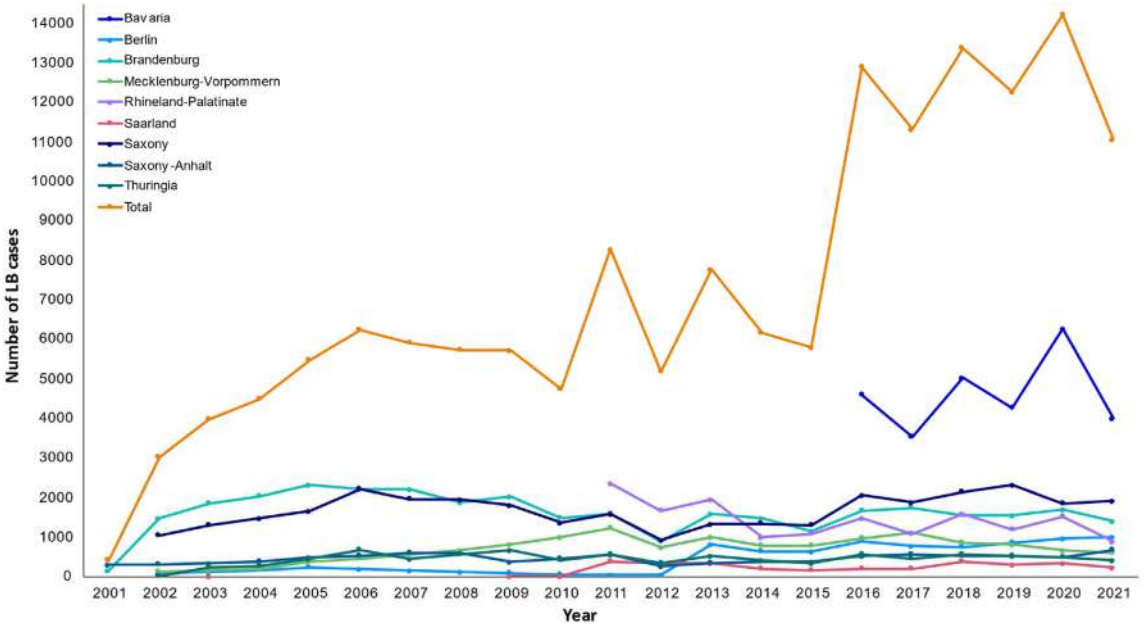

Fig. 2. Number of reported LB cases in the nine German states that conduct public health surveillance for LB from 2001 to 2021.[26] LB, Lyme borreliosis.

Table 1
A. Estimated number of incident cases in children, by state, Germany, 2005. **B.** Estimated number of incident symptomatic LB cases in adults, by state, Germany, 2011.

A. Children					
State	2005 Seroprevalence		2005 children (0–17) population size[31]	Estimated number of incident cases in 2005	
	East vs West	North vs Middle vs South		East vs West	North vs Middle vs South
Bavaria	3.9%	4.9%	2,320,986	4526	5686
Berlin	4.5%	3.6%	509,591	1147	917
Brandenburg	4.5%	3.6%	375,950	846	677
Mecklenburg-Vorpommern	4.5%	3.6%	249,769	562	450
Rhineland-Palatinate	3.9%	4.9%	748,960	1460	1835
Saarland	3.9%	4.9%	176,165	344	432
Saxony	4.5%	3.5%	590,319	1328	1033
Saxony-Anhalt	4.5%	3.5%	343,064	772	600
Thuringia	4.5%	3.5%	326,972	736	572
Total	–	–	5,641,776	11,721	12,202
B. Adults					
State	2011 Seroprevalence		2011 adult (18–79) population size[31]	Estimated number of incident cases in 2011	
	East vs West	North vs Middle vs South		East vs West	North vs Middle vs South
Bavaria	9.1%	11.2%	9,703,505	44,151	54,340
Berlin	10.4%	9.0%	2,689,013	13,983	12,101
Brandenburg	10.4%	9.0%	1,985,034	10,322	8933
Mecklenburg-Vorpommern	10.4%	9.0%	1,306,373	6793	5879
Rhineland-Palatinate	9.1%	11.2%	3,108,241	14,142	17,406
Saarland	9.1%	11.2%	790,451	3597	4427
Saxony	10.4%	8.1%	3,238,640	16,841	13,116
Saxony-Anhalt	10.4%	8.1%	1,894,122	9849	7671
Thuringia	10.4%	8.1%	1,765,620	9181	7151
Total	–	–	26,480,999	128,859	131,024

257,960–261,518 symptomatic LB cases among all ages in the nine states in 2021 for a multiplier of 24 (Supplement Table 10). When a 20 year duration of antibody detection was used, there were an estimated 64,490–65,380 symptomatic LB cases in the nine states in 2021, for a multiplier of six.

Discussion

After adjusting for under-ascertainment by public health surveillance, Germany has a high population-based incidence of symptomatic LB (408/100,000 population per year) in the states

Table 2
A. Under-ascertainment multipliers and estimates of LB cases in children, by state, Germany, 2021. **B.** Under-ascertainment multipliers and estimates of LB cases in adults, by state, Germany, 2021.

A. Children

State	Total number of reported LB cases in 2005 or average of first 3 years of surveillance	Estimated number of incident LB cases in 2005		Multiplier *(based on 2005 data)*		Total number of reported cases in 2021	Estimated number of LB cases in 2021		
		East vs West	North vs Middle vs South	East vs West	North vs Middle vs South		East vs West	North vs Middle vs South	Average
Bavaria	564	4526	5686	8	10	620	4975	6251	5613
Berlin	40	1147	917	29	23	76	2179	1743	1961
Brandenburg	218	846	677	4	3	137	532	425	478
Mecklenburg-Vorpommern	36	562	450	16	12	59	921	737	829
Rhineland-Palatinate	287	1460	1835	5	6	151	768	964	866
Saarland	118	344	432	3	4	43	126	158	142
Saxony	155	1328	1033	9	7	129	1105	860	983
Saxony-Anhalt	56	772	600	14	11	40	551	429	490
Thuringia	75	736	572	10	8	49	481	374	427
Total	1549	11,721	12,202	–	–	1304	11,637	11,940	11,789

B. Adults

State	Total number of reported LB cases in 2011 or average of first 3 years of surveillance	Estimated number of incident LB cases in 2011		Multiplier *(based on 2011 data)*		Total number of reported cases in 2021	Estimated number of LB cases in 2021		
		East vs West	North vs Middle vs South	East vs West	North vs Middle vs South		East vs West	North vs Middle vs South	Average
Bavaria	3731	44,151	54,340	12	15	3269	38,680	47,607	43,144
Berlin	648	13,983	12,101	22	19	918	19,819	17,151	18,485
Brandenburg	1448	10,322	8933	7	6	1258	8968	7761	8364
Mecklenburg-Vorpommern	1144	6793	5879	6	5	542	3218	2785	3002
Rhineland-Palatinate	1681	14,142	17,406	8	10	709	5964	7340	6652
Saarland	200	3597	4427	18	22	162	2913	3585	3249
Saxony	1432	16,841	13,116	12	9	1782	20,957	16,322	18,640
Saxony-Anhalt	514	9849	7671	19	15	626	11,996	9343	10,669
Thuringia	485	9181	7151	19	15	349	6607	5146	5876
Total	11,283	128,859	131,024	–	–	9615	119,122	117,040	118,081

LB, Lyme borreliosis.

Table 3
Estimates of LB cases and population-based incidence among all ages, by state, Germany, 2021.

State	Total number of reported LB cases in 2021			Estimated total number of LB cases in 2021			Population in 2020[a] (0–79)	Population-based LB incidence (LB cases per 100,000 in 2021)
	Children (0–17)	Adults (≥18)	Total	East vs West	North vs Middle vs South	Average		
Bavaria	620	3269	3889	43,656	53,858	48,757	12,268,594	397
Berlin	76	918	994	21,998	18,894	20,446	3,442,846	594
Brandenburg	137	1258	1395	9499	8186	8843	2,322,407	381
Mecklenburg-Vorpommern	59	542	601	4139	3522	3831	1,477,358	259
Rhineland-Palatinate	151	709	860	6731	8304	7518	3,804,965	198
Saarland	43	162	205	3039	3743	3391	905,903	374
Saxony	129	1782	1911	22,062	17,182	19,622	3,694,954	531
Saxony-Anhalt	40	626	666	12,547	9772	11,159	1,989,373	561
Thuringia	49	349	398	7087	5519	6303	1,941,067	325
Total	1304	9615	10,919	130,758	128,980	129,870	31,847,467	408

LB, Lyme borreliosis.
[a] 2020 was the most recent year of available population data from Destatis.

that conduct LB surveillance. Furthermore, these data indicate that there are 12 cases of symptomatic LB for every surveillance-reported case in Germany. In Finland, the only other country where under-ascertainment multipliers for LB have been estimated using the seroprevalence-based approach, a similarly high incidence of symptomatic LB was reported: 520/100,000 population per year after adjusting for underdetection.[9] In Finland, however, it was estimated that there are 2.7 symptomatic LB cases for every surveillance-reported LB case, illuminating a high degree of under-ascertainment of symptomatic LB cases by Germany's public health surveillance despite mandatory notification of cases.

As expected, our seroprevalence-based estimate of the incidence of symptomatic LB cases in Germany is higher than the medical claims–based incidence estimates of medically attended LB in Germany. Using the medical claims–based approach, the incidence of medically attended LB cases estimated by Akmatov was 113 to 346 per 100,000 population in 2019[7] and by Müller was 261/100,000 population in 2008.[8] These incidence estimates are compatible with our incidence estimate of symptomatic LB cases because not all persons with symptomatic LB seek medical attention.

The quality of the estimated under-ascertainment multipliers depends on the availability of high-quality seroprevalence and public health surveillance data. Our estimation of the multipliers in Germany was facilitated by the availability of nationally representative seroprevalence studies with credible regional estimates of the infected proportion of children and adults. Both studies used a two-tier testing approach, with sera samples tested by ELISA and confirmatory line blot testing. Although LB surveillance is not nationwide in Germany, the available LB surveillance data in nine states enabled the application of this seroprevalence-based under-ascertainment multiplier approach.

Our study has several limitations. The child seroprevalence study was conducted in 2003–2006, and the adult seroprevalence study was conducted in 2008–2011. The assumption inherent in applying the under-ascertainment multipliers derived in earlier years to the surveillance data in 2021 to estimate the number of symptomatic LB cases in 2021 is that the factors associated with being a reported case in the surveillance system (e.g. frequency at which an infected person sought care, frequency of reporting of LB cases by clinicians and laboratories) remained unchanged from earlier years to 2021. This assumption is supported by a preliminary analysis of a more recent iteration of the adult seroprevalence study. This more recent adult seroprevalence study, which was conducted in 2018–2020 using similar methods as the previous survey, found little change in the overall seroprevalence (4.4% vs 4.1%) despite occurring 11 years later.[27] However, more recent child and adult seroprevalence data would enable us to derive multipliers with greater confidence. Two other key assumptions used to derive multiplier estimates were the proportion of asymptomatic infections and the duration of antibody detection. Although no data were available specifically for Germany, data from elsewhere in Europe suggest that the percentage of infected persons who possess an asymptomatic infection is approximately 50%. If a higher proportion of infected cases are asymptomatic, the estimated number of symptomatic cases would be lower, and vice versa. However, the studies used to estimate this proportion are not without limitations; more research, ideally conducted in Germany, is needed to better understand the true proportion of asymptomatic LB infections in Germany. Data from one German study and from studies conducted elsewhere in Europe indicated a 10 year duration of IgG antibody detection. To evaluate the impact of a shorter or longer duration of IgG antibody detection, we conducted a sensitivity analysis. Given that the literature on the duration of IgG antibody detection is limited, we used a conservative approach with the sensitivity analysis, considering the extremes of five and 20 year durations of IgG antibody detection. As demonstrated in the results, the duration of IgG antibody detection can have a substantial impact on the estimates of symptomatic incident cases. Further research on the duration of IgG antibody detection is needed and would enable us to derive more definitive estimates of under-ascertainment. Finally, a key limitation of our study is that only nine of 16 German states conduct LB surveillance. Thus, we were only able to derive multipliers, and population-based incidence estimates, for these nine states.

LB is endemic in much of Europe. In 2006, the World Health Organization estimated that ~85,000 cases of LB are reported annually across the 25 countries in the European Union[28]; however, this is likely a substantial underestimate due to reasons stated earlier that result in under-ascertainment of symptomatic LB cases by surveillance systems. Two systematic reviews have previously estimated LB incidence in Western Europe. Sykes found a wide range of national LB incidences across Western Europe, concluding that the LB incidence in Western Europe was 56.3/100,000 population per year.[29] Vandekerckhove et al. found a similarly wide range of national LB incidences and concluded the incidence is increasing in some countries, especially in the northern and central regions.[30] Our incidence estimate of 408 symptomatic LB cases/100,000 per year in Germany indicates it is likely that the LB disease burden is remarkably underestimated in Germany and presumedly elsewhere in Europe.

In conclusion, we identified a high incidence of symptomatic LB in Germany and a high degree of underdetection of symptomatic LB by public health surveillance. This seroprevalence-based approach for estimating the actual number of symptomatic LB cases could be applied in other countries that have representative LB seroprevalence data and conduct LB surveillance. Applying this seroprevalence-derived under-ascertainment multiplier approach in other European countries would likely demonstrate a higher population-based incidence of symptomatic LB than is currently recognized. Given the high disease burden of LB, public health efforts are needed. Such efforts should include enhancing LB surveillance in Europe, including the nationwide expansion of LB surveillance in Germany. In our analysis, we estimated the incidence of symptomatic LB among the nine states that conduct public health surveillance for LB. It is probable that the incidence of symptomatic LB is similarly high in the seven states that do not conduct LB surveillance, although this lack of surveillance makes it more challenging to understand the epidemiological picture of LB in these states. The high burden of LB in Germany and elsewhere is an important public health problem, and additional disease prevention options, such as the availability of an efficacious LB vaccine, are needed.

Author statements

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Ethical approval

No ethical approval was obtained because this study did not involve a prospective evaluation nor experiments on animals.

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Competing interests

J.O., F.J.A., A.P., K.H., P.K., G.B., J.S., and L.J. are employees of Pfizer and may hold stock or stock options.

Author contributions

J.O. and F.J.A. contributed to conceptualization, methodology, formal analysis, investigation, writing, and visualization. A.P., K.H., P.K., and G.B. contributed to investigation, writing, and visualization. J.S. and L.J. contributed to conceptualization, formal analysis, investigation, writing, visualization, and supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.002.

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Original Research

Evaluation of the reach and impact of a UK campaign highlighting obesity as a cause of cancer among the general public and Members of Parliament

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ABSTRACT

Objectives: 'Overweight and obesity' is the second biggest preventable cause of cancer after smoking. In 2018, Cancer Research UK launched an awareness raising campaign about the link between overweight and obesity and cancer risk. This study aimed to evaluate the reach and impact of the campaign.
Study design: This study was a repeated cross-sectional online survey.
Methods: The campaign consisted of six elements including the main message that 'Obesity is a cause of cancer'. UK adults and Members of Parliament (MPs) were surveyed before the campaign (W1; $n = 2124$ and $n = 151$), 1 month (W2; $n = 2050$ and $n = 151$) and 3 months after the campaign (W3; $n = 2059$ and MPs not surveyed). Outcome measures were campaign reach, awareness of overweight and obesity as risk factors for cancer, attitudes towards individuals who are overweight or obese, support for policies to reduce obesity and reactions to the campaign.
Results: Overall, 76.2% of MPs and just under half of the public (47.5% in W2 and 36.8% in W3) reported having seen the campaign. Unprompted awareness of obesity as a risk factor increased among the public from 17.1% at W1 to 43.3% in W2 (odds ratio 3.71, 95% confidence interval 3.18–4.33) and 30.3% in W3 (odds ratio 2.11, 95% confidence interval 1.80–2.47). A similar pattern was seen for prompted awareness and among MPs. There were no consistent changes in attitudes towards overweight individuals or support for policies to reduce obesity.
Conclusions: This evaluation suggests that the campaign achieved the primary objective of increasing awareness of the link between obesity and cancer without increasing negative attitudes towards individuals who are overweight or obese.

Introduction

'Overweight and obesity' is the second biggest preventable cause of cancer after smoking.[1,2] In 2019, 63.8% of all adults in the United Kingdom were overweight or obese, and a recent report by Cancer Research UK and the UK Health Forum report predicts that three in four adults in the United Kingdom will be overweight or obese by 2035.[3] Overweight and obesity together increase the risk of 13 different types of cancer, with around 23,000 cases of cancer each year in the United Kingdom currently attributable to being overweight or obese.[4]

Despite overweight and obesity being the second biggest preventable causes of cancer, public awareness of this link is relatively low: in 2014, only 10.3% of a sample of the UK public were able to recall obesity as a factor that might affect a person's chance of developing cancer,[5] and in 2017, this had only risen to 14.9%.[6] This low level of public awareness, along with evidence that increased awareness of specific risk factors for cancer, can lead to increased public support for related policy measures that could improve health,[7] led Cancer Research UK to launch a campaign in 2018 to increase awareness of overweight and obesity as a cause of cancer. Shortly after launch, the campaign generated controversy within the medical community[8] and media[9] and was criticised for being 'fat shaming',[10] failing to respect the British public's autonomy and

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stigmatising those who are overweight or obese while failing to acknowledge the complex causes of obesity.[11]

The aims of this study were to evaluate the reach of the campaign; changes in awareness of overweight or obesity as a risk factor for cancer; any unintended changes in attitudes towards overweight or obese individuals; and reactions to the campaign, including intention to change health behaviours and support for a range of government and manufacturer actions to reduce obesity.

Methods

Design and sample

The campaign evaluation was a repeated cross-sectional study. Approximately 2000 adult members of the general public, nationally representative by age, gender, social grade and region, were recruited by YouGov, a Market Research Society company partner, at three time points from across the United Kingdom.

1) Precampaign (wave 1 [W1]; 9 February 2018 to 20 February 2018; $N = 2124$)
2) Immediately postcampaign (wave 2 [W2]; 27 March 2018 to 4 April 2018; $N = 2050$)
3) 2 months postcampaign (wave 3 [W3]; 21 May 2018 to 29 May 2018; $N = 2059$).

Those who took part in the survey were awarded with points for their participation that could be saved and exchanged for a voucher. Two thousand participants were estimated to give 90% power to detect an increase in prompted and unprompted awareness of overweight/obesity as a risk factor for cancer of ±5%.

A pragmatic sample of Members of Parliament (MPs) were recruited from across the United Kingdom by Savanta (formally ComRes) at two time points.

1) Precampaign (wave 1 [W1]; 31 January 2018 to 28 February 2018; $N = 151$)
2) Postcampaign (wave 2 [W2]; 16 April 2018 to 14 May 2018; $N = 151$).

Intervention

The campaign ran from 26 February 2018 to 25 March 2018 and consisted of six elements: a poster, a radio advert, two Facebook static adverts, and two video clips. The messaging across all elements aimed to raise awareness of obesity as a cause of cancer and included the main message of 'Obesity is a cause of cancer' (Supplementary File 1). The target was all adults in the United Kingdom of all weights, and the campaign had been pilot tested in 2016 as a regional campaign in the West Midlands.[12]

Measures

In all three waves of the survey for the general public, unprompted free-text and prompted awareness of overweight and obesity as a risk factor for cancer were assessed using questions from the Cancer Awareness Measure.[13] Attitudes towards individuals who are overweight or obese, views on whether tackling obesity is the responsibility of individuals or the government and agreement with policies to reduce obesity were assessed with a series of questions adapted from a previous campaign evaluation.[14]

In W2 and W3, participants were shown each element of the campaign in turn and asked if they had seen it before. The survey ended with questions asking how they felt about the campaign, and for those who had reported seeing at least one element, what, if anything, they had done as a result. Full details on the survey questions are given in Supplementary Files 2 and 3.

Unprompted free-text and prompted awareness of overweight and obesity were similarly assessed among MPs. MPs were then shown three elements of the campaign and asked if they had seen any before and a series of questions about their views and actions or potential actions. Full details are given in Supplementary Files 4 and 5.

Analysis

Responses to questions about awareness of the association between obesity and cancer were dichotomised into 'Yes' vs 'No'/'Don't know'. Responses to all questions based on a Likert scale were dichotomised into 'strongly agree' and 'agree' vs 'neither agree nor disagree'/'disagree'/'strongly disagree'/'don't know'.

For analysis of awareness of the association between obesity and cancer, attitudes towards overweight individuals and views on responsibility for tackling obesity, we compared responses between pre- and post-campaign surveys using logistic regression. We then compared responses postcampaign between those who reported having seen at least one element of the campaign with those who had reported not having seen the campaign.

To enable us to identify characteristics of participants associated with having seen the campaign and with different responses to the campaign, we performed multivariable logistic regression across both W2 and W3. Finally, we compared the actions respondents reported to have taken following the campaign stratified by self-reported weight status (underweight/healthy weight/overweight).

We report all regression analysis results as odds ratios (ORs) with 95% confidence intervals (CIs), and the results presented from the general population data are weighted to be representative of the United Kingdom in respect of age, sex and region based on the census 2011 and estimated social grade (ABC1C2DE) by the National Readership survey. All questions were compulsory; therefore, there were no missing data. STATA version 14 was used for analysis with statistical significance set at $P < 0.05$.

Results

General population surveys

The characteristics of the populations for the three surveys of the general public are shown in Table 1. Overall, 51.3% were female, and 54% were in social class ABC1. The education levels, smoking status and body mass index were similar across the three waves.

Exposure and reach of campaign

Just less than half of respondents in both postcampaign waves (47.5% in W2 and 36.8% in W3) reported having seen any elements of the campaign. The poster was the most frequently seen with 36.9% and 27.5% of respondents recalling seeing it. In multivariable regression, being older (OR 0.97 [0.97–0.98] for each increasing year) and being in lower social classes (C2DE) compared with higher classes (ABC1; OR 0.80 [0.69–0.94]) were associated with reduced odds of seeing the campaign. There were no differences by sex, smoking status, weight status or region of the country (Supplementary Table 1).

Table 1
Demographics of participants within the three public surveys.

Characteristic	Unweighted			Weighted		
	Precampaign ($n = 2124$)	Wave 2 ($n = 2050$)	Wave 3 ($n = 2059$)	Precampaign ($n = 2124$)	Wave 2 ($n = 2050$)	Wave 3 ($n = 2059$)
Age (years)						
18–24	8.52	11.61	12.53	11.3	11.3	11.3
25–34	16.29	16.44	13.74	17.2	17.2	17.2
35–44	17.28	15.41	16.85	16.1	16.1	16.1
45–54	18.97	18.39	18.94	17.9	17.9	17.9
55–64	16.29	15.61	15.78	14.7	14.7	14.7
65+	22.65	22.54	22.15	22.8	22.8	22.8
Sex						
Male	45.81	43.46	45.60	48.8	48.7	48.7
Female	54.19	56.54	54.40	51.2	51.3	51.3
Region of country						
East	9.60	9.41	8.21	9.3	9.3	9.3
London	10.92	10.24	10.83	14.6	14.6	14.6
Midlands	15.77	15.76	15.93	15.7	15.7	15.7
North	24.29	24.29	25.01	22.8	22.8	22.8
Northern Ireland	2.40	2.05	3.11	2.8	2.8	2.8
Scotland	8.57	10.15	9.28	8.4	8.4	8.4
South	23.21	22.78	22.68	21.9	21.9	21.9
Wales	5.23	5.32	4.95	4.5	4.5	4.5
Social class[a]						
ABC1	57.86	57.51	60.76	54.00	54.00	54.00
C2DE	42.14	42.49	39.24	46.00	46.00	46.00
Education level						
High	36.06	38.29	38.37	34.21	36.16	36.14
Medium	40.44	41.02	39.29	41.45	41.65	39.61
Low	23.49	20.68	22.34	24.34	22.19	24.25
Smoking status						
Never smoker	50.66	53.46	54.44	50.76	52.39	52.98
Ex-smoker	35.03	32.00	32.73	34.37	33.15	33.20
Current smoker	14.31	14.54	12.82	14.87	14.46	13.82
Weight status (BMI in kg/m^2)						
<18.5 (underweight)	3.05	3.64	2.67	3.31	3.50	2.75
18.5 to <25 (healthy weight)	39.60	42.53	43.00	39.83	42.55	42.09
≥25 (overweight)	57.35	53.83	54.33	56.86	53.95	55.16

All data presented as percentages.
[a] Social class grouped based on the NRS social grades where A = upper middle class, B = middle middle class, C1 = lower middle class, C2 = skilled working class, D = working class, E = non-working, BMI, body mass index; NRS, National Readership Survey.

Awareness of obesity and being overweight as risk factor for cancer

In unprompted free text, 17.1% listed obesity or being overweight as a risk factor precampaign (Fig. 1a). This increased to 43.3% in W2 and 30.3% in W3. Compared with precampaign, participants in W2 were 3.71 (3.18–4.33) times more likely to mention obesity and participants in W3 2.11 (1.80–2.47) times more likely. A similar pattern of increase was seen in those who listed being overweight or obese in their top three risk factors for cancer (8.1% W1, 28.6% W2 and 16.5% W3).

When asked directly if being overweight or obese is associated with cancer risk, 66.6% strongly agreed/agreed before the campaign. This increased to 78.9% in W2 (OR 1.87 [1.61–2.18] compared with W1) and 74.0% in W3 (OR 1.43 [1.24–1.65] compared with W1) among all respondents and 88% in W2 and 84% in W3 for those who had seen the campaign.

There was a corresponding increase in those who strongly agreed/agreed that it is equally important to tackle obesity as smoking (62.4% at baseline, 69.1% at W2 and 67.3% at W3, OR 1.35 [1.17–1.55] for W2 compared with baseline and OR 1.24 [95% CI 1.08–1.43] for W3 compared with baseline).

Attitudes towards people who are overweight and responsibility for tackling obesity

While one-third of the public respondents believed that people who are overweight are to blame for their health problems, no changes were observed in the percentage of respondents who held this belief between pre- and post-campaign. There were small increases between precampaign and W2 in the percentages strongly agreeing/agreeing that people who are overweight tend to have less energy or tend to be less successful than people with a healthy weight, but these were not seen at W3 (Table 2) and were not dependent on having seen the campaign (Supplementary Table 2). Similarly, no consistent changes between waves or between those had or had not seen the campaign were observed in the percentage of participants agreeing with certain government or manufacturer controls (Supplementary Tables 3 and 4).

Reactions to the campaign

Fig. 2a shows responses after being shown all the components of the campaign. The most common reactions across both waves combined were either feeling neutral (29.8%) or surprise (25.3%), with a further 13.6% not thinking any of the options reflected their view. Notably 2.8% felt anger, 2.0% felt contempt and 1.7% felt disgust, with odds of such feelings decreasing with increased age (OR per 1 year 0.986 [0.976–0.995]; Supplementary Table 5).

More than 75% strongly agreed/agreed that the campaign was believable, informative, an important message and responsible advertising (Fig. 2b). Notably, however, 64% had found the campaign worrying, and 8% had found the campaign offensive. Those in lower social classes (C2DE) were more likely to have found the campaign offensive (OR 1.41 [1.05–1.89]), and women, current smokers and those underweight were less likely to find the campaign worrying. No associations were seen with finding the

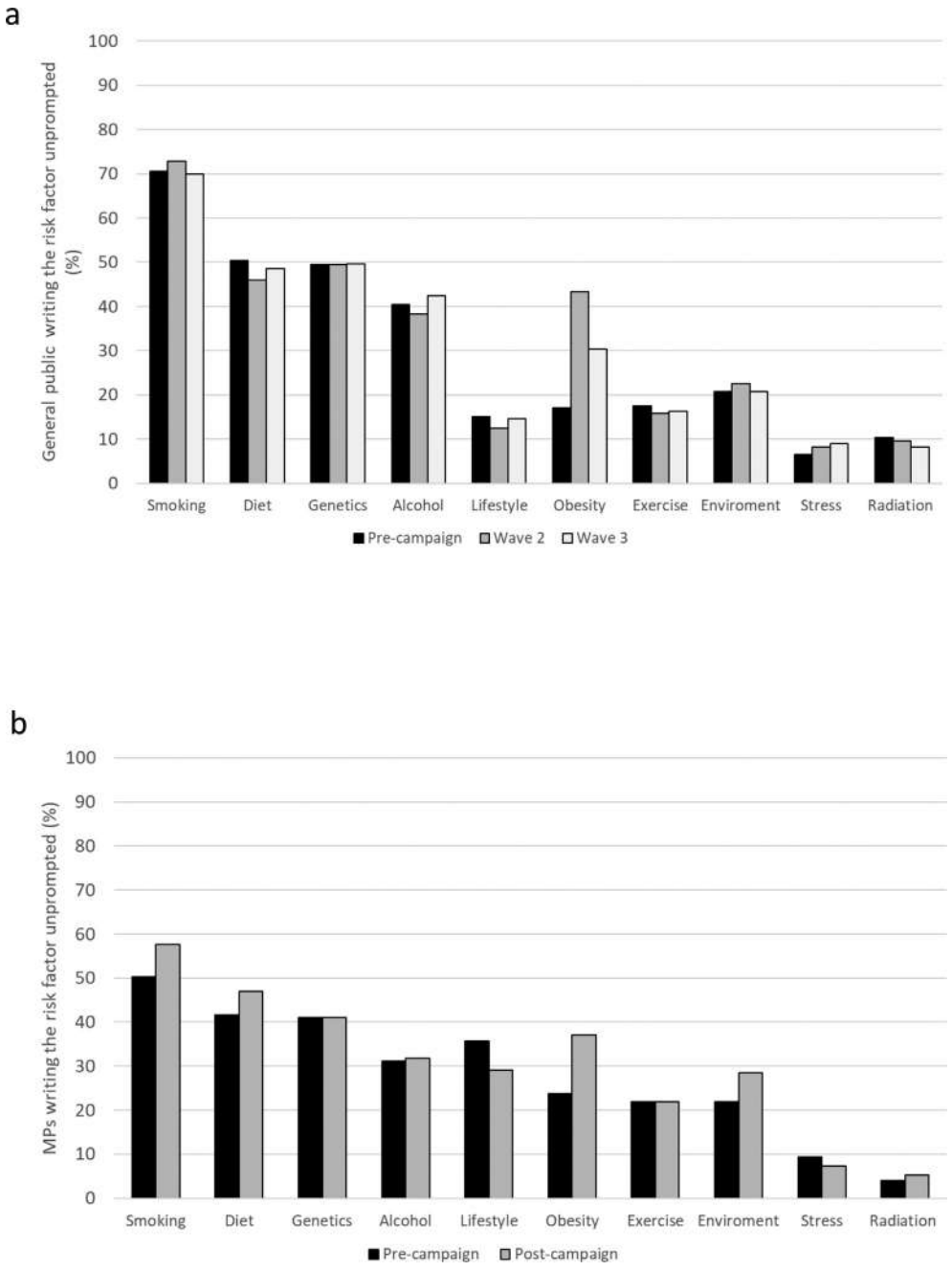

Fig. 1. Frequency of mentioning risk factors in response to an unprompted question about risk factors associated with cancer amongst (a) the public and (b) MPs before and after the campaign.

campaign worrying or offensive and age, education level or region of the country (Supplementary Table 5).

Table 3 presents the actions those who recalled seeing at least one element of the campaign had taken. Across both waves, 30% had thought about changing their eating behaviours and 20% had thought about changing their physical activity behaviours. In multivariable analysis (Supplementary Table 6), participants who were overweight or obese were more likely to have thought about changing their eating behaviours or physical activity behaviours than those of a healthy weight (OR 1.97 [1.53–2.54] for eating behaviours and OR 1.71 [1.27–2.30] for physical activity).

MP surveys

A total of 151 MPs took part in both the precampaign and postcampaign surveys. Most were within the labour (49.7% and 53%) or conservative (37.8% and 34.4%) parties.

Exposure and reach of campaign

When asked if they had seen elements of the campaign, 51.0% ($n = 77$) recalled seeing the poster, 59.6% ($n = 90$) recalled seeing newspaper coverage and 7.3% ($n = 11$) recalled seeing a still image. Moreover, 23.8% ($n = 36$) had not seen any of the elements, with

Table 2
Attitudes towards overweight individuals and responsibility for tackling obesity amongst members of the public.

Wave	Strongly agreeing/agreeing (%)	Odds ratio (95% CI)
People who are overweight are to blame for their health problems		
Precampaign	34.6	1 (Ref)
Wave 2	35.6	1.04 (0.91–1.20)
Wave 3	34.9	1.01 (0.88–1.16)
People who are overweight or obese tend to have less energy		
Precampaign	71.2	1 (Ref)
Wave 2	75.4	**1.24 (1.07–1.45)**
Wave 3	73.5	1.12 (0.97–1.30)
People who are overweight or obese tend to lack will power		
Precampaign	40.9	1 (Ref)
Wave 2	42.8	1.08 (0.95–1.24)
Wave 3	45.0	**1.18 (1.03–1.35)**
People who are overweight or obese tend to be less successful		
Precampaign	25.7	1 (Ref)
Wave 2	30.2	**1.25 (1.08–1.45)**
Wave 3	28.2	1.14 (0.98–1.32)
People who are overweight or obese tend to have less friends		
Precampaign	12.0	1 (Ref)
Wave 2	14.1	1.21 (0.99–1.47)
Wave 3	13.6	1.16 (0.95–1.42)
Authorities exaggerate the harmful effects of being overweight		
Precampaign	18.0	1 (Ref)
Wave 2	16.4	0.90 (0.75–1.07)
Wave 3	15.9	0.87 (0.73–1.03)
Tackling obesity is the responsibility of the individual rather than the government		
Precampaign	67.5	1 (Ref)
Wave 2	66.8	0.97 (0.84–1.12)
Wave 3	65.3	0.91 (0.79–1.04)

Bold values indicate statistically significant differences.

40.4% ($n = 61$) seeing one element, 29.8% ($n = 45$) seeing two elements and 6.0% ($n = 9$) seeing all three.

Awareness of obesity and being overweight as risk factor for cancer

In unprompted free-text, 23.8% listed being overweight or obese as a risk factor for cancer precampaign. This increased to 37.1% postcampaign, with MPs in the postcampaign survey 1.88 (95% CI 1.14–3.10) times more likely to mention being overweight or obese than those in the precampaign survey (Fig. 1b). There was no difference postcampaign between those who had and had not seen the campaign (OR 1.73 [0.76–3.93]).

When prompted, in the baseline survey, 86.7% ($n = 131$) strongly agreed/agreed that there was a link between obesity and cancer. In the follow-up survey, the proportion who thought that being overweight or obese can increase a person's chances of developing cancer increased to 94.7% ($n = 142$; OR 2.71 [1.15–6.36]). As for unprompted responses, there was no difference postcampaign between those who had seen the campaign and those who had not (OR 0.45 [0.05–3.82]).

Attitudes towards people who are overweight and responsibility for tackling obesity

There was no change in the percentage of MPs who strongly agreed/agreed that it was equally important to tackle obesity as smoking (70.9% at baseline, 77.5% at follow-up, OR 1.42 [0.84–2.38]) or who believed tackling obesity was the responsibility of the individual (45.0% at baseline, 52.7% at following, OR 1.36 [0.86–2.14]), and no differences between those who had seen the campaign and those who had not (OR 0.68 [0.31–1.46] for the responsibility of the individual and OR 1.46 [0.62–3.43] for equally important to tackle obesity as smoking).

Reactions to the campaign

In general, MPs were supportive of the campaign. Overall, 95.3% ($n = 144$) strongly agreed/agreed that the campaign has an important message, 90.7% ($n = 137$) supported campaigns like it and 83.4% ($n = 126$) considered the campaign relevant to them in their role as an MP. However, only 29.1% ($n = 44$) had discussed the campaign with their colleagues or constituents, and only 43.7% ($n = 66$) intended to do so.

Discussion

Key findings

Our findings demonstrate an increased awareness of overweight and obesity as a cause of cancer among members of the public and MPs up to 2 months after an awareness raising campaign. Despite the cross-sectional design of the study, our finding that the postcampaign awareness among the public was greater in those who reported having seen the campaign and that no changes were seen in awareness of other risk factors suggests that at least some of the increase in awareness was likely related to the campaign. There is also suggestion that the campaign may have impacted some individuals' intentions to change their behaviour, and respondents who were overweight or obese were approximately twice as likely to have thought about changing their eating or physical behaviours as those of a healthy weight.

Despite the negative media coverage of the campaign, we found no consistent evidence of an increase in negative attitudes towards people who are overweight or obese after the campaign. Our findings do, however, highlight widespread negative attitudes and stigma towards overweight or obese individuals that were present from precampaign. In addition, although the majority of respondents were positive about the campaign, a significant minority (8%) of the public thought the campaign was offensive, and 6.5% felt anger, contempt or disgust in response to it. Notably, these reactions to the campaign did not differ by weight status.

Comparison with existing literature

The population reach of the campaign, with approximately half of the respondents reporting that they had seen at least one element, is comparable with other obesity prevention campaigns[14–17] and the baseline awareness in this study population consistent with other recent UK population–based studies in which prompted recall for obesity as a risk factor was between 61% and 73%.[18,19] The increases in awareness observed in this study are also similar to those in a community-based cancer awareness roadshow in the United Kingdom, where prompted awareness increased from 72.4% at baseline to 78.8% two months post-intervention[18] and following a state-wide public health intervention designed to improve awareness and knowledge of the link between alcohol and cancer in Australia.[20]

Our finding that there was no persistent increase in negative attitudes towards people who are overweight or obese after the campaign is consistent with a similar evaluation of the 'LiveLighter' campaign in Australia in which graphic anatomical images of visceral fat were used to illustrate the negative health effects of being overweight.[14] Respondents who were overweight in that study were also no more likely to experience a negative emotional response to the campaign than those of a recommended healthy weight.

Strengths and limitations

A strength of this evaluation is the use of national samples of the public and MPs before and after the campaign and the inclusion of questions to assess any potential unintended consequences of the campaign on attitudes towards individuals who are overweight or

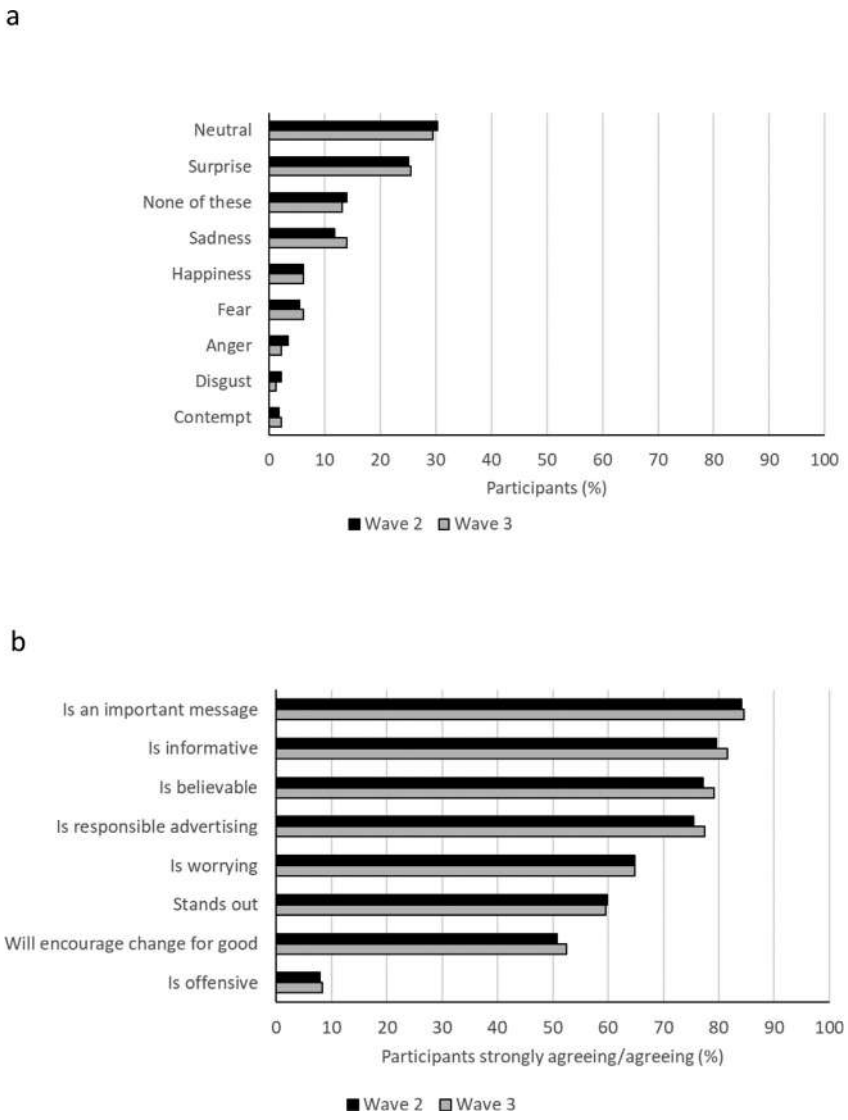

Fig. 2. Public participants' (a) emotional responses to and (b) beliefs about the campaign.

Table 3
Actions following the campaign amongst members of the public who recalled seeing at least one element of the campaign.

Action	Wave 2 ($n = 934$)	Wave 3 ($n = 753$)
Talked to friends/family about the campaign	15.5	17.7
Shared the campaign on social media	1.7	2.7
Talked about the campaign on social media	3.1	3.0
Visited the CRUK website to find out more	1.5	1.8
Looked somewhere else for information	0.1	0.6
Contacted a GP or health professional	0.7	2.0
Thought about changing physical activity behaviours	20.2	19.9
Thought about changing eating behaviours	30.3	30.7
Something else	3.5	2.4
Nothing	52.1	50.2

All data presented as percentages.

obese. The absence of a control or unexposed sample and the cross-sectional design of the study, however, mean that the changes observed cannot be attributed to the campaign. The nature of the surveys additionally relied on self-report, meaning the responses may have been affected by social desirability bias. We also did not assess internalised weight stigma, for example, body dissatisfaction, and were unable to measure the effect of the campaign on change in health behaviours. Although the analysis was weighted to key characteristics of the UK population, those who completed the survey may also not be representative of the United Kingdom.

Implications for policy and research

This evaluation suggests that the Cancer Research UK (CRUK) public campaign successfully achieved the primary objective of increasing awareness of the link between obesity and cancer. Awareness of obesity as a risk factor for cancer, however, remains low: even among those who had seen the campaign, only 39.1% of the public participants in W3 included overweight or obesity as a risk factor in unprompted free-text and only 22.9% included obesity or being overweight in their top three risk factors. While the month long campaign is potentially an important first step in raising awareness, additional interventions will be needed to achieve levels of awareness of obesity similar to those for smoking.

It has been proposed previously that mass population campaigns such as this may have the greatest impact by influencing the agenda for discussion by the public and policy makers.[14,21] We found an increase in the percentage of the public who strongly

agreed/agreed that it is equally important to tackle obesity as smoking but little evidence that the campaign had influenced support for a range of potential policy measures.

Although we found no clear evidence of a sustained increase in negative attitudes towards people who are overweight and obese, the widespread negative attitudes present both before and after the campaign, along with prior evidence that weight stigma may negatively impact weight-related health behaviours[22] and body mass index,[23] support previous calls for obesity prevention efforts to include strategies to prevent weight stigma.[22–24] Further research to identify which specific components of the campaign were perceived as offensive alongside careful communication plans may also help to mitigate against negative reactions in future campaigns.

In conclusion, this repeated cross-sectional study suggests that the CRUK campaign achieved the primary objective of increasing awareness of the link between obesity and cancer without increasing negative attitudes towards individuals who are overweight or obese. Whether these increases in awareness translate into changes in behaviour or greater support for policies to reduce obesity is not known.

Author statements

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Ethical approval

All research for this health marketing campaign evaluation was conducted in accordance to the Market Research Societies (MRS) Code of Conduct (2014 and is also compliant with superseding MRS 2019 code of Conduct). Specifically, all participants provided written consent to be contacted for participation by signing up or being a member of the research panels. Participants took part voluntarily and were provided with some basic information about the context of the survey. They could withdraw from participation at any time by choosing to discontinue the survey. Adherence to the MRS Code of Conduct was confirmed before data collection by the Cancer Research UK Cancer Intelligence and Data Governance teams. The Market Research agency used to collect the data were also members of the MRS and so bound by the MRS Code of Conduct. The data were anonymised, stored and maintained in accordance with data protection regulations (Data Protection Regulations, 1994 and superseding GDPR, 2018).

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Competing interests

C.I. and K.B. are employed by Cancer Research UK. J.U.S. has received research grants for other projects from Cancer Research UK in the previous 3 years. All authors declare that (1) they have no other support from or relationships with companies that might have an interest in the submitted work in the previous 3 years; (2) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (3) they have no non-financial interests that may be relevant to the submitted work.

Authors' contributions

The campaign was initiated by Cancer Research UK, and the evaluation was managed by C.I.W. J.U.S. and M.F. completed the data analysis. All authors contributed to the final analysis and interpretation of the data. J.U.S. wrote the first draft of the article with contributions from V.P.S., S.N. and C.I.W. All authors critically reviewed the article and have approved the final version.

Availability of data and materials

The data sets analysed during the present study will be made available on the UK data Archive (https://ukdataservice.ac.uk/) following acceptance of the present paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.026.

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Review Paper

Factors influencing organised faecal occult blood test screening participation in culturally and linguistically diverse populations: a scoping review

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ABSTRACT

Objective: This review aims to provide a comprehensive overview of the literature examining factors influencing participation in organised faecal occult blood test (FOBT) screening programmes in culturally and linguistically diverse populations. This article addresses gaps in the literature by providing a mixed methods review of the multilevel influences on FOBT screening in culturally and linguistically diverse (CALD) populations. This review was guided by the question "What are the factors influencing participation in organised FOBT screening programs in CALD populations?"

Study design: Scoping review.

Methods: A scoping review methodology was used to summarise the available evidence. A thematic analysis of the included studies was undertaken to identify factors influencing organised FOBT screening participation in CALD populations from the literature.

Results: FOBT screening participation was lower by ethnicity, religion, birthplace and language spoken. Barriers to screening included, faecal aversion, fatalism, fear of cancer, language and literacy barriers, difficulty accessing translated materials and low colorectal screening knowledge and awareness. CALD populations also had lower perceived benefits, susceptibility and cues to action, higher perceived barriers and greater perceived external health locus control than non-CALD populations. Facilitators of screening included positive attitudes to screening, general practitioner recommendations and social support. Group education sessions and narrative-based screening information were found to increase screening participation.

Conclusion: This review highlights the range of interrelated factors influencing participation in organised FOBT screening programmes in CALD populations and proposes multicomponent interventions to address low screening uptake. Features of successful community-level interventions should be explored further. Narratives show promise for engaging CALD populations. Accessibility of screening information should be addressed at the system level. Leveraging the general practitioner relationship in promoting FOBT screening programmes may also be an effective strategy to target 'hard-to-reach' populations.

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer deaths responsible for more than 900,000 deaths and an estimated 1.9 million new cases of CRC globally in 2020.[1,2] Between 1990 and 2019, the global age-standardised incidence has increased from 22.2 to 26.7 cases per 100,000, whereas age-standardised mortality has decreased from 14.3 to 13.7 deaths per 100,000.[3] In high-income countries, the CRC burden is decreasing due to dietary changes, improved treatments and the implementation of organised screening programmes.[4] Population-level screening programmes using self-administered faecal occult blood tests (FOBT) are a cost-effective strategy for reducing CRC incidence and mortality.[1] However, uptake rates in screening programmes implemented in Europe, the United Kingdom, Canada and Australia are frequently reported to be below 50%.[5]

Culturally and linguistically diverse (CALD) populations are reported to participate in mail-out screening programmes at lower rates than the general population.[6] Despite lower CRC incidence

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than the majority population, lower screening rates often result in later-stage diagnosis.[7] As a result, poorer CRC health outcomes have been observed by ethnicity, language spoken and immigration status.[8] Addressing the needs of CALD populations is of increasing importance, especially in countries with increasing levels of diversity.[6]

The term culturally and linguistically diverse describes non-Indigenous populations that identify with a cultural, religious, ethnic or linguistic group outside of the predominant culture of their country of residence.[9–11] The term was introduced by the Australian Bureau of Statistics to capture the diversity of multicultural populations in Australia.[11,12] In the United States and the United Kingdom, terms such as minority, ethnicity or race are used to capture similar groups. To capture the diversity of populations in an international context, the term CALD has been adapted for this review to describe participants; born outside their country of residence, who speak a language other than the main language spoken in their county of residence or have a self-identified connection to their place of birth, ancestry, ethnic origin, religion, preferred language or language spoken at home.[11]

Previous reviews have focused on identifying sociodemographic, ethnic inequalities and factors influencing screening uptake in the general population.[13–16] This review addresses gaps in the literature by providing a comprehensive, mixed methods overview of the sociodemographic, individual, environmental and system-level factors influencing FOBT screening in CALD populations. Identifying the factors influencing the uptake of organised FOBT screening programmes in CALD populations is critical to informing interventions to increase participation, improve CRC health outcomes and reduce health inequalities. This review is guided by the question "What are the factors influencing participation in organised FOBT screening programs in CALD populations?"

Methods

A scoping review using Arksey and O'Malley's[17] framework was used to examine the range, nature, and key concepts in the literature.[18] Arksey and O'Malley's[17] framework involves formulating a research question, conducting a comprehensive literature search, selecting relevant studies, charting data, summarising and reporting the findings. The quality of the included studies was not appraised as the focus of the review was to provide an overview of the range and types of evidence and develop a comprehensive model of factors influencing FOBT screening participation in CALD populations.

This review included studies investigating screening using self-administered, faecal-based tests (iFOBT, gFOBT and FiT) in countries with organised CRC screening programmes. Studies examining screening by colonoscopy, sigmoidoscopy, virtual colonoscopy or polymerase chain reaction were excluded. This review included participants who were born outside their country of residence, speak a language other than the main language in their county of residence or with self-identified connection to their birthplace, ancestry, ethnic origin or religion.[11] Qualitative, quantitative and mixed methods studies were included to uncover a comprehensive overview of the factors influencing screening uptake. Reviews, editorials, commentary, case reports and case series were excluded.

CINAHL, PubMed, Scopus and Web of Science were searched from 2002 to April 2022. Keywords included 'colorectal cancer', 'screening', 'participation','barriers', 'faecal occult blood test' and 'culturally and linguistically diverse' and their synonyms (Appendix A).[19] Titles and abstracts were first reviewed to exclude irrelevant articles. Full-text articles of the remaining studies were extracted and assessed for eligibility. The literature search identified 3946 articles after removing duplicates. After screening titles and abstracts, 43 articles were included from 155 full-text articles assessed for eligibility (Fig. A1).

A thematic analysis of the included studies was undertaken using NVivo 12.[20] A full reading and charting of the studies served as the familiarisation process. Each study was then coded using an inductive approach. The codes were collated into descriptive themes and subthemes, amalgamating and discarding codes where appropriate.

Results

Study characteristics

Forty-three papers reporting 45 studies were selected for inclusion (Fig. A1). Studies were exclusively from high-income countries; the United Kingdom (14), Australia (10), Canada (3), Denmark (3), New Zealand (3), Israel (3), the Netherlands (2), Singapore (2), Belgium (1), Finland (1) and Spain (1). Study designs comprised 33 quantitative studies, 11 qualitative studies and one mixed methods study. The quantitative studies included 26 cross-sectional studies, three randomised controlled trials, two cohort studies, one pretest/posttest study and one interrupted time series analysis. Qualitative studies collected data through interviews (5), focus group discussions (4) and both interviews and focus group discussions (2). CALD populations were identified by ethnicity,[21–39] birthplace,[40–50] language spoken,[45–51] religion[36–39] and migration status[52–54] (study characteristics; Table A1).

Theoretical frameworks

Thirteen studies explicitly used theoretical frameworks to inform their research.[21,24,26,34,40,42,44–47,55–57] The most cited framework was the Health Belief Model.[21,26,29,34,42,44,45] Other frameworks included the Transtheoretical model,[47,55] Social Cognitive Theory,[47,56] Social-ecological model,[47] Behavioural Reasoning Theory,[45] Theoretical Domains Framework,[24] Precaution Adoption Process Model,[55] Continuum of Resistance model[55] and the Extended Parallel Process Model.[57]

Factor influencing participating in FOBT screening programmes

Factors influencing FOBT screening are reported at the individual, interpersonal, community and system levels (Fig. A2).

Individual-level factors

Sociodemographic factors. In total, nine studies investigated screening uptake by ethnicity, of which eight reported lower screening by ethnicity compared with the general population.[22,23,27,36,39,50,56,58] Three studies reported lower screening participation in all ethnic groups other than Chinese participants who had higher screening uptake than the reference population.[22,23,36] Lower screening was reported among non-European participants except for Asian-born participants who had higher screening uptake than European participants.[27] Hirst et al. reported a gradient of participation by area-level ethnic diversity with the highest participation in the least diverse areas.[58] Of eight studies reporting screening by birthplace,[41,46–50,52,59] five reported lower rates of screening in those born outside their country of residence.[41,48,49,52,59] In contrast to findings by ethnicity, two studies reported lower screening among Asian-born participants compared with the reference population.[41,49] Only two of six studies examining screening by language found lower screening participation among those who spoke a language other than the main language in their country of residence.[36,46–50]

Religion was found to be a determinant of screening uptake in four studies[36,37,39,43] with significantly lower screening participation amongst Muslim,[36,37,39,43] Hindu,[36,37,39] Sikh,[36,37,39] Jewish,[36] Roman Catholic[36] and 'other' religions[36] compared with the respective reference religion in each study. In all four studies, Muslim participants had the lowest FOBT screening participation of all religious groups.[36,37,39,43] In contrast, Campbell et al.[36] reported that screening amongst Buddhist participants did not differ significantly from the reference Church of Scotland group.

FOBT screening was influenced by age, gender and socioeconomic status (SES). Screening participation by age typically followed an inverted 'U'-shaped pattern, with the lowest participation in the lower range of screening eligibility, increasing toward the middle, then decreasing toward the end of the eligibility range.[21–23,39,47–50,52,56,59] Gender was assessed in 17 studies. The influence of gender on FOBT screening uptake differed between populations.[21–23,30,36,37,39,43,46,47,49,50,52,56,58,59] Eight studies found no significant association between gender and screening uptake.[21,22,30,37,46,47,50,56] Six studies found significantly lower screening participation among male participants.[30,39,43,49,58,59] Two studies reported significantly lower screening participation amongst female participants.[23,52] One study reported that participation by gender varied between different ethnicities and religions.[36] Fourteen studies examined screening uptake by SES, education and income.[22,23,37,39,43,46–50,52,56,58,59] The expected social gradient was found with screening participation increasing with increasing level of education,[22,48,49,52,59] income[22,52,59] and SES.[37,39,56,58]

Social cognitive factors

Knowledge and awareness. Ethnicity was associated with lower CRC knowledge, FOBT screening knowledge and screening programme awareness in six studies.[30,42,51,55,56,60] In the qualitative literature, a lack of CRC screening awareness was also a barrier to screening uptake.[24,25,28,33,35,38,40,44,61] The need for asymptomatic screening was often poorly understood in CALD populations with good health and lack of symptoms cited for non-participation in 10 studies.[25,28,35,40,44,45,53,55–57] The belief that asymptomatic screening was not required was significantly associated with lower screening uptake and lower screening intention.[56,57]

Beliefs and attitudes. Faecal aversion was a barrier to FOBT screening in 12 studies.[25,29,33,35,38,40,44,45,55–57,61] Disgust was significantly associated with lower screening uptake[56] and lower screening intention.[57] Embarrassment was also significantly associated with lower screening uptake.[57] A negative association was also found between 'response cost' (embarrassment, hygiene and disgust) and screening participation among South Asian participants.[37] In qualitative research, participants expressed feelings of disgust and embarrassment with faecal collection.[29,55,61] In a study of a South Asian population in the United Kingdom, participants attributed faecal aversion to cultural factors.[40] In contrast, African and Caribbean participants in the United Kingdom and Spanish Roma participants reported no aversion to faecal collection.[24,33]

Fatalistic beliefs such as illness being in the hands of God, spiritual aetiology of cancer, and the belief cancer could not be prevented or cured were reported in nine studies.[24,25,33–35,40,44,55,61] In a study comparing Jewish and Arab-Israeli participants, external health locus control, a concept similar to fatalism, was associated with lower screening intention and participation.[21] Similarly, the belief that health was a result of chance was associated with lower screening intention.[47]

In some populations, religious beliefs promoted health maintenance. Faith was found to motivate preventative health behaviours among African and Caribbean participants in the United Kingdom.[24] Despite fatalistic beliefs, Turkish, Moroccan and Surinamese participants in the Netherlands felt required by their faith to protect their health.[44] Similarly, Greek, Vietnamese and Iranian Australians viewed prevention as a sign of respect for God.[25]

Fear was a barrier to screening participation in 12 studies,[25,28,29,33–35,38,40,45,53,55,61] with two studies significantly associated with lower screening uptake.[29,55] Fear of cancer was identified as a theme in eight studies.[25,34,35,38,40,53,55,61] The word cancer itself was reported to elicit fear amongst participants in seven studies.[25,28,33,34,40,53,61] Fear of colonoscopy also inhibited screening in three studies.[34,40,45] Conversely, positive attitudes toward prevention were cited as promoting screening uptake in seven studies.[24,25,33,34,40,44,57] Screening was seen to offer 'peace of mind' in three studies.[24,40,57]

Health behaviour constructs. Seven studies examined FOBT screening using theoretical frameworks to explain FOBT screening behaviour.[21,26,37,44,46,47,57] Health behaviour constructs represent various individual perceptions that together influence health behaviour according to a particular theoretical framework. The Health Belief Model was the most commonly used health behaviour theory in the literature.[21,26,29,34,42,44,45] Screening intention was associated with perceived benefits,[21,26] perceived barriers,[47,56] FOBT self-efficacy,[37,56] perceived susceptibility,[21] cues to action[21] and health locus of control.[47] Screening participation was associated with perceived benefits,[21,26] perceived barriers,[26,47] perceived susceptibility,[26,47] cues to action[21,26] and health locus of control.[21,47] Natan et al.[26] found that Health Belief Model constructs explained 46% of the variance in FOBT screening uptake among Arab Israelis.

Skills and capabilities

Lack of time was cited as a barrier to FOBT screening in seven studies.[24,29,34,45,53,55,56] Being busy,[45] everyday pressures,[24] work commitments[61] and forgetting[34] were amongst the time-related barriers. Literacy was a barrier to engaging with screening invitations and FOBT instructions in four studies.[28,33,38,61] Difficulty with written communication in any language was also a barrier to engaging with screening information.[28,38,61]

Social-ecological level factors

Interpersonal relationships. Knowing someone with cancer was found to promote FOBT screening in seven studies.[21,24,26,40,46,47,61] Knowing a person with CRC was found to be significantly associated with screening in three studies.[21,46,47] Social influences were also reported by Lo et al.,[56] where knowing someone who screened and believing others think you should screen increased uptake. In some communities, responsibility to family and the community promoted screening participation.[24,25,44] Two studies also found that participants were motivated by civic duty.[24,25] Social support was also found to facilitate screening participation in five studies.[33,38,40,44,56]

The general practitioner (GP) relationship was one of the strongest predictors of screening participation.[21,24–26,28,33,34,40,42,44,53,61] Two studies found that those receiving a GP recommendation were significantly more likely to complete an FOBT.[21,42] Likewise, Natan et al.[26] also reported a significant positive association between screening intention and health practitioner recommendation. GP trust,[25,61] good GP relationship,[61] same culture GP[40] and same gender GP[40] also facilitated screening.

Community-based promotion and education. Culturally tailored group education interventions were examined in five studies.[38,40,44,45,53] South Asian participants suggested that

addressing faith groups would more effectively engage the community.[38] Interaction and FOBT demonstrations were noted benefits of group education.[38,44,53] Settings such as churches, temples, mosques, ethnic community groups and social groups were suggested as suitable settings for community programmes.[38,40,44,45,53]

Targeted community awareness campaigns were also suggested. In a study of an ethnically diverse Australian population, Koo et al.[42] found that campaign recall was associated with higher screening participation (odds ratio [OR] 2.41, 95% confidence interval [CI] 1.38–4.18). Koo et al.[42] also found lower campaign recall associated with lower screening knowledge (OR 2.65, 95% CI 1.79–3.92). In qualitative research, radio, television and cultural newspapers were suggested channels for awareness campaigns.[28,34,38,40]

System-level factors

Accessing translated material. Difficulties understanding invitations and accessing translations hindered screening participation.[25,28,33,34,44,53,61] Five studies found that being unable to read the screening invitation language inhibited screening.[25,28,34,53,61] Two studies reported that CALD populations had difficultly accessing or were unaware that translations were available.[25,28] Ghanouni et al.[62] reported that not reading the screening leaflet was associated with rarely or never screening (OR 0.34, 95% CI 0.19–0.59). Similarly, Kobayashi et al.[63] found that those who had never participated in the UK Bowel Screening Program were 39 (OR 39, 95% CI 26.2–58.1) times more likely to have not read the screening pamphlet than those who had ever participated in the programme. In both studies, non-White participants were significantly less likely to read the screening information than White participants.[62,63]

Complex FOBT process and instructions. CALD population expressed difficulty completing the FOBT. CALD men in Australia and Roma participants in Spain found the procedure too difficult.[33,61] Difficulties with the FOBT were reflected in higher 'spoil' rates among Pacific participants of the New Zealand Bowel Cancer Screening Program.[27] Instructions were also difficult to understand.[25,28,35] In contrast with English-speaking participants, non-English-speaking participants expressed difficulty following FOBT instructions.[25] Serbian and Macedonian background participants suggested reducing the amount of text in instructions and including illustrations.[28] Similarly, Woudstra et al.[44] reported that Turkish and Moroccan participants suggested verbal and visual materials.

Interventions

Interventions to increase FOBT participation included group education,[29,45] one on one education,[55] narrative invitations,[57] telephone reminders[32] and a community FOBT drop-off.[31] In doctor-led Arabic language group education sessions, Rainis et al.[29] reported an increase in FOBT screening participation from 17.8% to 61%. Cullerton et al.[45] also reported that culturally tailored group education increased screening intention from 25% to 49%. Cullerton et al.[45] reported that a culturally tailored group education programme resulted in changes in perceived risk, perceived lack of time, perceived inconvenience, lack of reminders, peace of mind and disgust.[45,57] Barriers that were not significantly changed by group education included faecal aversion, fatalism, fear and self-efficacy.[45,55,57]

McGregor et al.[57] found the inclusion of a narrative pamphlet with an FOBT screening invitation significantly increased screening intention compared with a standard invitation ($P = 0.04$). Using face-to-face education, Foo et al.[55] reported that the 'acceptance' rate for FOBT increased from 1.7% to 33%; however, the number of participants 'deciding not to act' also increased from 3.1% to 51%. Sandiford et al.[31] found that same-ethnicity telephone reminders significantly increased screening amongst Māori and Pacific participants, but not Asian participants.[31] A community drop-off option for FOBT did not increase overall screening participation; however, it did increase participation among men and those aged 50–59 years.[32]

Discussion

Lower rates of screening suggest that screening programmes are not meeting the needs of CALD populations. Disparities in screening were widespread but varied in magnitude from country to country by ethnicity, religion, birthplace and gender. The influence of gender on FOBT uptake varied between CALD populations differing from the wider literature where men tend to participate in CRC screening at a lower rate than women.[6] Lower screening among younger cohorts may be attributable to lower screening awareness, suggesting efforts to target early uptake would yield benefits.[30,42] Consistent with the wider literature, socioeconomic measures (SES, income, and education) were also positively associated with FOBT screening uptake.[6,64]

FOBT screening was influenced by a range of interrelated factors at the individual, interpersonal and system levels. Except for language and accessibility of translated materials, the barriers identified in this review are often present in the broader population; however, many beliefs and attitudes associated with lower screening uptake are more common in CALD populations.[15] Furthermore, the interaction between knowledge gaps, low screening programme awareness, misconceptions about screening and health beliefs are likely the result of exposure to the key antecedents of health communication, including media exposure, low engagement and lower perceived susceptibility.[26,42,47,63,65]

Faecal aversion, embarrassment and disgust appear to be more prevalent in CALD populations. Disgust has been found to have a low to moderate effect on FOBT screening in the general population.[66] The greater prevalence of faecal aversion may be because of cultural beliefs in some communities.[40,33,44,55–57,66–68] It is noteworthy that faecal aversion was not universal among all CALD groups.[24,31,33]

Fear of cancer was also more prominent in CALD populations.[15] Fatalistic beliefs also appear to be more prevalent in CALD populations mirroring that seen in the breast cancer screening literature.[15,21,55,38,40,61,69] Importantly, emotion-laden attitudes, such as faecal aversion, fatalism and fear, proved difficult to overcome.[45,55,57]

Culturally tailored group education shows promise for increasing screening in CALD populations. Two interventions in this review found that community-based, education programmes were able to increase CRC screening knowledge, awareness, screening intention and uptake.[29,45] Breast and cervical cancer studies have shown that culturally tailored education is effective in increasing screening uptake with ethnic minorities.[70,71] Community settings are particularly suitable for delivering culturally tailored interventions to CALD populations.[72]

Narratives may also help overcome the lack of engagement with fact-based information identified in Kobayashi et al.[63] Robb et al.[73] who also found that non-White ethnicity was associated with a lower preference for deliberation associated with evaluating fact-based information. In a realist review, Woudstra and Suurmond[74] have identified the mechanisms by which narratives can influence CRC screening behaviour. Further research is needed to explore the suitability of narratives for engaging CALD populations.

At the system level, efforts to make screening information accessible are required. Collection of language preferences could facilitate tailored screening invitations and reminders.[31] The GP may also be able to fulfil a role in promoting screening to hard-to-

reach groups.[75] GP endorsement letters have been used successfully in the general population.[76] Research to test translated invitations and preferred language telephone reminders should also be explored.[77]

The results of this review should be interpreted with caution. CALD populations consist of a diverse range of communities with differing needs. The results are not generalisable to all CALD populations. This scoping review identifies common factors influencing FOBT screening in CALD populations to inform research identifying the needs of specific CALD populations and formative research to develop interventions for specific subgroups.

Conclusion

This review highlights the relationship between the levels of influence and proposes multicomponent interventions to increase screening uptake. Features of successful community-level interventions should be explored further. In particular, the use of narratives shows promise for engaging CALD populations. Accessibility of screening information should be addressed at the system level. Leveraging the GP relationship in promoting FOBT screening programmes may also be an effective strategy to target 'hard-to-reach' populations. Fear, fatalism and disgust remain difficult barriers to overcome.

Author statements

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Competing interests

The authors report no conflicts of interest.

Appendix A. Supplementary data

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Guest Editorial

Health inequalities: responding to the challenge

Health inequalities or inequities can be defined as the "systematic, avoidable and unfair differences in health outcomes that can be observed between populations, between social groups within the same population, or as a gradient across a population ranked by social position."[1] The causes and appropriate policy responses to reduce health inequalities have been repeatedly described, but there has been little to no progress in reducing them or mitigating their effects.[2,3] Indeed, the economic policy decisions following the 2007 financial crash, which led to the implementation of austerity measures across many countries, the COVID-19 pandemic and repeated inflationary increases in the costs of living have continued to exacerbate the scale of health inequalities. This special issue seeks to make a contribution to how we understand and respond to persistent health inequalities.

Understanding the problem

The scale of the health inequalities challenge is illustrated in several articles in this issue, including the stark and avoidable mortality inequalities amongst children aged <5 years old in Colombia,[4] breast cancer mortality by ethnicity in Brazil[5] and by the inequalities in self-reported health across older adults in China.[6] In 2023, inequalities in health outcomes are not unexpected, given systemic inequalities in exposure to the wide array of influences that support and damage health. This is showcased in this special issue in terms of well-known health behaviours, such as inequalities in breastfeeding[7] and handwashing,[8] as well as digital determinants of health, such as internet broadband access.[9] Furthermore, it remains relevant to demonstrate the links between harmful exposures and health outcomes and how these are experienced unequally. To this end, one of the studies in the special issue demonstrated residents exposed to traffic-related air pollution, energy-related drilling, older housing stock and a lack of greenspace in Texas, USA, were more likely to visit hospital for exacerbations of asthma.[10]

The importance of a nuanced understanding of how inequalities operate is explored in the special issue using national survey data in the United States, which finds that the association between body mass index and diagnosis of type II diabetes, was found to vary substantially by ethnicity.[11] This has important implications for future research and practice, as it may represent differential access to services and diagnoses mediated via structural racism or real differences in how exposures are embodied intersectionally, further emphasising the need for context-specific understandings of disease processes and how they are structured by social and economic contexts.

Tools to support an improved research on intersectional health inequalities are now available,[12] which allow best use to be made of local health survey data,[13] and more novel data sources such as wearable technology,[14] to identify needs and provide a locus for intervention. However, the limitations of existing data remain all too apparent, as demonstrated by the problems in using area-based deprivation measures in Scotland to frame place-based approaches to reduce health inequalities.[15]

Evaluating interventions

However well we understand the scale and causes of health inequalities, it is even more important to understand what does and does not work to reduce them and the contexts in and populations for which policies and interventions are, and are not, effective. In this issue, we publish examples of both successes and failures.

In Chile, the provision of maternity leave was found to be insufficient to increase exclusive breastfeeding,[16] whilst in the United States, the imposition of tighter voting restrictions was associated with increases in teenage pregnancy, plausibly linked by reduced access to family planning services,[17] something likely to be further exacerbated by recent Supreme Court rulings. Even the delivery of preventive health care can exacerbate inequalities when the delivery systems do not sufficiently protect against structural discrimination, as was identified for COVID-19 vaccination coverage in Japan.[18]

On the other side, there are glimmers of hope. Innovative work to provide mobile phone technology to displaced Afghan evacuees in the United States speaks to the importance of addressing the modern determinants of health, particularly for populations with high needs for social connection and access to information.[19] That said, we have only one study in this special issue, which actually evaluates a substantive intervention and demonstrates a reduction health inequality trends. This study evaluated the impact of the health inequalities strategy in England between 1997 and 2010 and shows an improving trend in inequalities in Years of Life Lost overall and for specific causes of death between 2000 and 2010. Although it is an ecological study with only time trend controls for the periods before and after the strategy, and although it only evaluates the impacts on absolute inequalities, it does suggest that such strategies can be effective.[20] Unfortunately, the period after 2010 has seen a rapid reversal of this previous progress across the UK nations (and in many countries beyond) as a result of the austerity policies introduced, which have damaged the social fabric of society through rising poverty and cuts to public services.[21,22]

Addressing the health inequalities challenge will require bold policymaking and action. As a public health community, we must do all that we can to catalyse and support the forms of action most likely to be effective[2,3] whilst continuing our pursuit of improved understanding and evaluation of current interventions.

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Doing this necessitates intervention strategies addressing the very structures that potentiate suboptimal outcomes in some communities and not others. The measures and methods and study designs are complex. But the potential for effective intervention strategies addressing health inequities is significant by optimising individual and social resilience in normal times as well as during public health emergencies.

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Original Research

How do forms and characteristics of Asian public housing neighbourhoods affect dementia risk among senior population? A cross-sectional study in Hong Kong

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ABSTRACT

Background: Public housing estate is a key determinant of community health risk in American/European cities. However, how forms/characteristics of compact/hilly public housing's neighbourhoods affect dementia among Asian seniors was underestimated.
Design: This was a cross-sectional study.
Methods: A total of 2,077 seniors living in Hong Kong's public housing estates were included. Dementia was measured by a Cantonese version of Montreal – Cognitive Assessment. Built environment was measured based on three dimensions (greenery, walkability, accessibility), including 11 metrics. Circular buffers (without walking paths) and service areas (considering walking paths) with two-dimensional/three-dimensional (terrain) adjustment were applied to quantify forms/characteristics of neighbourhoods. Two spatial buffers were applied: immediate distance (200 m) and walkable distance (500 m). Exposure-by-exposure regressions were applied to evaluate the associations between form/characteristics of neighbourhood and dementia.
Results: Forms/characteristics without considering walking paths may overestimate health benefits from built environment. For circular buffers, higher percentage of building coverage, higher land use mix and more community/transportation/leisure facilities were negatively associated with dementia. All measures of greenery were positively associated with dementia. For service areas, measures of walkability and accessibility became insignificant except more community facilities at the immediate distance. Furthermore, terrain effect was insignificant when it was compared with the impacts of walking paths.
Conclusion: Dementia among seniors in hilly public housing estates was negatively associated with neighbourhood's walkability and accessibility and was influenced by walking paths. For healthy ageing, improved forms/characteristics of public housing neighbourhoods should include more accessible spaces and community facilities along walking paths for physical activities and basic daily needs.

Introduction

"Public housing estate" was originally conceived for pragmatic reasons.[1] Housing estate tended to fulfil basic living, with limited health/social support for vulnerable people (e.g. seniors). Public

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housing residents even in high-income countries were associated with health issues.[2,3]

Seniors with dementia could be more vulnerable among all subpopulations. As a common disorder related to senior's cognitive function in high-income countries,[4] dementia could directly influence self-management, physical activities and daily living,[5,6] resulting in unhealthy diet, low levels of mobility and physical activity. Recent studies have investigated the association between built environment and dementia among seniors based on the following dimensions: greenery, building form and local accessibility.[7–10] However, few studies have evaluated these environment–health relationships in public housing estates, perhaps because of their physical homogeneity in American/European cities. Thus, the socioenvironmental nexus of low-income housing estates influencing residents' dementia needs to be investigated.

Specifically, housing estates in Asian cities are not as homogeneous as those in European/American cities. Hilly terrain and compact environment may vary the environment–health associations. This living environment can be stressful. Seniors constitute the least mobility among all subpopulations, and their decreasing financial means may accentuate immobility. They are neighbourhood bound and are frequent users of local facilities for exercise and socialising. However, the “older residents” can be low socioeconomic status, and the earlier estates were generally of low quality and lacked community/health facilities. Thus, variations of forms and characteristics in these public housing estates could yield dementia risk among older residents.

This study evaluated how form/characteristics in public housing neighbourhoods may be associated with dementia among seniors in Hong Kong. Particularly, we evaluated whether slope/terrain and walking paths in hilly environment would yield the association between built environment and dementia.

Data and methods

Data collection

These data were retrieved from a baseline survey of an existing cohort.[23,24,31] After removing four subjects with invalid data, a total of 2,077 subjects were included.

Specifically, the cohort study was originally conducted between 2014 and 2017, with participants aged ≥65 years living in 12 selected estates managed by Hong Kong Housing Society (Fig. 1). These included estates in urbanised areas and suburbs. More than half of these estates were located in the hilly environment (Fig. 2).

For baseline survey, all subjects were Cantonese-speaking Chinese tenants interviewed in 2014 and were randomly sampled within the following age strata: 65–74, 75–84 and ≥85. The target sample sizes for these age strata were 50, 60 and 70, respectively, resulting in a total of 180 subjects per estate. Oversampling for 75–84 and ≥85 years were taken into account due to the higher attrition rates. In addition, all interviews were conducted during home visits by trained researchers. More information regarding data collection's procedures has been noted in previous studies.[23]

Data collection was approved by the Human Research Ethics Committee, The University of Hong Kong (No: EA050814). All participants signed a written informed consent.

Health outcome

Dementia was measured based on a Cantonese version of Montreal – Cognitive Assessment.[11] Subjects with Cantonese version of Montreal – Cognitive Assessment ≤19 were with dementia symptoms.

Forms/characteristics of neighbourhoods

Four types of neighbourhoods were determined: (1) two-dimensional/three-dimensional (2D/3D) circular and (2) 2D/3D service area. *Circular* is a traditional measurement of neighbourhood based on a circular buffer drawn from the central point of a building. Environmental characteristics within the buffer were included without consideration of walking paths. *Service area* was an advanced measurement based on walking paths. 2D buffers did not adjust for slope/terrain. 3D buffers were with terrain adjustment. Two different scales were applied to determine the living environment: immediate distance (200 m) and walkable distance (500 m) from their residence. Immediate distance was associated with approximately six minute walk of seniors in Hong Kong. Walkable distance was associated with approximately 15-min walk. The above buffers have been used in other local studies.[21–24]

Built environment metrics

Built environment were measured based on the following dimensions: greenery, walkability and accessibility (Fig. 3).

Measures of Greenery included (1) % greenery, (2) greenness and (3) green heterogeneity. *%greenery* referred to percentage of natural greenery. It was mapped with a supervised classification with Google Earth Engine.[12] *Greenness* referred to the intensity of natural greenery and was calculated by the average of Normalized Difference Vegetation Index (NDVI). NDVI was calculated from red and near-infrared bands of a 2016 SPOT-6 multispectral satellite image.[13] Higher NDVI indicated more greenness. *Green heterogeneity* represented the mixture of natural greenery/non-greenery.[14] This measure was estimated based on the standard derivation of NDVI.

Measures of walkability included (1) %public space, (2) %building coverage and (3) land use mix. All measures were associated with Jane Jacob's theory of vitality and diversity.[15] *%public space* represented vitality and diversity of public open space designed and managed by the local government, including spaces for leisure, culture and sport activities. Higher percentage of public space implied a neighbourhood with better social connection and mobilisation. *%building coverage* represented the percentage of building footprint. According to Jacob's theory, small building blocks could enhance physical and social contacts among people, and sufficient concentration of buildings could sustain social connection. *Land use mix* was estimated by the equation noted elsewhere.[16] Five types of land use were included: residential lands, commercial/industrial lands, institutional lands, public space and others. Land use mix indicated diversified building types/services and attraction to walk around the neighbourhoods. Greater land use mix indicated higher walkability. All walkability measures were retrieved from Hong Kong's 1:1000 topographic (ib1000) map (https://data.gov.hk/en-data/dataset/hk-landsd-openmap-development-hkms-digital-b1k).

Measures of accessibility included (1) major transportation facilities, (2) facilities for municipal services, (3) community facilities, (4) leisure facilities and (5) health facilities. The spatial information was retrieved from the Hong Kong's GeoCommunity Database 3.0.

We set intervals of %greenery, %public space and %building coverage as 10% and intervals of greenness, green heterogeneity and land use mix as 0.1.

Covariates

Following our prior study using the same cohort,[31] covariates of medical history included cardiovascular disease, stroke, osteoporosis, chronic obstructive pulmonary disease, pain, depression,

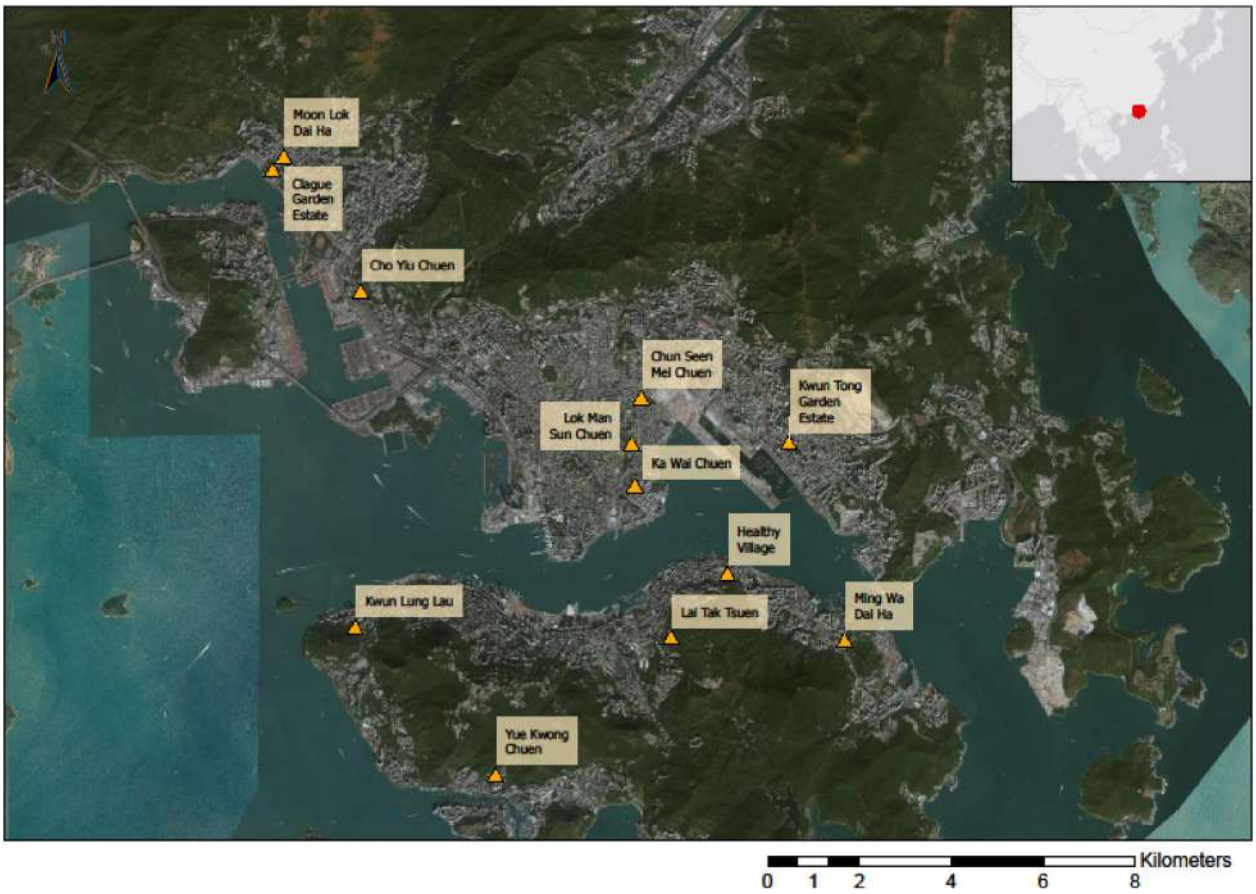

Fig. 1. Study area: twelve selected public housing estates in Hong Kong.

Fig. 2. Hilly environment of the selected public housing estates. Lai Tak Tsuen (left) is a public housing estate in a suburb near a middle-class neighbourhood. Cho Yiu Chuen (middle) is a public housing estate in a new town. Kwun Tong Garden Estate (right) is a public housing estate in an urbanised area near a low-income neighbourhood and industrial area.

walking ability and frailty. Depression was measured based on a Chinese version of Geriatric Depression Scale-15.[17] Frailty was estimated by the five item FRAIL Questionnaire.

Covariates regarding sociodemographic information and lifestyle characteristics included age, gender, body mass index (BMI), sleep quality, smoking status, alcohol consumption, low education, unhealthy diet, quality of life and activities of daily living. Quality of life was calculated based on the EUROHIS-QOL eight item index. The score of activities of daily living was calculated based on the Chinese version of Lawton Instrumental Activities of Daily Living scale (IADLs).[18] Low education was defined as individuals who only completed primary school or below .[19] Missing information was replaced with the average score of each measure.[20]

Statistical analyses

Exposure-by-exposure binomial regressions were used to evaluate the relationship between built environment metrics and

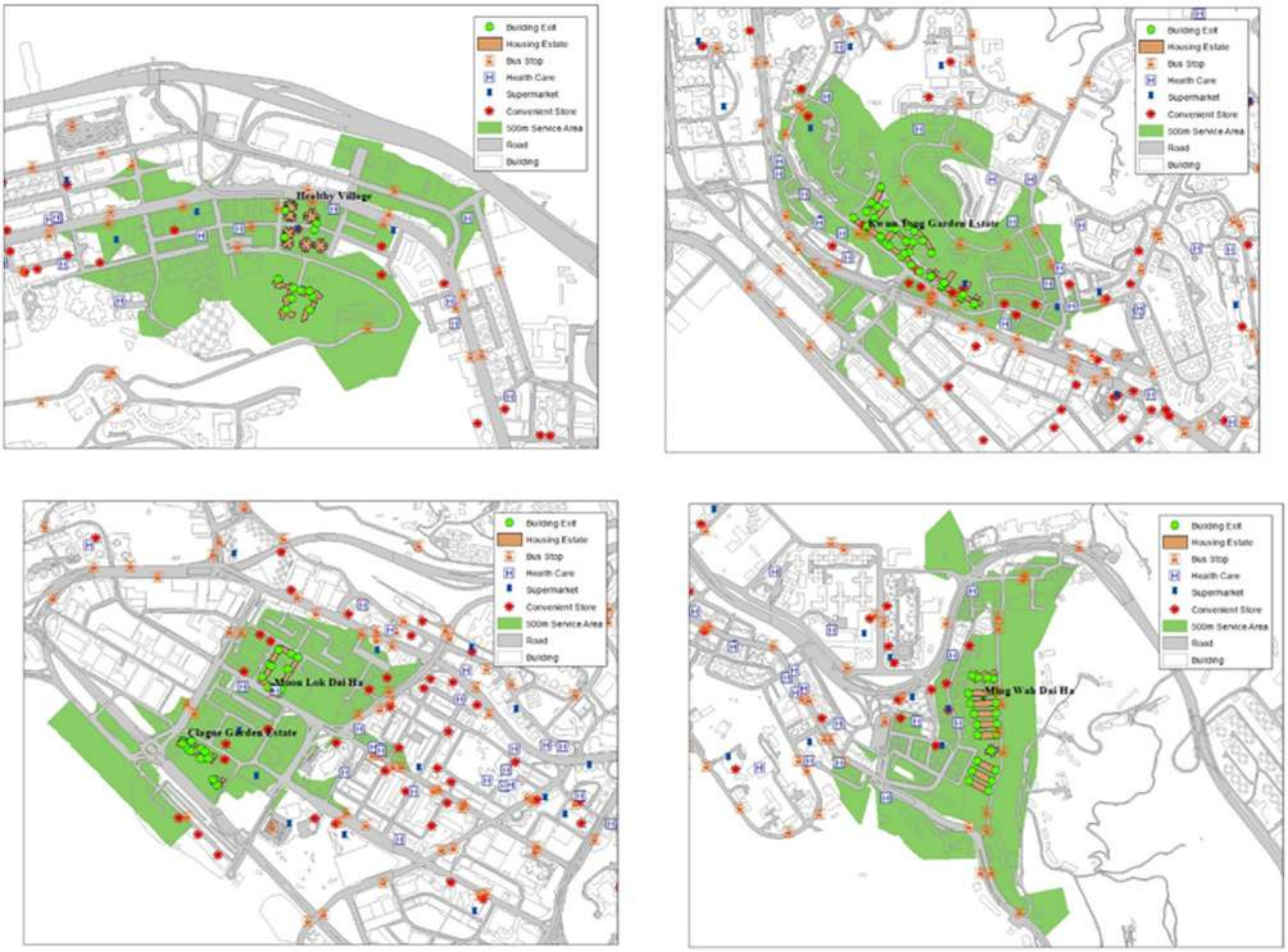

Fig. 3. Examples of greenery and facilities surrounding five of the 12 selected public housing estates. Healthy village (top left) and Ming Wah Dai Ha (bottom right) are public housing estates located in urbanised areas of Hong Kong Island. Kwun Tong Garden Estate (top right) is a public housing estate in an urbanised area near a low-income neighbourhood and industrial area of Kowloon. Clague Garden Estate and Moon Lok Dai Ha are public housing estates located in a new town of new territories.

dementia. Crude and adjusted odds ratios (ORs) for all regressions with 95% confidence intervals (CIs) were reported. Covariates regarding medical history, lifestyle and sociodemographic characteristics were selected based on Variance Inflation Factor <2 to minimise multicollinearity. Based on the results of Variance Inflation Factor, covariates for final models included IADLs, age, cardiovascular disease, stroke, chronic obstructive pulmonary disease, pain, depression, walking ability, frailty, low education, gender, BMI, quality of life, sleep quality, smoking status, alcohol consumption, unhealthy diet and osteoporosis. The previously mentioned factors were associated with dementia or cognitive functions.

Results

Data summary

Among 2,077 subjects, 859 subjects (41.4%) were associated with dementia (Table 1). These subjects were generally overweight (average BMI >23 kg/m^2). Subjects with dementia had significant differences in lifestyle and sociodemographic characteristics from those without dementia (Table 1). Particularly, the subjects with dementia were older ages (83.0 vs 77.3), more likely to be female (60.1% vs 55.2%), lower BMI (23.5 vs 23.8), less educated (88.4% vs 71.3%), lower quality of life (28.6 vs 29.31) and lower IADLs (13.8 vs 15.6). However, *t*-tests did not show significant differences in smoking status and alcohol consumption among subjects with and without dementia.

T-test results for medical history indicated that subjects with dementia were more associated with depression, lower ability to walk and frailty compared with subjects without dementia. About 12.8% of subjects with dementia found to have depressive symptoms, but only 9.2% subjects without dementia were associated with depression (*P*-value <0.05). Approximately 14.3% subjects with dementia reported to have problems to walk independently, but only 8.3% subjects without dementia reported to have this issue (*P*-value <0.05). Approximately 16.5% of subjects with dementia were associated with frailty, but only 8.7% of subjects without dementia were associated with frailty (*P*-value <0.05).

Local characteristics of built environment

Without consideration of walking paths and terrain/slope, all subjects were living in a high-density environment with mixed land uses (Table 2). The results of 2D circular buffers showed that the seniors of public housing estates were living with average 27.1% building coverage, 33.2% greenery and 8% public spaces within a 500-m radius. The land use mix within 500 m was 0.64, indicating a multifunctional neighbourhood. There were mostly more than two facilities for municipal services (e.g. bazaar, cooked fool stall,

Table 1
Summary of lifestyle and sociodemographic characteristics and medical history of all subjects (N = 2,077) in the analytic data set.

Dimension	Variable	With dementia	Without dementia	*t*-test
		n = 859	*n* = 1,218	*P*-value
Lifestyle and sociodemographic characteristics	Age	**83.0**	**77.3**	**<0.05**
	Gender	**60.1%**	**52.2%**	**<0.05**
	BMI	**23.5**	**23.8**	**<0.05**
	Sleep quality	16.5%	14.7%	0.26
	Smoking status	7.0%	7.0%	0.996
	Alcohol consumption	0.8%	1.5%	0.15
	Low education	**88.4%**	**71.3%**	**<0.05**
	Unhealthy diet	3.7%	4.5%	0.37
	Quality of life	**28.6**	**29.3**	**<0.05**
	Instrumental activities of daily living (IADLs)	**13.8**	**15.6**	**<0.05**
Medical history	Cardiovascular disease	18.3%	16.8%	0.40
	Stroke	7.6%	6.1%	0.19
	Chronic obstructive pulmonary disease	1.0%	0.9%	0.74
	Pain	9.4%	8.0%	0.27
	Depression	**12.8%**	**9.2%**	**<0.05**
	Walking ability	**14.3%**	**8.3%**	**<0.05**
	Frailty	**16.5%**	**8.7%**	**<0.05**
	Osteoporosis	11.5%	12.0%	0.75

Bold values indicate a significant difference between subjects with and without physical/cognitive functions based on t-test.

Table 2
Summary: local characteristics of built environment among all subjects (N = 2,077) in the analytics.

Built environment	2D circular				3D service area			
	Minimum	Maximum	Mean	SD	Minimum	Maximum	Mean	SD
Greenery (200 m)	3.6%	66.5%	**29.9%**	16.6%	1.0%	36.8%	**16.8%**	10.3%
Greenery (500 m)	8.0%	68.9%	**33.2%**	20.5%	5.8%	56.7%	**26.9%**	15.0%
Greenness (200 m)	0.14	0.57	**0.32**	0.11	0.15	0.40	**0.25**	0.07
Greenness (500 m)	0.15	0.59	**0.33**	0.14	0.15	0.51	**0.30**	0.10
Green heterogeneity (200 m)	0.09	0.30	**0.22**	0.06	0.07	0.25	**0.16**	0.05
Green heterogeneity (500 m)	0.14	0.32	**0.24**	0.06	0.11	0.29	**0.21**	0.06
% Public space (200 m)	0.0%	31.9%	**6.9%**	6.2%	0.0%	24.5%	**4.9%**	7.4%
% Public space (500 m)	1.0%	27.0%	**8.0%**	6.9%	0.5%	25.7%	**5.2%**	4.9%
% Building coverage (200 m)	10.6%	47.7%	**29.2%**	9.0%	18.5%	45.5%	**30.4%**	6.9%
% Building coverage (500 m)	11.3%	43.7%	**27.1%**	10.5%	11.3%	46.3%	**30.4%**	8.3%
Land use mix (200 m)	0.47	0.89	**0.70**	0.09	0.24	0.98	**0.72**	0.17
Land use mix (500 m)	0.48	0.84	**0.64**	0.08	0.55	0.84	**0.69**	0.08
Major transportation (200 m)	0	9	**2.5**	2.8	0	7	**0.7**	1.3
Major transportation (500 m)	2	20	**10.4**	5.5	0	12	**3.8**	3.3
Municipal services (200 m)	0	4	**0.8**	1.0	0	1	**0.1**	0.3
Municipal services (500 m)	0	5	**2.6**	1.4	0	4	**1.3**	1.2
Community facilities (200 m)	4	28	**14.8**	6.5	0	13	**5.5**	3.6
Community facilities (500 m)	26	84	**57.1**	14.3	8	47	**23.8**	9.8
Leisure facilities (200 m)	1	14	**6.2**	2.7	0	6	**1.5**	1.6
Leisure facilities (500 m)	11	57	**30.2**	9.5	1	18	**8.2**	3.6
Health facilities (200 m)	0	8	**2.2**	2.2	0	5	**0.6**	1.1
Health facilities (500 m)	0	21	**11.0**	5.6	0	10	**4.2**	3.1

2D, two-dimensional; 3D, three-dimensional; SD, standard deviation.
Two definitions of neighbourhoods separately applied to measure the local characteristics.

municipal complex, market, refuse collection point, toilet, wholesale market) within this walkable distance, as well as multiple spots of major transportation facilities, community facilities, leisure facilities and health facilities.

Considering walking paths and terrain/slope, all subjects were actually living in a more compact environment than the estimations from 2D models. The results of 3D services showed that seniors were living with averagely 30.4% building coverage, 26.9% greenery and 5.2% public spaces within a 500-m radius. Compactness did not eliminate land use diversity. Land use mix within 500 m was 0.69, which was even higher than the value calculated based on 2D circular. Furthermore, seniors averagely had at least one facility of municipal service within walkable distance. The number of other types of facilities was significantly lower than the results of 2D circular. However, there was still at least one spot of each type of facility within the walkable distance.

Built environment and dementia

There were significant differences in results when we compared the groups of circular buffers and service areas. Without consideration of walking paths (2D/3D circular), most measures related to walkability and accessibility were negatively associated with dementia (Table 3). Higher %building coverage in an immediate distance and a walkable distance were negatively associated with dementia (adjusted ORs for 2D circular: 0.90 [0.80, 0.998], 0.88 [0.80, 0.96]). Higher land use mix in a walkable distance was also negatively associated with dementia (adjusted OR for 2D circular: 0.84 [0.75, 0.95]). Furthermore, more community facilities and major transportation facilities within an immediate distance/walkable distance and more leisure facilities within an immediate distance had negative association with dementia. However, when walking paths were considered (2D/3D service area), most

Table 3
Association between built environment and dementia.

Built environment	2D circular		2D service area		3D circular		3D service area	
	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR
% Greenery (200 m)	**1.09 [1.04, 1.15]**	**1.11 [1.05, 1.18]**	1.04 [0.95, 1.13]	1.06 [0.97, 1.16]	**1.09 [1.03, 1.16]**	**1.12 [1.05, 1.19]**	1.04 [0.95, 1.13]	1.06 [0.97, 1.16]
% Greenery (500 m)	***1.09 [1.05, 1.14]***	***1.10 [1.05, 1.15]***	**1.11 [1.05, 1.18]**	**1.12 [1.05, 1.20]**	**1.10 [1.05, 1.14]**	**1.10 [1.05, 1.16]**	***1.11 [1.05, 1.17]***	***1.12 [1.05, 1.20]***
Greenness (200 m)	**1.14 [1.05, 1.23]**	**1.18 [1.08, 1.28]**	1.07 [0.94, 1.22]	1.13 [0.98, 1.30]	**1.13 [1.04, 1.23]**	**1.18 [1.08, 1.30]**	1.07 [0.94, 1.23]	1.13 [0.97, 1.31]
Greenness (500 m)	***1.13 [1.06, 1.20]***	***1.14 [1.07, 1.22]***	**1.16 [1.06, 1.26]**	**1.19 [1.08, 1.31]**	**1.13 [1.06, 1.21]**	**1.15 [1.07, 1.23]**	***1.15 [1.06, 1.26]***	***1.18 [1.07, 1.30]***
Green heterogeneity (200 m)	**1.29 [1.11, 1.48]**	**1.32 [1.13, 1.55]**	1.14 [0.96, 1.34]	1.20 [0.995, 1.44]	**1.27 [1.09, 1.47]**	**1.31 [1.12, 1.54]**	1.13 [0.96, 1.34]	1.20 [0.99, 1.44]
Green heterogeneity (500 m)	***1.30 [1.12, 1.50]***	***1.32 [1.13, 1.55]***	**1.35 [1.16, 1.58]**	**1.38 [1.16, 1.64]**	**1.31 [1.13, 1.52]**	**1.34 [1.14, 1.59]**	***1.34 [1.15, 1.57]***	***1.37 [1.15, 1.63]***
% Public space (200 m)	1.02 [0.88, 1.17]	0.96 [0.83, 1.13]	0.95 [0.85, 1.07]	0.97 [0.86, 1.13]	0.99 [0.84, 1.15]	0.95 [0.80, 1.12]	0.96 [0.85, 1.08]	0.99 [0.87, 1.13]
% Public space (500 m)	1.05 [0.92, 1.19]	1.02 [0.88, 1.17]	0.96 [0.80, 1.16]	0.94 [0.77, 1.14]	1.04 [0.92, 1.18]	1.01 [0.89, 1.16]	0.96 [0.80, 1.15]	0.94 [0.77, 1.14]
% Building coverage (200 m)	0.94 [0.85, 1.03]	**0.90 [0.80, 0.998]**	1.12 [0.99, 1.27]	1.02 [0.88, 1.17]	0.94 [0.86, 1.04]	0.91 [0.82, 1.00]	1.13 [0.99, 1.28]	1.03 [0.89, 1.18]
% Building coverage (500 m)	**0.90 [0.83, 0.98]**	**0.88 [0.80, 0.96]**	0.97 [0.87, 1.07]	0.93 [0.83, 1.04]	**0.90 [0.82, 0.98]**	**0.88 [0.80, 0.97]**	0.97 [0.87, 1.07]	0.93 [0.83, 1.05]
Land use mix (200 m)	0.997 [0.89, 1.11]	0.97 [0.86, 1.09]	0.9996 [0.95, 1.05]	0.99 [0.94, 1.05]	0.99 [0.91, 1.08]	0.99 [0.90, 1.10]	0.999 [0.95, 1.05]	0.99 [0.94, 1.05]
Land use mix (500 m)	**0.86 [0.77, 0.96]**	**0.84 [0.75, 0.95]**	0.91 [0.82, 1.02]	0.92 [0.82, 1.04]	**0.83 [0.74, 0.93]**	**0.80 [0.71, 0.91]**	0.91 [0.81, 1.02]	0.92 [0.81, 1.04]
Major transportation (200 m)	**0.97 [0.95, 0.9996]**	**0.97 [0.94, 0.995]**	0.97 [0.90, 1.04]	0.94 [0.87, 1.01]	**0.96 [0.92, 0.99]**	**0.95 [0.91, 0.99]**	0.97 [0.90, 1.04]	0.94 [0.87, 1.01]
Major transportation (500 m)	**0.98 [0.97, 0.997]**	**0.98 [0.97, 0.997]**	1.01 [0.99, 1.04]	1.00 [0.97, 1.03]	**0.98 [0.97, 0.999]**	**0.98 [0.96, 0.997]**	1.01 [0.99, 1.04]	1.00 [0.97, 1.03]
Municipal services (200 m)	1.00 [0.92, 1.10]	0.95 [0.86, 1.04]	1.11 [0.86, 1.45]	1.09 [0.82, 1.46]	1.01 [0.91, 1.13]	0.96 [0.85, 1.07]	1.11 [0.86, 1.45]	1.09 [0.82, 1.46]
Municipal services (500 m)	0.96 [0.90, 1.02]	0.94 [0.88, 1.01]	1.01 [0.93, 1.08]	0.98 [0.90, 1.06]	0.98 [0.91, 1.05]	0.96 [0.89, 1.04]	1.01 [0.93, 1.08]	0.98 [0.90, 1.06]
Community facilities (200 m)	0.99 [0.97, 1.00]	***0.98 [0.97, 0.998]***	**0.98 [0.95, 0.9998]**	**0.97 [0.94, 0.997]**	**0.98 [0.97, 0.996]**	**0.98 [0.96, 0.995]**	***0.97 [0.95, 0.997]***	***0.97 [0.94, 0.99]***
Community facilities (500 m)	0.99 [0.99, 1.00]	**0.99 [0.99, 0.999]**	0.997 [0.989, 1.01]	0.99 [0.98, 1.00]	**0.99 [0.98, 0.995]**	**0.99 [0.98, 0.99]**	0.997 [0.99, 1.01]	0.99 [0.98, 1.00]
Leisure facilities (200 m)	**0.97 [0.94, 0.99]**	**0.96 [0.94, 0.99]**	1.03 [0.98, 1.09]	1.01 [0.95, 1.07]	0.99 [0.95, 1.02]	0.97 [0.93, 1.01]	1.03 [0.98, 1.09]	1.01 [0.95, 1.07]
Leisure facilities (500 m)	0.997 [0.99, 1.01]	0.999 [0.99, 1.01]	0.99 [0.97, 1.02]	0.98 [0.96, 1.01]	1.00 [0.99, 1.01]	1.00 [0.99.1.02]	0.99 [0.97, 1.01]	0.98 [0.96, 1.01]
Health facilities (200 m)	1.01 [0.98, 1.05]	1.01 [0.97, 1.04]	1.06 [0.98, 1.15]	1.02 [0.94, 1.11]	1.01 [0.97, 1.06]	0.997 [0.95, 1.05]	1.06 [0.98, 1.14]	1.02 [0.94, 1.11]
Health facilities (500 m)	0.9997 [0.99, 1.01]	0.998 [0.98, 1.01]	1.02 [0.99, 1.05]	1.01 [0.98, 1.04]	1.01 [0.99, 1.02]	0.998 [0.98, 1.02]	1.02 [0.996, 1.05]	1.01 [0.98, 1.04]

2D, two-dimensional; 3D, three-dimensional; CI, confidence interval; OR, odds ratio.
Bold values indicate a significant result from a model for a specific type of neighbourhood measurement. Bold and italicised values indicate the result with consistency for a measure of built environment based on whether OR and 95% CI from all model.

measures of walkability and accessibility became insignificant, except community facilities. For 3D service area, adjusted OR for more community facilities at the immediate distance was 0.97 [0.94, 0.99].

All measures of greenery from all types of spatial buffers had positive associations with dementia. For 3D service area, 10% increase in greenery within a walkable distance was positively associated with dementia (adjusted OR: 1.12 [1.05, 1.20]). An increase by 0.1 in greenness and green heterogeneity also resulted in adjusted ORs of 1.18 (1.07, 1.30) and 1.37 (1.15, 1.63).

In addition, the results did not show significant differences when we compared 2D and 3D service areas. The results between 2D and 3D circular buffers also did not indicate significant differences. It indicated that terrain effect was insignificant when walking paths were included in modelling.

Discussion

This study used four forms/characteristics of neighbourhoods (2D/3D circular and 2D/3D service area) with two spatial distances (200 m and 500 m) to evaluate the association between built environment and dementia across hilly public housing estates in Hong Kong. Overall, measures of walkability and accessibility were negatively associated with dementia, but measures of greenery were positively associated with dementia. Specifically, public spaces were not associated with dementia, whereas leisure and transportation facilities as well as land use mix and building coverage were only significant in the case of circular buffers where no consideration was given to walking paths. In the case of service area by which attention was given to walking paths, the only significant result related to walkability and accessibility was the negative association between community facilities and dementia.

These results were somewhat consistent with dementia research in American cities. For example, neighbourhoods in North America with better community resources and higher proximity to public transport and public space were associated with slower rate of cognitive decline.[7] These findings have particular relevance to public housing estates in Asian metropolitans, as they were often more compact and more densely populated than cities in the West,[32] including denser networks of community facility provision and public transport services.

Our results were also somewhat consistent with local studies[9,24] and several studies in other Asian cities.[10,25] Specifically, Guo et al.[9] found that neighbourhood library accessibility and neighbourhood walkability in Hong Kong were negatively associated with dementia, but neighbourhood recreational accessibility was not associated with dementia. Liu et al.[25] conducted a large population-based study in Taiwan (n = 26,206) and found that community centre availability was significantly associated with 8% decreased odds for dementia. However, greenery was not associated with dementia. Echoing the above results as well as the discussion of Guo et al.,[9] the contradictory association of walkability and greenery/public space with dementia could be due to the unfriendly design of urban greenery. In our study area, natural greenery was an unfavourable and inaccessible environment mainly found on the hilly slope (Fig. 4). Furthermore, our descriptive statistics showed a great difference in percentages of greenery and public spaces from the circular and service area's results, which further implied that public spaces in Hong Kong may not necessarily be “green” and urban greenery may be inaccessible. This specific characteristic of Hong Kong has also been noted in recent studies.[22,26] In addition, our subjects with dementia were individuals with lower quality of life and IADLs. Subjects with dementia were also associated with depression, frailty and lower walking ability. Thus, rurality and inaccessibility as well as sense of fear could be reasons behind these results. Linking to local context, Hong Kong's hilly terrain and inaccessible greenery may negatively affect the seniors' fear and the motivation to move around, which further influencing their abilities of spatial navigation. As a result, dementia risk was increased.

Fig. 4. Example of inaccessible greenery on the hilly slope nearby the selected public housing estates.

Advancing from previous studies, we considered various forms/characteristics of neighbourhoods with/without terrain and walking path's adjustment. Our results indicated that neighbourhood mapping without considering walking paths (2D/3D circular) might over-highlight health benefits of local built environment. Although the differences in effect sizes between results in circular buffers and service areas were not large (<10%), bias in using circular buffers was still notable. Specifically, most built environment metrics found to be significantly associated with dementia in circular buffers were insignificant in 2D/3D service area's analyses. This indicated the needs in considering walking paths. Based on our results, community plans for the facilitation of health care and resources should focus on enhancing spatial navigation and physical activities among seniors. For better healthy living, we suggested that improvements regarding design of public housing estates should include building more community facilities, major transportation facilities and leisure facilities along walking paths. With the walking paths, negative effects of steep slopes could be minimised. Otherwise, the functionality of these facilities might be reduced because of inaccessibility even the spatial distance may be close.

Several limitations should be noted. First, we followed previous studies to use home address to map the living environment. However, activity spaces of urban population could be different from living environment surrounding home.[27,28] Previous studies also found differences in daytime and night-time human behaviours in Asian cities, which induced various scenarios of environmental inequality.[27] However, seniors generally had lower ability to walk and were more locally bound, especially those with dementia. Thus, using home address to map the neighbourhoods may still be appropriate.

Our subjects were Cantonese-speaking Chinese tenants without known psychiatric disorder due to a prescreening test. This prescreening excluded individuals medically diagnosed with dementia. As these patients had high difficulties in self-management, they would mostly be living in institutional settings or staying in indoor environments. As our study focused on the associations between outdoor environment and dementia, exclusion was considered appropriate.

We followed previous studies to assume a linear relationship between built environments and dementia. However, relationships between environmental factors (e.g. greenspace) and health outcomes could be non-linear[29] and may be mediated by other neighbourhood effects.[30] Path analysis and non-linear models should be considered to further explore the relationships between built environment and dementia.

Conclusions

We evaluated how forms/characteristics of hilly public housing neighbourhoods may affect the association between built environment and dementia among low-income seniors in Hong Kong. We found that walking paths could affect the results, and this effect was much more significant than influences from terrain. Along walking paths, more community facilities within an immediate distance were negatively associated with dementia, but more greenery, greenness and green heterogeneity within a walkable distance were positively associated with dementia. This indicated that a walkable neighbourhood with more spaces for physical activities as well as for meeting basic requirements of daily living (e.g. groceries, local healthcare) is needed. Furthermore, measurement of neighbourhood effect should be linked with local terrain and road networks so that community plans to optimise a self-managed lifestyle could be developed effectively and appropriately.

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Original Research

‘I don't really associate climate change with actual people's health’: a qualitative study in England of perceptions of climate change and its impacts on health

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ABSTRACT

Objectives: The health impacts of climate change are increasing, but qualitative evidence on people's perceptions is limited. This qualitative study investigated people's perceptions of climate change and its impacts on health.
Study design: This was an online study using semistructured interviews.
Methods: A total of 41 semistructured interviews were conducted in 2021 with members of the public aged ≥15 years living in England, recruited via community-based groups. Data were analysed using reflexive thematic analysis.
Results: Participants were concerned about climate change, which was often perceived as extreme weather events happening elsewhere. Changes in the UK's seasons and weather patterns were noted, but participants were uncertain whether these changes resulted from climate change. Participants often struggled to identify health impacts of climate change; where health impacts were described, they tended to be linked to extreme weather events outside the United Kingdom and their associated threats to life. The mental health impacts of such events were also noted.
Conclusions: The study found that most participants did not perceive climate change to be affecting people's health in England. This raises questions about whether framing climate change as a health issue, an approach advocated for countries less exposed to the direct effects of climate change, will increase its salience for the British public.

Introduction

Climate change is placing people's health at increasing risk, both globally[1–3] and within the United Kingdom.[4,5] Rising global temperatures are increasing the frequency, duration and severity of extreme weather events,[1,6,7] including flooding and heat waves in the United Kingdom,[8,9] exposures set to increase over time and across generations.[10] Highlighting the health impacts of climate change is advocated as a way of bringing climate change ‘closer to home’,[11,12] particularly in high-income countries that, to date, have been less exposed to the direct effects of climate change.[13–15] A ‘health framing’ is seen to provide a way for public health policy and practice to connect climate change with people's everyday concerns.[12,16,17]

However, evidence for such a framing is mixed. A 2018 review of studies of public perceptions of the health impacts of climate change noted that in English-speaking countries, there was a divergence between studies using closed- and open-ended questions. In response to closed questions, the majority of participants perceived climate change as harmful to human health, a finding in line with UK surveys.[18,19] However, responses to open-ended questions indicated that participants struggled to make connections between climate change and health.[20] In the single UK study within the review,[21] the majority did not perceive themselves to be at risk. Updating this review (additional file, Table S1), we located a further qualitative study in Canada,[22] where the majority of participants perceived climate change as a problem from which they were spatially and temporally distant. Our qualitative study adds to

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this small evidence base by exploring perceptions of climate change and its impacts on people's health in England.

Methods

The study was approved by the Health Sciences Research Governance Committee, University of York (ref: HSRGC/2020/409/C; 11/9.20).

Setting and participants

Participants aged ≥15 years were recruited via community groups, including local residents' groups, activity- and identity-based groups (e.g. walking and faith groups) and age-related groups (e.g. young people's groups). The groups were selected to reach into different communities, including members of the public from different age groups and social backgrounds and living in different areas (rural villages, small towns, and cities). We included participants aged <18 years to ensure the voice of future generations was represented in the study.

COVID-19 and the associated restrictions on people's everyday lives[23] meant many community groups were either suspended or limited to core support for members, restricting the range of community groups participating in the study. The pandemic context – with government-imposed 'lockdowns' requiring the public to 'stay at home' and limit social contact to a minimum – also required a change in the study design. We shifted from in-person, community-based focus groups to one-to-one online and telephone interviews.[24–26] Online interviews complied with government regulations and, arranged at a time of the individual's choosing, minimised the participant burden during a period of major disruption in people's everyday lives.

A poster circulated via group coordinators (Table S2) invited potential participants to seek further information about the study. This information (Table S3) noted that '*We are wanting to speak to people across England about their thoughts on climate change and whether they think climate change has an impact on their health. We are wanting to speak with people who have different experiences and views of climate change.*' Informed consent (assent and parental consent for participants aged 15 years) was obtained. Participants received a voucher of £10 to thank them for their time.

The sample comprised 41 participants recruited from 19 community groups (Tables S4 and S5). More than half of the participants were aged ≥60 years (compared with 23% in the wider population), and more than 60% were male. Based on the Index of Multiple Deprivation, a measure of relative deprivation at local level, participants were overrepresented in the more and less deprived deciles; with respect to its health profile, the sample was more evenly distributed across deciles[27] (Table S6).

Interview schedule

The interview guide was informed by the review of the perceptions literature and developed iteratively by the wider project team. Interviews began with open-ended questions about perceptions of climate change and people's health. UK photographs of *'climate-related events likely to become more common with climate change'* were then introduced as prompts to elicit further thoughts and accounts of experiences (Table S7).

Data collection

Between January and October 2021, individual semistructured interviews of ≤60 min were conducted online/by telephone (with one participant providing responses by email) by J.M.K., an Australian/British White female qualitative researcher whose previous research had not focused on climate change. Interviews were digitally recorded, transcribed and pseudonymised by participant number. J.M.K. maintained a summary of interviews with notes made immediately after each interview.

Data analysis

Using NVivo,[28] reflexive thematic analysis was conducted.[29,30] This iterative process involves data familiarisation, line-by-line coding, generation of initial themes and review, further development and refinement of themes. Following Braun and Clarke's methodology,[31] one researcher (J.M.K.) undertook the analysis, generated initial codes and developed themes relating to perceptions of climate change and its health impacts. Themes were discussed and refined with P.L., H.G. and the wider project team. Trustworthiness[32,33] was protected by each of these analysis stages, including in-depth immersion in the data, and ensuring that the themes captured recurring patterns across the data set. An iterative process of internal triangulation was undertaken, and themes were discussed and refined collectively by the project team. We consistently reviewed the themes and the supporting data to ensure that our findings were based on what people said and that each theme was cohesive. In addition, rich verbatim accounts are included to support the findings. A summary of findings was made available to the study participants; all opted to receive it.

Results

Our analysis produced themes related to perceptions of climate change (two themes) and to perceptions of health impacts (two themes).

Perceptions of climate change

Although most participants reported being 'very concerned' about climate change, they did not perceive it as an immediate threat to people in the United Kingdom. It was seen as distant from participants' lives, unfolding in other areas of the world and across future generations. Britain's temperate climate and the unpredictability of its weather added to uncertainties about whether climate change was affecting the United Kingdom. These two themes are discussed below and illustrated in Table 1.

Theme 1: Climate change at a distance

When asked about climate change, participants often described extreme impacts beyond the United Kingdom. They talked about cyclones in Bangladesh, wildfires, drought and flooding in *'developing countries'* and countries with *'more extreme climates'* (e.g. Australia) with *'vast areas'* impacted by wildfires (e.g. California), heatwaves (France) and flooding (Germany). They described *'severe'* and *'devastating'* impacts in these countries, often referring to images in the media. In addition, the term 'global warming' implied a process located beyond the United Kingdom, while in the United Kingdom, '*we can't put our finger on it [climate change], you know, we can't*' (P16, male, aged 40–49 years). Some participants commented on their experiences, either direct experiences or via the media, of extreme weather events in the United Kingdom, particularly floods, but were not sure these were related to climate change.

With climate change described in terms of extreme weather events in other countries, it tended to be perceived as a future, rather than a current, threat to the United Kingdom. Participants with children described '*worry*', '*concern*' and '*fear*' about future generations of their family: '*End of the world. Not for me, but more*

Table 1
Perceptions of climate change.

Theme	Supporting quotes
Climate change at a distance: happening elsewhere and in the future	*Images on the news come to mind straight away. It's those kind of images that I see, you know, forest fires in California and that, and those places in Florida and stuff, and just to see all that happening, it's those images that come to mind straight away.* (P17, male, aged 40–49 years) *In Britain, we're not so affected really … If I thought about it for longer, I'd be thinking about how it seems to affect everywhere but us, unfortunately, and maybe that's why people don't care, cos it doesn't immediately affect them.* (P27, female, aged 30–39 years) *It [global warming] kind of talks about as being something over there, not something local, and we know that we get flooded, we know that we get mild winters now and blazing hot record breaking days in the summer, and, and that's local.* (P28, male, aged 70–79) *We do have climate change … but the extremes of changes are much more likely to happen in the extremes of climate, and we're a moderate climate.* (P02, male, aged 70–79 years) *I don't have children but it's something that is obviously so precious to them, a child's health is such a huge precious thing that we think about children as the next generation, as the future, so therefore when I'm thinking about climate change obviously I'm thinking about the future.* (P12, female, aged 30–39 years)
Uncertainty about whether the UK is experiencing climate change …	*I don't know … I guess the weather in the UK is kind of up and down at the moment; I guess it was really, really warm on Sunday and then it's like, then it goes really, really cold again. But I don't know if that's just unpredictable UK weather or that's related to global warming.* (P04, female, aged 15–19 years) *There are times when the weather does seem to play tricks with us; whether that's climate change or, I don't know.* (P15, male, aged 70–74 years) *It's quite hard to kinda pin it down in the UK; I think it'll probably be more apparent in places where you get like very definite seasons like a dry season and a wet season or whatever that's usually pretty predictable. Their extremes are a lot more apparent when rains don't turn up or they come three months later and things like that.* (P30, male, aged 40–47 years) *I would expect there not to be that much awareness [about climate change] for people in Britain, cos I think we're quite lucky, being a temperate country.* (P14, female, aged 60–62 years)

for probably my son's children if he decides to have any' (P01, male, aged 60–69 years).

Theme 2: Uncertainty about whether the United Kingdom is experiencing climate change

Many participants described the seasons *'changing'* and *'shifting'*, with more winter snow in the past and hotter summers now: '*I feel like the seasons have shifted, like they're not quite in line from what I remember like growing up*' (P12, female, aged 30–39 years). However, participants often expressed uncertainty about whether these changes were driven by climate change or were part of *'the variability'* of *'the British weather'*. Britain's *'temperate'* and *'moderate'* climate was seen to protect the country and its people from the changes seen elsewhere: as participants put it, '*I think we're quite lucky, being a temperate country*' (P14, female aged 60–69 years) without '*definite seasons like a dry season and a wet season (where) rains don't turn up*' (P30, male, aged 40–49 years).

UK photographs of climate-related events prompted some participants to talk about experiences of flooding and heatwaves, but these did not appear to inform their responses. For example, in response to the photograph of flooding, a participant noted that the river near her village '*was flooded for weeks last year*', but when asked earlier in the interview about her thoughts on climate change, she talked about the Pacific Islands (P14, female, aged 60–69 years).

Perceptions of the health impacts of climate change

Two interconnected themes were identified. First, participants spoke of the difficulty of linking climate change to people's health: *'I don't really associate climate change with actual like people's health'* (P04, female, aged 15–19 years). Secondly and relatedly, they were uncertain about whether the human impacts that came to mind would qualify as 'health impacts': as one participant put it, *'it depends how you define health impact'* (P16, male, aged 40–49 years). These themes are discussed below and illustrated in Table 2.

Theme 1: It's hard to see connections between climate change and people's health

Participants often struggled to link climate change to people's health: '*despite the fact that I've had notice of this conversation for quite some time, people's health isn't very high up what I think about'* (P10, male, aged 60–69 years). Instead, it was other impacts of climate change that participants spoke about, particularly impacts on wildlife and the natural environment: "*for me, I keep thinking 'oh it's the animals, the animals, and how long will it take'. I mean some species will be wiped out*" (P37, female, aged 70–79 years).

Theme 2: Uncertainty about what is meant by 'health' in the context of climate change

Where health impacts were noted, they tended to relate to *'dramatic'* events outside the United Kingdom and associated threats to life (*'death', 'survivability'*). As a participant put it, '*it seems to be that the impacts of climate change are having a gradual impact on the physical world which then has a catastrophic event that then kills people rather than making them less healthy*' (P17, male, aged 30–39 years). However, participants expressed uncertainty about whether such impacts fell within the concept of health: *'So the health impacts that we might expect to become prominent would be more like starvation, but then is that really health?'* (P10, male, aged 60–69 years).

It appeared to be easier to identify mental health impacts, linking these both to events outside the United Kingdom and to flooding within it. Participants described *'the anxiety'* of living on '*one of these low lying islands'* (P14, female, aged 60–69 years) and in flood risk areas in the United Kingdom, noting '*the stress of that certainly, I mean it's stress-related things which are probably gonna be felt more than actual illnesses'* (P07, male, aged 70–79 years).

Discussion

Main findings

Climate change was seen as primarily affecting people in other places and in future times. These perceptions were related to understandings of climate change as an extreme phenomenon, manifested in major meteorological events and their associated impacts: extensive flooding and wildfires and intense heatwaves. Perceptions of the inherent variability of the British weather – its *'ups and downs'* and '*tricks'* – appeared to add to uncertainty about whether climate change was yet affecting the United Kingdom. This

Table 2
Perceptions of the health impacts of climate change.

Theme	Supporting quotes
Hard to see the connections between climate change and people's health …	*Until you mentioned this interview thing, I never thought of it in terms of the consequence for human life because other life took precedence in my mind.* (P03, male, aged 60–69 years) *I don't know, I don't really associate climate change with actual like people's health. Cos we don't really see climate change within the UK, you see it in like developing countries rather than the UK, and countries like America who aren't developing [laughs]. So yeah, lack of nutrition, under-developed people. You get like those adverts on TV that are advertising; this is where I've got it from.* (P04, female, aged 15–19 years) *I wouldn't say I've seen it [climate change] so far on people's health. So I don't think health-wise I've seen it so far. I mean some people may get very deeply worried about it and think that we're going to disappear in the next year or two. I don't know that I've got to that position yet.* (P15, male, aged 70–79 years) *I think there's the kind of more visible destruction, so like the destruction of rain forests or the destruction of the coral reef or all the kind of things that come to mind when people talk about climate change, so whether that's, you know, ice disappearing or whatever it might be, those kind of more visible things.* (P12, female, aged 30–39 years) *I mainly think about, like the wild, like the animals and like how as humans like climate change is destroying like habitats that were once there and the animals are getting extinct … I think about stuff like that.* (P18, female, aged 15–19 years) *I just feel like with that kinda of thing, what these environmental issues have on people's health, they think more about its affecting the earth than how it's affecting humans.* (P11, female, aged 15–19 years)
Uncertainty about what is meant by 'health' in the context of climate change … but greater certainty about the mental health impacts of climate change	*So the health impacts that we might expect to become prominent would be more like starvation, but then is that really health? I would label that slightly differently, I think.* (P10, male, aged 60–69 years) *I suppose survivability is maybe not health so I won't go down the route of, you know, it's endangering lives.* (P17, male, aged 30–39 years) *I guess I don't think about it in terms of individual health, it's more that kind of big impacts on like lack of food and water, impacts of heat on people. So yeah, I guess I don't think about it in terms of people's personal like health and fitness but more of a kind of global, social scale.* (P30, male, aged 40–49 years) *So it depends how you define health impact, because there's definitely psychological impact and mental health and I think the way people react to it and, as I say, flooding and everything else and so on.* (P16, male aged 40–49 years) *For those people who are living in flood risk areas, I would expect that would have a pretty significant impact on mental health on the basis that they're going through, horrific, you know, trauma from having their houses destroyed, and rebuilding and then destroying them again and then rebuilding. So I'd expect there'd be a pretty significant mental health impact.* (P17, male, aged 30–39 years) *I think probably the biggest one at the moment is the anxiety; it's actually that intangible, but, you know, birds and wildlife, and then that knock-on effect of you've lost that wellbeing from the natural environment, but it's the anxiety of not knowing what's gonna happen, when it's gonna happen. If you're on one of these low lying islands or if you're one of these farmers, if you were me trying to, you know, have my garden and worry about my garden birds and my hedgehogs, it's the anxiety of not knowing exactly how far it's gonna go, how far it's going to tip. I mean it's the anxiety level of the uncertainty.* (P14, female, aged 60–69 years)

perception may be because while 'talking about the weather' is a reassuring part of everyday social interactions, reframing the UK's changing weather patterns as part of long-term changes in the climate could move the conversation into highly charged political territory.[22,34,35]

Participants' perceptions of climate change as episodic, unexpected and life-threatening appeared to inform their perceptions of its health impacts. Seen in this way, they *'didn't see much of a connection'* between climate change and people's health, particularly in a UK context. This may in part reflect a conceptualisation of health that does not include its negation ('*starvation*', *'death'*) and where positive health is seen as influenced by individual-level factors, such as health behaviours, rather than wider environmental determinants.[36]

It has been argued that in countries relatively protected from climate change, perceiving it as a phenomenon happening in other places and times is a manifestation of 'psychological distancing'.[37,38] While such a distancing is evident in our study, it appears, at least in part, to be shaped by participants' exposure to media representations of extreme weather events (cyclones in Bangladesh, wildfires in California and Australia, flooding in Germany), a central factor in how the public understand climate change and its human impacts.[39–41] A qualitative study in Canada similarly noted that perceptions of climate change drew on what participants had seen in the media.[22]

The pandemic context may also have reduced the potential salience of climate change and its health impacts. During the interview period, the United Kingdom experienced high rates of infection and long periods of lockdown.[23] In a UK survey conducted in July 2021, participants were asked to identify the three 'biggest threats' to their health from a list that included 'the effects of climate change'; the list was dominated by 'chronic diseases such as cancer, obesity and diabetes' and 'the COVID-19 pandemic', with only a small minority identifying climate change.[50]

What is already known about this topic?

The limited evidence suggests that in high-income countries less directly affected by climate change, the public have a low perception of personal risk and perceive climate change as being worse in other places and times.[22] Framing it as a health issue is advocated as a way of increasing its personal salience.[11,14,15] But the evidence to support this approach is limited, particularly with respect to qualitative studies of the general public where participants express their thoughts and understandings in their own words.[20,22]

What this study adds

Our study adds to the small qualitative literature on public perceptions of the health impacts of climate change. It adds to an even smaller evidence base exploring people's perceptions of the health impacts of climate change in the United Kingdom.

Our findings are in line earlier studies in the United Kingdom, and Canada where climate change was understood to be happening elsewhere in place and time, and the public were often uncertain about whether it was affecting people's health.[14,51] Our study adds to these findings by noting how perceptions of 'the British weather' as inherently variable contributed to uncertainty about whether the United Kingdom was experiencing climate change. We also note how participants' perceptions of climate change appear to draw on media images of life-threatening events beyond the United Kingdom. This suggests that climate change is understood, not as a change in climate patterns from the late 20th century affecting all regions of the world but as sudden and extreme periods of flooding, wildfires and heatwaves. Understood in this way, study participants found it difficult to identify impacts on people's health, pointing instead to risks to life.

The study contributes to wider discussions within public health policy and practice about how to communicate climate risks in ways that connect with people's understandings and concerns.[12,17] A health-centred approach is seen to hold promise in countries less vulnerable to the direct effects of climate change. In our study, participants struggled to connect climate change and people's health, pointing to potential challenges in engaging the public through a health framing of climate change.

Limitations of the study

Our study was conducted before the UK's heatwaves in June to August 2022,[42] a prolonged period of extreme heat that may have brought climate change and its health risks closer to home.

Conducted during the COVID-19 pandemic, study recruitment was restricted to community groups remaining open during lockdown and with capacity to circulate study details. The range of groups – which included groups with an environmental (e.g. neighbourhood forums, cycling groups) or health (e.g. young person's advisory groups) focus – may have skewed the participant profile to those more engaged in climate change and health. However, while like the general population,[43] most participants were concerned about climate change, their accounts suggest uncertainty about whether climate change is happening in the United Kingdom and whether it is affecting people's health. It could therefore be argued that these perceptions would be evident, and possibly to a greater extent, in the wider population. While participants spanned a wide age range (15–80 years), there was a higher proportion of older and male participants than in the general population. However, the themes were informed by the full range of interviews, including younger and female participants.

COVID-19 and its associated restrictions on people's lives required a shift from in-person focus groups to individual online and telephone interviews. While the dynamics of focus groups can generate jointly produced accounts and discourses,[44,45] one-to-one interviews may have enabled a wider range of individual views to be expressed. Nonetheless, the thematic analysis pointed to consistency of perspectives and opinions across the study participants. Most UK adults (95%) have online access, but digital exclusion is associated with multiple social and health disadvantages.[46,47] We offered telephone interviews to enable participation by those without internet access or who were not comfortable with online interviews.

Conclusions

In democratic societies, policies require public support. An understanding of people's perceptions of climate change is therefore integral to ethical and effective policy-making. Connecting climate change to health is seen as a way to bring climate change closer to people's lives,[11,14,15] particularly in countries currently less exposed to climate change. While quantitative surveys point to the potential for such a framing, qualitative studies paint a more nuanced picture. Our study in England adds to this small qualitative evidence base.

Participants mainly understood climate change in terms of extreme weather events beyond the United Kingdom, which were sudden, widespread and devastating in their impacts. Perceived in this way, they located climate change as a process from which they were spatially and temporally distant and with limited health implications for the United Kingdom. In this context, alternative framings of climate change may have greater personal resonance. Climate change's impacts on the natural environment and future generations were ones that participants spontaneously discussed and in ways that suggested these impacts were more meaningful to them. A 'coupling' of climate change with environmental change and children's futures is supported by evidence: damage to the Earth's natural systems is undermining human and planetary health[48,49] and lifetime exposure to climate extremes will increase across birth cohorts at both global and country levels.[10] Our findings suggest that in countries less exposed to the health impacts of climate change, such 'couplings' may speak more directly to people's concerns and values. We recommend that future UK studies explore health alongside other framings of climate change to inform public messaging and public health policies to protect people and the planet.

Author statements

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Ethical approval

Ethical approval was received from the Health Sciences Research Governance Committee, University of York on 11 September 2020 (ref: HSRGC/2020/409/C).

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Competing interests

None declared

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.020.

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Original Research

Non-linear relationship between dietary vitamin E intake and cognitive performance in older adults

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ABSTRACT

Objectives: This study aimed to explore the relationship between dietary vitamin E (VE) intake and cognitive function in older adults.
Study design: This was a cross-sectional study.
Methods: We applied data from the National Health and Nutrition Examination Survey obtained during 2011–2014 that met our requirements. The cognitive ability assessments included the Consortium to Establish a Registry for Alzheimer's Disease Word Learning (CERAD-WL) and Delayed Recall (CERAD-DR) tests, the animal fluency test, the Digit Symbol Substitution Test, and a composite z-score calculated by summing z-scores of individual tests. We used binary logistic regression analysis to explore the relationship between VE intake and cognitive performance. The results are reported using odds ratios and 95% confidence intervals. Our study also included sex-stratified analyses and sensitivity analysis. A restricted cubic splines model was used to evaluate the dose–response relationship between dietary VE intake and cognitive function.
Results: This study found that a higher intake of dietary VE was associated with a lower risk of cognitive impairment in patients. Sensitivity analysis shows stable results. The results of the gender stratification analysis showed that dietary VE intake was negatively related to the risk of cognitive disorder among females. An irregular L-shaped dose–response relationship was observed between dietary VE intake and cognitive impairment risk.
Conclusions: Dietary VE intake was negatively related to the risk of cognitive disorder in older adults, with a higher VE intake lowering the risk.

Introduction

The advent of an aging society has resulted in cognitive decline in older adults, becoming a global problem that cannot be ignored.[1] Research projections indicate that by 2050, the number of people with cognitive impairment will reach approximately 152 million worldwide.[2] In the near future, the increasing incidence rates of cognitive impairment and dementia will become a major public health challenge for humanity, with a heavy socio-economic burden.[3]

There is currently no clear way to treat or slow down the deterioration of mild cognitive impairment (MCI).[4] Controlling, delaying, and preventing cognitive decline is therefore of great significance. Factors that can affect this deterioration, such as an appropriate vitamin E (VE) intake, may have a positive effect on the risk of cognitive impairment.[5–8]

Animal experiments have indicated that VE has a positive effect on cognitive impairment.[9,10] Many frequently consumed foods are rich in VE.[11] Plants synthesize eight different forms of VE. Its available form (alpha-tocopherol) is important for scavenging free radicals in the body[11] and helps prostaglandin synthesis in the brain and regulates nucleic acid synthesis, which may have protective effects on cognitive function. Animals (including humans) cannot interchange between forms of VE, so humans can only maintain normal VE levels through dietary or supplement intake.[12] The form of VE intake in our study was also in the form of alpha-tocopherol. Many studies on humans have examined the role of

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VE intake in cognitive impairment, but the results have been inconsistent.[6,13–15] Engelhart et al. concluded that a higher VE intake was associated with a lower risk of Alzheimer's disease (AD).[6] Luchsinger et al. conducted a study on 980 participants and concluded that diet, vitamin supplementation, and total VE intake did not affect cognitive impairment.[13] In other words, the connection between dietary VE intake and cognitive performance in older people has not been conclusive, which makes it significant to explore reasonable dietary VE intake thresholds.

We therefore used data from the National Health and Nutrition Examination Survey (NHANES) to assess the relationship between VE intake and cognitive impairment risk in older adults in the United States. Our study demonstrated dose–response relationships and sex-stratified outcomes. This may lead to ways of reducing cognitive impairment, which would have significant social implications.

Methods

Data sources

The data used for our study were from the NHANES, a public database on the United States population. The NHANES database includes demographic, dietary, examination, laboratory, questionnaire, and limited-access data. All participants or their proxies provided written informed consents.[16] The project information and survey data of NHANES are updated in real time on the Web site, and it is completely free for public access.[17]

Study population

The study included data on dietary VE intake and cognizance assessments from NHANES during 2011–2012 and 2013–2014. We included subjects aged > 60 years with complete data on four cognitive assessment tests, demographic characteristics, marital status, education level, poverty-income ratio, body mass index, smoking, drinking, hypertension, and outdoor activity.[18] After further exclusion screening, 2267 participants in NHANES were suitable for this study (Fig. 1).

Cognitive function assessment

Cognitive performance was assessed using four tests in the following sequence: Consortium to Establish a Registry for Alzheimer's Disease Word Learning (CERAD-WL) test, Animal Fluency Test (AF), Digit Symbol Substitution Test (DSST), and CERAD Delayed Recall (CERAD-DR) test.

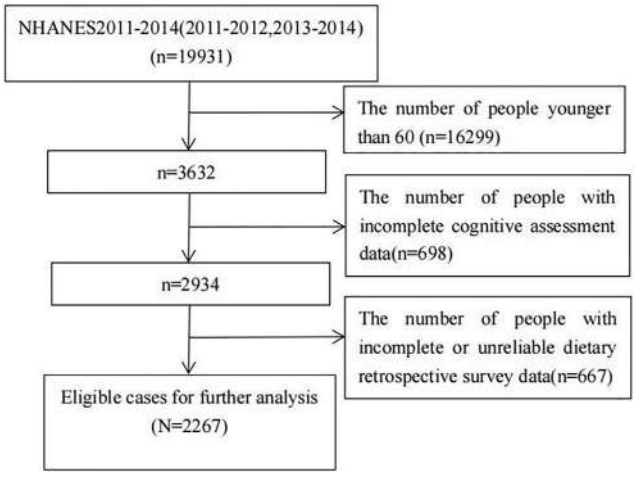

Fig. 1. Case inclusion process.

The CERAD test consists of three learning test phases and one delayed recall test phase.[19] The CERAD-WL test was administered by asking participants to recall as many of the words read aloud as possible immediately after reading 10 unrelated words aloud, then changing the order of those words and testing them two more times, for a total of 30 points. After completing the AF and DSST, the CERAD-DR test was administered, and cases were asked to recall 10 words from the CERAD-WL test for a maximum of 10 points. Based on previous studies,[17] thresholds <17 for CERAD-WL and <5 for CERAD-DR were used to distinguish potential cognitive impairment from healthy cognitive function and lack of cognitive impairment.

Before the AF, the assessor first asked the participant to name any three garments, and those who could do so successfully entered the formal test. In the formal test, the participants said the names of as many animals as possible within one min, with a correct answer giving a score of one.[20,21] According to previous studies,[17] a threshold of AF <14 was used to distinguish potential cognitive impairment.

For the DSST, we asked participants to paste the corresponding symbols into the 133 boxes next to the numbers within two min, scoring one point for a correct set, with a minimum of zero points and a maximum of 133 points.[22] According to previous studies,[17] a threshold of <34 for DSST was used to distinguish potential cognitive impairment.

In addition, a composite z-score was created by summing the z-scores [(individual test score − mean score)/SD] of these three individual tests (DSST, AF, and CERAD). For all the tests, higher scores represent better cognitive performance. Individual and global standardized cognitive scores <−1 were characterized as "low cognitive performance" for their respective cognitive measure.

Dietary VE intake

VE intake was obtained in the NHANES by calculating the average of two 24-h dietary recall recordings.[23] We divided the VE intake into four groups based on intake quartiles ($0.06 \leq Q1 \leq 2.188$ mg/day, $2.188 < Q2 \leq 3.47$ mg/day, $3.47 < Q3 \leq 5.442$ mg/day, and $5.442 < Q4 \leq 57.475$ mg/day).

Covariates

Confounders were assessed for the following variables: age (continuous), sex (male and female), race (Mexican American, Other Hispanic, non-Hispanic White, non-Hispanic Black, and other race-including multiracial), marital status (married, living with a partner, widowed/divorced/separated, and never married), education level (<9th grade, 9th to 11th grade, high school graduate/General Educational Development, a college or Associate of Arts (AA) degree, and college graduate or above), poverty-to-income ratio (<1, ≥1), body mass index (<25 kg/m^2; 25–30 kg/m^2; ≥30 kg/m^2), smoked at least 100 cigarettes in life (yes and no), had at least 12 alcohol drinks per 1 year (yes and no), ever told you had high blood pressure (yes and no), and vigorous recreational activities/1week (yes and no).

Statistical analysis

According to the analysis guidelines of the NHANES, we recalculated the sample weights to ensure the accuracy and stability of the study.[24] We used the Kolmogorov–Smirnov method to test whether continuous variables conformed to the normal distribution. We used mean (±standard error) values to describe variables that conformed to the normal distribution, with median and

Table 1
Characteristics of the dietary VE and cognition study population.

Characteristics	Number of subjects (*N*)	CERAD-WL			CERAD-DR			AF			DSST			z-score		
		Normal cognitive function	Low cognitive function	*P*-value	Normal cognitive function	Low cognitive function	*P*-value	Normal cognitive function	Low cognitive function	*P*-value	Normal cognitive function	Low cognitive function	*P*-Value	Normal cognitive function	Low cognitive function	*P*-Value
Number of subjects[a], *n* (%)		1667 (73.53)	600 (26.47)		1730 (76.31)	537 (23.69)		1638 (72.25)	629 (27.75)		1765 (77.86)	502 (22.14)		1476 (65.11)	791 (34.89)	
Age[b]	2267	68.07 ± 0.21	72.37 ± 0.45	<0.0001	67.99 ± 0.20	72.70 ± 0.41	<0.0001	68.29 ± 0.19	71.69 ± 0.32	<0.0001	68.34 ± 0.20	73.21 ± 0.49	<0.0001	67.81 (0.18)	72.64 (0.41)	<0.0001
Sex[a], *n* (%)	2267			<0.001			<0.001			0.66			0.71			
Male		736 (43.37)	351 (54.50)		765 (43.15)	322 (55.38)		788 (45.92)	299 (44.42)		812 (45.50)	275 (46.56)		644 (43.97)	443 (51.03)	0.04
Female		931 (56.63)	249 (45.50)		965 (56.85)	215 (44.62)		850 (54.08)	330 (55.58)	1038	953 (54.50)	227 (53.44)		832 (56.03)	348 (48.97)	
Race[a], *n* (%)	2267			<0.0001			0.04			<0.0001			<0.0001			<0.0001
Mexican American		125 (2.56)	63 (4.77)		136 (2.72)	52 (4.11)		141 (2.77)	47 (3.97)		121 (2.21)	67 (8.67)		105 (2.24)	83 (5.51)	
Non-Hispanic White		881 (83.54)	283 (75.62)		884 (82.34)	280 (80.31)		937 (85.56)	227 (66.73)		1003 (85.25)	161 (58.37)		851 (85.93)	313 (68.90)	
Non-Hispanic Black		389 (7.27)	135 (9.42)		397 (7.45)	127 (8.72)		310 (5.66)	214 (16.26)		353 (5.94)	171 (20.23)		286 (5.66)	238 (14.38)	
Other Hispanic		135 (2.54)	74 (5.54)		155 (2.91)	54 (4.06)		138 (2.53)	71 (5.72)		122 (2.09)	87 (10.67)		99 (1.96)	110 (7.00)	
Other races		137 (4.10)	45 (4.66)		158 (4.58)	24 (2.80)		112 (3.47)	70 (7.32)		166 (4.52)	16 (2.07)		135 (4.21)	47 (4.22)	
Material status[a], *n* (%)	2267			0.04			0.5			0.13			0.002			0.01
Married		968 (65.34)	306 (54.76)		986 (64.03)	288 (59.88)		937 (64.40)	337 (58.15)		1033 (64.91)	241 (50.96)		865 (65.46)	409 (55.80)	
Living with partner		39 (2.33)	27 (4.34)		45 (2.71)	21 (2.83)		53 (2.95)	13 (1.83)		47 (2.64)	19 (3.39)		40 (2.59)	26 (3.19)	
Divorced and separated and widowed		547 (27.03)	220 (34.79)		573 (27.70)	194 (32.17)		531 (27.31)	236 (34.05)		563 (27.06)	204 (39.58)		472 (26.73)	295 (34.70)	
Never married		113 (5.30)	47 (6.12)		126 (5.56)	34 (5.12)		117 (5.35)	43 (5.98)		122 (5.38)	38 (6.07)		99 (5.21)	61 (6.30)	
Education[a], *n* (%)	2267			<0.0001			<0.001			<0.0001			<0.0001			<0.0001
Less than 9th grade		88 (2.89)	125 (12.73)		122 (3.85)	91 (8.98)		113 (3.25)	100 (11.74)		54 (2.08)	159 (24.80)		37 (1.72)	176 (15.20)	
9th−11th grade		194 (8.06)	107 (16.07)		218 (8.89)	83 (12.83)		179 (8.34)	122 (15.34)		190 (8.13)	111 (20.76)		145 (7.45)	156 (16.97)	
High school graduate/GED or equivalent		395 (20.50)	136 (25.32)		392 (20.40)	139 (25.73)		351 (19.04)	180 (31.70)		412 (20.74)	119 (26.71)		323 (18.79)	208 (30.22)	
Some college or AA degree		536 (33.85)	131 (26.32)		548 (33.85)	119 (26.31)		522 (34.07)	145 (24.98)		587 (34.16)	80 (19.26)		508 (35.30)	159 (22.64)	
College graduate or above		454 (34.70)	101 (19.56)		450 (33.02)	105 (26.15)		473 (35.30)	82 (16.24)		522 (34.89)	33 (8.47)		463 (36.75)	92 (14.99)	
Poverty-income ratio[a], *n* (%)	2267			<0.0001			0.03			<0.0001			<0.0001			<0.0001
<1		227 (6.60)	131 (14.70)		259 (7.64)	99 (10.63)		209 (6.45)	149 (15.75)		208 (6.14)	150 (23.21)		171 (5.68)	187 (16.58)	
≥1		1440 (93.40)	469 (85.30)		1471 (92.36)	438 (89.37)		1429 (93.55)	480 (84.25)		1557 (93.86)	352 (76.79)		1305 (94.32)	604 (83.42)	
Body mass index[a], *n* (%)	2267			0.17			0.11			0.51			0.65			0.33
<25 kg/m^2		420 (25.15)	169 (28.83)		444 (25.80)	145 (26.30)		406 (25.25)	183 (28.63)		453 (25.64)	136 (27.73)		377 (25.26)	212 (27.97)	
25−30 kg/m^2		567 (35.29)	221 (38.01)		574 (34.58)	214 (40.82)		580 (35.98)	208 (35.26)		619 (36.23)	169 (33.08)		505 (35.25)	283 (37.78)	
30 kg/m^2		680 (39.56))	210 (33.16)		712 (39.63)	178 (32.88)		652 (38.77)	238 (36.10)		693 (38.13)	197 (39.19)		594 (39.49)	296 (34.25)	
Smoke at least 100 cigarettes in life[a], *n* (%)	2267			0.51			0.18			0.91			0.67			0.26
Yes		856 (51.26)	296 (49.70)		884 (51.74)	268 (47.83)		838 (51.00)	314 (50.69)		894 (51.13)	258 (49.59)		737 (50.28)	415 (53.11)	
No		811 (48.74)	304 (50.30)		846 (48.26)	269 (52.17)		800 (49.00)	315 (49.31)		871 (48.87)	244 (50.41)		739 (49.72)	376 (46.89)	
Had at least 12 alcohol drinks per year[a], *n* (%)			<0.001				0.09			<0.0001			<0.0001			<0.0001
Yes		1172 (75.35)	402 (66.30)		1208 (74.30)	366 (70.42)		1170 (75.83)	404 (63.80)		1259 (75.56)	315 (58.97)		1065 (76.36)	509 (64.23)	
No		495 (24.65)	198 (33.70)		522 (25.70)	171 (29.58)		468 (24.17)	225 (36.20)		506 (24.44)	187 (41.03)		411 (23.64)	282 (35.77)	
Hypertension[a], *n* (%)	2267			0.02			0.02			<0.001			<0.0001			<0.0001

Yes	1022 (56.60)	397 (65.46)		1066 (56.75)	353 (64.90)		985 (56.36)	434 (66.94)		1059 (56.12)	360 (74.57)		882 (55.24)	537 (68.68)	
No	645 (43.40)	203 (34.54)		664 (43.25)	184 (35.10)		653 (43.64)	195 (33.06)		706 (43.88)	142 (25.43)		594 (44.76)	254 (31.32)	
Vigorous recreational activities per week[a,c], n (%)			<0.0001			0.01			0.041			<0.001			0.003
Yes	207 (15.14)	47 (8.20)		210 (14.87)	44 (9.26)		210 (15.05)	44 (8.20)		216 (14.76)	38 (6.44)		191 (15.35)	63 (8.46)	
No	1460 (84.86)	553 (91.80)		1520 (85.13)	493 (90.74)		1428 (84.95)	585 (91.80)		1549 (85.24)	464 (93.56)		1285 (84.65)	728 (91.54)	
VE (mg/day)[b]			<0.0001			<0.001			<0.0001			<0.001			<0.001
	5.01 ± 0.14	4.10 ± 0.18		5.02 ± 0.14	4.06 ± 0.21		5.01 ± 0.13	4.07 ± 0.14		4.96 ± 0.14)	3.86 ± 0.22		5.07 ± 0.15	4.03 ± 0.15	

AF, Animal Fluency Test; CERAD-DR, Consortium to Establish a Registry for Alzheimer's Disease Delayed Recall; CERAD-WL, Consortium to Establish a Registry for Alzheimer's Disease Word Learning; DSST, Digit Symbol Substitution Test; VE, vitamin E.

[a] Chi-squared test was used to compare the difference between normal and low cognitive function participants, and data are number of subjects (percentage).

[b] Values are mean ± standard error.

[c] Does strenuous activity that causes a significant increase in breathing or heart rate, such as lifting or carrying heavy objects, excavation or construction work, for at least 10 consecutive minutes per week? In this study, a cutoff of <17 for CERAD-WL, <5 for CERAD-DR, <14 for AF, <34 for DSST, and <1 for z-score was used to define a potential cognitive impairment.

interquartile range values used for other variables. For the data in Table 1, if the variable was normally distributed, the Student t-test was used to compare the mean levels between the low cognitive performance group and the normal cognitive performance group. If the variable was not normally distributed, Mann–Whitney U test was used. The Chi-squared test was selected to compare the percentage of categorical variables between different groups, and data are number of subjects (percentage) or medians (interquartile ranges).

The Q1 group was used as a reference. Logistic regression analysis was used to review the relationship between VE intake and cognitive performance. We quantified the results using odds ratios (ORs) and 95% confidence intervals (95% CIs). We first conducted regression analyses that were adjusted for age, sex, and race (Model 1) and then regression analyses that were adjusted for all of the included covariates (Model 2). We also performed sex-stratified analyses. A restricted cubic splines model was used to review the dose–response relationship between dietary VE and cognitive performance after adjusting for all variables. Three nodes were located at the 5th, 50th, and 95th percentiles of dietary VE intake. Probability values of $P < 0.05$ were assumed to indicate significantly different results. All analyses were performed using R software (version 4.0.2, https://www.r-project.org/).

Results

Sample characteristics

The cognitive performance characteristics of participants in the dietary VE intake survey are listed in Table 1. In all cognitive tests, we found that older, non-Hispanic White participants with lower education levels, lower incomes, hypertension, no outdoor activity, and lower VE intake had lower cognitive ability.

Association between dietary VE and cognitive performance

All results are presented with Q1 as a reference. In the non-adjusted model, the OR (95% CI) values for a low CERAD-WL score were 0.66 (0.47–0.95), 0.54 (0.41–0.71), and 0.45 (0.34–0.58) in groups Q2, Q3, and Q4, respectively. The OR (95% CI) values for a low CERAD-DR score were 0.72 (0.53–0.96) and 0.43 (0.29–0.62) in groups Q3 and Q4, respectively. The OR (95% CI) values for a low AF score were 0.49 (0.34–0.71), 0.49 (0.31–0.75), and 0.43 (0.32–0.58) in groups Q2, Q3, and Q4, respectively. The multivariate-adjusted OR (95% CI) values for a low DSST score were 0.59 (0.41–0.84), 0.41 (0.27–0.63), and 0.36 (0.23–0.54) in groups Q2, Q3, and Q4, respectively. The OR (95% CI) values for a low z-score were 0.54 (0.36–0.80), 0.60 (0.43–0.83), and 0.35 (0.24–0.51) in groups Q2, Q3, and Q4, respectively.

After adjusting for age, sex, and race only (Model 1), the multivariate-adjusted OR (95% CI) values for a low CERAD-WL score were 0.65 (0.44–0.95), 0.53 (0.39–0.70), and 0.48 (0.35–0.65) in groups Q2, Q3, and Q4, respectively. The OR (95% CI) values for a low CERAD-DR score were 0.70 (0.50–0.97) and 0.44 (0.30–0.64) in groups Q3 and Q4, respectively. The multivariate-adjusted OR (95% CI) values for a low AF score were 0.51 (0.35–0.75), 0.53 (0.34–0.83), and 0.53 (0.40–0.71) in groups Q2, Q3, and Q4, respectively. The multivariate-adjusted OR (95% CI) values for a low DSST score were 0.63 (0.41–0.96), 0.44 (0.27–0.72), and 0.48 (0.31–0.73) in groups Q2, Q3, and Q4, respectively. The OR (95% CI) values for a low z-score were 0.53 (0.34–0.82), 0.62 (0.43–0.90), and 0.40 (0.28–0.59) in groups Q2, Q3, and Q4, respectively.

After adjusting for all variables (Model 2) listed in Table 2, the multivariate-adjusted OR (95% CI) values for a low CERAD-WL score were 0.60 (0.44–0.81) and 0.56 (0.40–0.78) in groups Q3 and Q4,

Table 2
Weighted dominance ratio (95% confidence interval) of CERAD-WL, CERAD-DR, AF, DSST, and global z-score in dietary VE intake.

Cognitive score	Dietary VE intake (mg/day)	Q1 (0.06–2.188)	Q2 (2.188–3.47)	Q3 (3.47–5.442)	Q4 (5.442–57.475)
CERAD W-L	Case/participants	190/567, 33.51%	147/567, 25.93%	134/566, 23.67%	129/567, 22.75%
	Crude	1.00 (Ref.)	0.66 (0.47–0.95)*	0.54 (0.41, 0.71)*	0.45 (0.34, 0.58)*
	Model 1	1.00 (Ref.)	0.65 (0.44, 0.95)*	0.53 (0.39, 0.70)*	0.48 (0.35, 0.65)*
	Model 2	1.00 (Ref.)	0.75 (0.48, 1.16)	0.60 (0.44, 0.81) *	0.56 (0.40, 0.78)*
CERAD D-R	Case/participants	161/567, 28.40%	136/567, 23.99%	141/566, 24.91%	99/567, 17.46%
	Crude	1.00 (Ref.)	0.71 (0.48, 1.03)	0.72 (0.53, 0.96)*	0.43 (0.29, 0.62)*
	Model 1	1.00 (Ref.)	0.68 (0.46, 1.03)	0.70 (0.50, 0.97)*	0.44 (0.30, 0.64)*
	Model 2	1.00 (Ref.)	0.74 (0.47, 1.17)	0.74 (0.51, 1.07)	0.46 (0.31, 0.69)*
AF	Case/participants	200/567, 35.27%	160/567, 28.22%	139/566, 24.56%	130/567, 22.93%
	Crude	1.00 (Ref.)	0.49 (0.34, 0.71)*	0.49 (0.31, 0.75)*	0.43 (0.32, 0.58)*
	Model 1	1.00 (Ref.)	0.51 (0.35, 0.75)*	0.53 (0.34, 0.83)*	0.53 (0.40, 0.71)*
	Model 2	1.00 (Ref.)	0.58 (0.38, 0.88)*	0.59 (0.36, 0.99)*	0.62 (0.44, 0.88)*
DSST	Case/participants	173/567, 30.51%	135/567, 23.81%	105/566, 18.55%	89/567, 15.70%
	Crude	1.00 (Ref.)	0.59 (0.41, 0.84)*	0.41 (0.27, 0.63)*	0.36 (0.23, 0.54)*
	Model 1	1.00 (Ref.)	0.63 (0.41, 0.96)*	0.44 (0.27, 0.72)*	0.48 (0.31, 0.73)*
	Model 2	1.00 (Ref.)	0.76 (0.45, 1.28)	0.54 (0.31, 0.96)*	0.59 (0.35, 0.99)*
z-score	Case/participants	248/567, 43.74%	198/567, 34.92%	185/566, 32.69%	160/567, 28.22%
	Crude	1.00 (Ref.)	0.54 (0.36, 0.80)*	0.60 (0.43, 0.83)*	0.35 (0.24, 0.51)*
	Model 1	1.00 (Ref.)	0.53 (0.34, 0.82)*	0.62 (0.43, 0.90)*	0.40 (0.28, 0.59)*
	Model 2	1.00 (Ref.)	0.61 (0.36, 1.02)	0.73 (0.50, 1.09)	0.48 (0.31, 0.74)*

AF, Animal Fluency Test; CERAD-DR, Consortium to Establish a Registry for Alzheimer's Disease Delayed Recall; CERAD-WL, Consortium to Establish a Registry for Alzheimer's Disease Word Learning; DSST, Digit Symbol Substitution Test; VE, vitamin E.
Binary logistic regression analyses were used to calculate weighted odds ratio values. Reference (Ref.); model 1 adjusted for age, race, and sex; model 2 adjusted for age, sex, race, marital status, education level, poverty-to-income ratio, body mass index, smoking, drinking, hypertension, and outdoor activity.
* $P < 0.05$.

respectively. The OR (95% CI) for a low CERAD-DR score was 0.46 (0.31–0.69) in group Q4. The multivariate-adjusted OR (95% CI) values for a low AF score were 0.58 (0.38–0.88), 0.59 (0.36–0.99), and 0.62 (0.44–0.88) in groups Q2, Q3, and Q4, respectively. The multivariate-adjusted OR (95% CI) values for a low DSST score were 0.54 (0.31–0.96) and 0.59 (0.35–0.99) in groups Q3 and Q4, respectively. The OR (95% CI) for a low z-score was 0.48 (0.31–0.74) in group Q4 (Table 2).

Previous studies[25] have shown that VK intake has a significant effect on cognition in older adults, so we performed sensitivity analyses, adjusting for all covariates and VK intake, and found that the association between dietary VE intake and low cognitive function remained significant, indicating that our results were more stable. Detailed information is provided in Supplementary Table 1.

The connection between dietary VE intake and cognitive performance was more pronounced in females, with no significant difference seen in males. Among females, the multivariate-adjusted OR (95% CI) values for a low CERAD-WL score were 0.48 (0.27–0.84) and 0.41 (0.24–0.69) in groups Q3 and Q4, respectively. The multivariate-adjusted OR (95% CI) values for a low CERAD-DR score were 0.47 (0.26–0.86) and 0.25 (0.13–0.50) in groups Q3 and Q4, respectively. The multivariate-adjusted OR (95% CI) for a low AF score was 0.41 (0.21–0.82) in group Q3. The multivariate-adjusted OR (95% CI) for a low DSST score was 0.45 (0.22–0.94) in group Q3. The multivariate-adjusted OR (95% CI) values for a low z-score were 0.45 (0.26–0.78) and 0.42 (0.24–0.74) in groups Q3 and Q4, respectively. Detailed information is provided in Supplementary Table 2.

Dose–response relationships

After adjusting for all included potential confounders, the association between VE intake and the cognitive performance had an irregular L shape (CERAD-WL and AF, $P_{\text{for non-linearity}} > 0.05$; CERAD-DR and DSST, $P_{\text{for non-linearity}} < 0.05$; global z-score, $P_{\text{for non-linearity}} < 0.05$; Figs. 2 and 3). In the CERAD-WL test, CERAD-DR test, and AF, the reduction in cognitive disorder risk slowed significantly when the VE intake increased above 7.1972, 5.5607, and 3.4788, respectively (Fig. 2A–C, respectively). In the DSST test, the risk of cognitive disorder no longer decreased for a VE of higher than 7.0910 mg/day (Fig. 2D). In the global z-score test, the risk of cognitive impairment almost ceased to decrease when VE was higher than 7.0210 mg/day (Fig. 3). Using z-scores from each cognitive test, we get the same results. Detailed information is provided in Annex Fig. 1A–D.

Discussion

In this study, we investigated the associations between dietary VE intake with cognitive performance in older adults. The correlation remained significant after adjusting for all of the included confounders. We also investigated the non-linear relationship between dietary VE intake and cognitive capabilities (CERAD-WL and AF, $P_{\text{for non-linearity}} > 0.05$; CERAD-DR and DSST, $P_{\text{for non-linearity}} < 0.05$; global z-score, $P_{\text{for non-linearity}} < 0.05$). The association between VE intake and cognitive performance had an irregular L shape. All three tests and global z-score indicated that the risk of developing cognitive disorder decreased with increasing dietary VE intake, except for the DSST that indicated that cognitive disorder risk no longer decreased with increasing VE intake, as it became >7.0910 mg/day. In a sex-stratified analysis, the correlation between dietary VE intake and cognitive performance was more pronounced in females.

Animal studies have found VE to have a positive effect on AD.[9,10] Studies involving humans have examined the role of VE intake (diet and supplementary) in cognitive impairment. The study by Engelhart et al. included 5395 participants aged >55 years with 6 years of follow-up data and concluded that a higher VE intake was associated with a lower AD risk.6 A prospective study by Morris et al. involving 815 participants aged ≥65 years concluded that foods that contain VE but no other antioxidants may reduce AD risk,[14] which was consistent with our findings. The study of Gray et al., which included 2969 participants with 5.5 years of follow-up data, also found that VE supplementation did not reduce cognitive impairment risk.[15] The reasons behind the contrasting results of our study and others may include differences in ages, with older

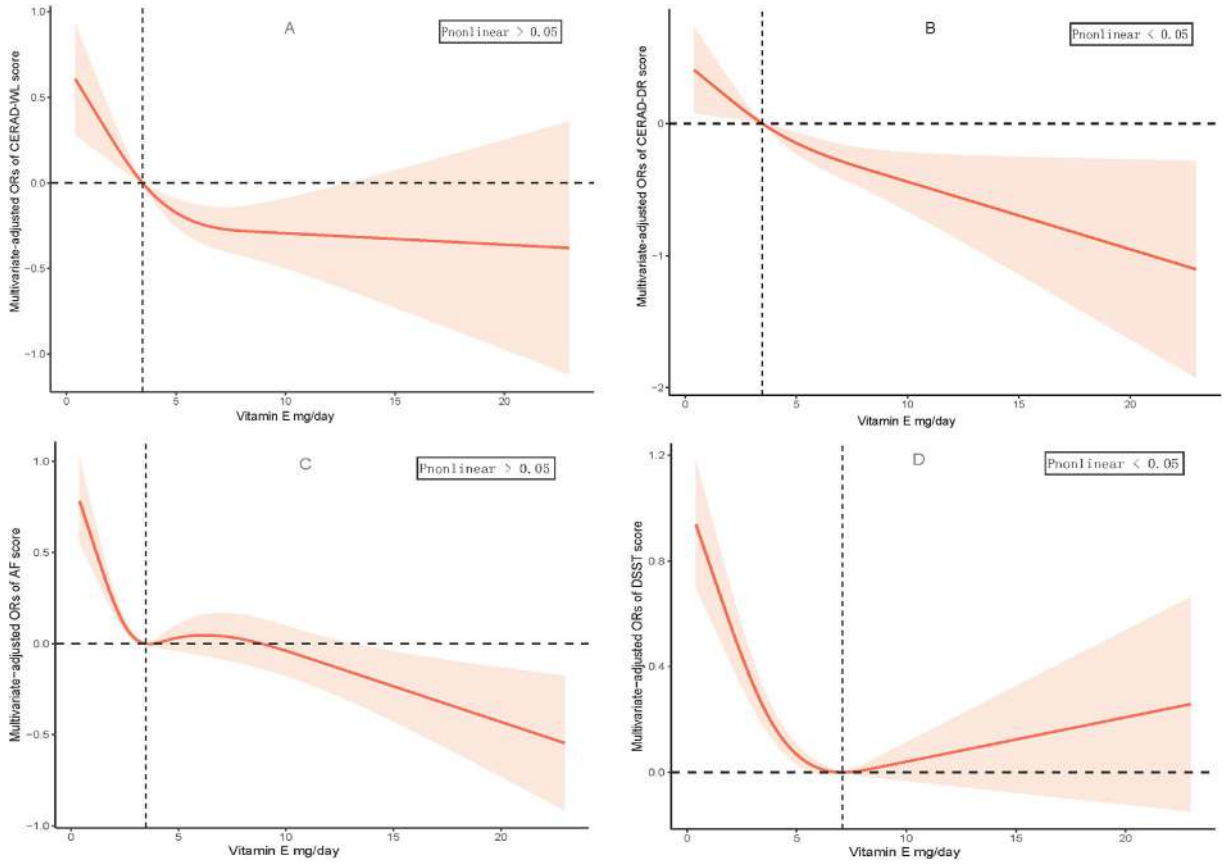

Fig. 2. Dose–response relationship between dietary VE intake and risk of low cognitive function CERAD-WL (A), CERAD-DR (B), AF (C), and DSST (D). AF, Animal Fluency Test; CERAD-DR, Consortium to Establish a Registry for Alzheimer's Disease Delayed Recall; CERAD-WL, Consortium to Establish a Registry for Alzheimer's Disease Word Learning; DSST, Digit Symbol Substitution Test; VE, vitamin E.

ages being included in the other studies (>65 years), the geographical area, and the cognitive assessment methods.

One possible mechanism by which VE might improve cognitive performance is that the nervous system has high oxygen consumption and is susceptible to oxidative stress, which leads to an increase in reactive oxygen species. Oxidative stress therefore plays a critical role in various neurological diseases, including ischemic stroke, and neurodegenerative diseases, including MCI and the prodromal stage of AD.[26–28] In humans, VE is a powerful antioxidant that promotes neurotransmission and carries out an important role in brain function by regulating the synthesis and release of neurotransmitters and thereby improving cognitive function.[29,30] Another basic study of a rat model found that VE restored memory impairment from chronic sleep deprivation through hippocampal molecules,[31] which could also be a possible mechanism for how VE improves cognitive impairment.

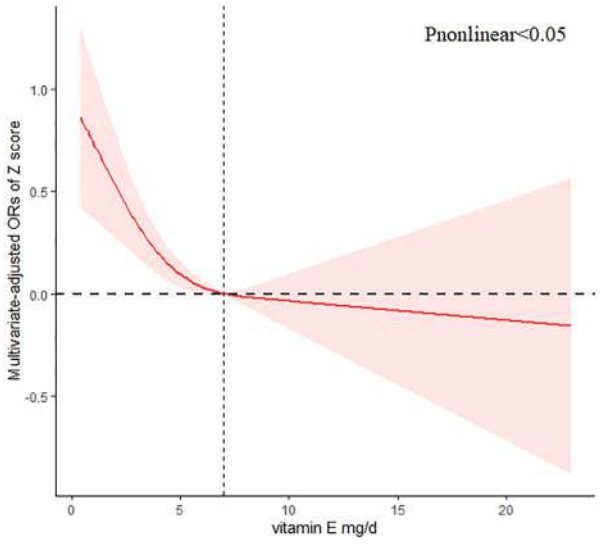

Fig. 3. Dose–response relationship between dietary VE intake and risk of low cognitive function global z-score. VE, vitamin E.

After adjusting for all variables, dietary VE intake was significantly associated with cognitive function in female participants. However, there was no significant correlation in male participants. These findings may indicate a sex difference in the relationship between dietary VE intake and cognitive function.[32,33] A rat model suggests that male rats respond more to reactive oxygen species produced during stress and ischemia than females due to brain vitamin loss. This is an important mechanism for the difference in vitamin reflexes between males and females.[34] In addition, males consume more alcohol than females, and studies have found an association between alcohol consumption and elevated oxidative stress, which is associated with reduced gray-matter volume in specific regions, such as the frontal lobe, which may be the mechanism behind the sex differences in the relationship between VE intake and cognitive impairment risk.[32] Many studies have also only included female participants, and studies on the relationship between VE intake and cognitive performance in males are lacking[35,36]; the relationship between VE and cognitive performance in males should therefore not be overlooked in future studies.

This study had some shortcomings. First, it had a cross-sectional design and so could not determine the causal relationship between VE intake and cognitive performance. Second, there may be recall bias in dietary VE intake obtained by finding the mean value from two 24-h dietary recalls. Third, we did not distinguish between causes of cognitive impairment, such as AD, Lewy-body dementia, and vascular dementia. Fourth, although we considered the main confounding factors to the greatest possible extent, the environments in which people live and eat are also possible confounding factors that we did not consider.

Conclusions

We found that dietary VE intake was negatively associated with the risk of low cognitive performance in older adults. Ideal vitamin VE supplementation is related to optimal cognitive function, so future studies should look more deeply into their causal relationship.

Author statements

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Competing interests

The authors declare no conflict of interest.

Author contributions

W.L., S.L., and W.Z. contributed to conceptualization. W.L. contributed to methodology and data curation. Y.S. contributed to software. W.L., S.L., and Y.Q. contributed to validation. W.L.,W.Z., and L.L. contributed to writing the article. W.L. and W.Z. wrote, edited, and reviewed the article. L.J. and Z.C. contributed to researching designs and revising manuscripts. All authors have read and agreed to the published version of the article.

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data availability

The data that support the findings of this study are openly available vis this link: http://www.cdc.gov/nchs/nhanes.htm (accessed on 28 June 2021).

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Appendix A. Supplementary data

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Population well-being and the COVID-19 vaccination program in Chile: evidence from Google Trends

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ABSTRACT

Objective: We analyze the dynamics of the mental well-being of the Chilean population in response to the progress of the vaccination strategy implemented by the government.
Study design: This study aims at investigating the possibility of using Google Trends as an instrument for tracking mental well-being of the Chilean population.
Methods: We use the volume of searches for keywords in Google Trends (GT) related to *Anguish, Anxiety, Depression,* and *Stress* as a proxy for population well-being. Using event study methods, we analyze social attention reactions to news about the vaccination program. We implement a Difference-in-Difference-in-Differences estimation to estimate changes in population welfare by socio-economic status induced by the progress of inoculation.
Results: We show that social attention to mental health problems is sensitive to news about the vaccination program. Moreover, and most importantly, we find that mental well-being responds positively to the percentage of inoculated people. This phenomenon appear to be permanent and affected by socio-economic status, with the wealthier population experiencing greater improvements than the less wealthy.
Conclusions: During the COVID-19 vaccination program in Chile, social attention to mental health problems appears to be sensitive to news about the vaccination program. There is also strong evidence of socio-economic status–induced heterogeneity in population responses to program implementation. The above phenomena appears to be permanent and cannot be attributed to either socio-economic segregation in access to vaccines or to the highly stratified schedule of the vaccination program.

Introduction

As the COVID-19 pandemic evolved and vaccines became available, most countries implemented mass vaccination programs. In retrospect, vaccination processes have not only reduced health risks and helped economic activity to recover but have also alleviated the deterioration in people's well-being resulting from social distancing, isolation, and uncertainty.[1–8]

Chile became an example worldwide in terms of the speed and effectiveness of its vaccination program.[9,10] The Chilean health authorities pursued an aggressive vaccination campaign, engaging in early negotiation and signing business contacts with Sinovac, Pfizer-BionTech, Janssen, and AstraZeneca, which guaranteed access to the vaccines to practically the whole population. A total of 2.7 million people, almost 14% of the country's 19 million inhabitants, were immunized in the first 15 days of the process, which began on February 3, 2021. On March 9, 2021, *Our World in Data* ranked Chile first among those countries that were vaccinating their population the fastest, and on March 24, 2021, Chile passed the milestone of having 6 million people, nearly one-third of its total population, vaccinated with their first or single dose. On July 30, 2021, 80% of the target population had completed their vaccination program. By year-end 2021, Chile had the highest level of vaccination against COVID-19 in Latin America and, with a rate of almost 90%, one of the best in the world (marcachile.cl).

In this article, we analyze the dynamics of the mental health well-being of the Chilean population in response to the progress of the vaccination strategy implemented by the government. We refer to the studies by Díaz et al.[8] and Brodeur et al.[11] and use Google Trends (GT) data to proxy for changes in the mental well-being of the population. The underlying hypothesis is that social attention to mental health

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problems is reflected in Internet searches, which in turn should provide representative information on the health status of users.[d]

The fact that the health authorities designed a highly stratified vaccination program, together with a high degree of demographic and socio-economic heterogeneity among Chilean counties, allows us to measure the differential effects that the vaccination process may have had on the well-being of people belonging to different socio-economic strata. Furthermore, the wide coverage of the Chilean vaccination program and the role played by the authorities in ensuring the early availability of vaccines for the entire population allow an estimate of the effects of the vaccination program that is not affected by inequalities in access to health care.

Our results have important implications for both policymakers and researchers. First, mental health responses to the vaccination process appear to be affected by socio-economic status (SES). Therefore, it is critical to incorporate such heterogeneity in the design of policies aimed at alleviating the consequences of COVID-19 on population well-being. Second, from an academic perspective, any attempt to measure changes in the mental well-being of a population induced by exogenous factors could yield biased results if such heterogeneity is not controlled for. Finally, our work highlights the utility of using online population metrics to analyze, with near real-time data, the actual state of a disease. In this sense, Google Trend data can help public health experts and policymakers to set priorities and establish long-term strategies to mitigate symptoms and address mental and other health disorders.

Methods

Sample

We consider all the counties in the country with a population larger than 13,000 people. This sample covers 120 counties with a population of 15.8 million people, accumulating approximately 83% of the country's total population. We are able to obtain complete socio-economic and vaccination data for 117 of these counties, from February 1, 2021, to September 30, 2021, which correspond to our final sample for estimation purposes. For this sample period, we obtained daily online search data on the following topics related to mental health wellness: *Anguish, Anxiety, Depression,* and *Stress*. To obtain a baseline measure of societal attention to these issues under pandemic conditions but without vaccine availability, we also obtained online search data for the analogous period during 2020.

Social attention to mental health problems

We obtained the daily volume of Google searches for the topics presented in Table 1, translated into Spanish. These terms are related to *the 4-Item Patient Health Questionnaire for Anxiety and Depression* and have recently been used in the study of the impact of the COVID-19 vaccine on mental health disorders. Our proxies for the population attention toward mental health disorders are based on GT.[e] This service produces time series data on *Search Volume Intensity* (SVI) to measure the popularity of a particular keyword in a specific period and location.[18] The SVI is measured on a scale that ranges from zero (complete disinterest) to 100 (peak of popularity). Search terms are literally typed words, whereas topics may be proposed by GT when the tool recognizes phrases related to popular queries.[f] We follow[8] and retrieve data on the search volume intensity of the above-mentioned keywords for the sample period between February and September 2021. To study how changing patterns in search activity are related to the vaccination process, we follow[19] and calculate an *Abnormal Search Volume Activity*, $ASVA_{s,t}$

$$ASVA_{s,t} = ln\left(\frac{SVI_{s,t}}{E(SVI_{s,t})}\right) \quad (1)$$

where *ln* denotes natural logarithm and the $E(SVI_{s,t})$ is computed as the monthly average of the corresponding SVI index for keyword *s* during the corresponding month in 2020. The $ASVA_{s,t}$ index can be interpreted as the change between the search volume intensity of a given keyword during the vaccination period and its expected value during the pandemic but before the vaccination process began. We aggregate search intensity across terms in Table 1 by taking the average across all individual keywords *s* for each day *t* to obtain and aggregate *Mental Health* Index (MHI).

Table 1
Search terms: search terms used for Google Trends searches and recent works in which they appear.

Keyword (*s*)	Article
Anguish	Perez-Arce et al. (2021)[3], Koltai et al. (2022)[2]
Anxiety	Agrawal et al. (2021)[1], Perez-Arce et al. (2021)[3]
Depression	Agrawal et al. (2021)[1], Perez-Arce et al. (2021)[3], Koltai et al. (2022)[2]
Stress	Manning et al. (2021)[20]

Socio-economic status

Our proxy for the SES of the population is the *Poverty Index (PI)*, reported by the *Ministry of Social Development (Ministerio de Desarrollo Social)* in the CASEN 2019 survey.[g] Following Díaz et al.[8] and Díaz and Henríquez,[21] we consider wealthy counties as those belonging to the 10th percentile according to the *PI* sorting, which correspond to 12 counties whose population comprise about 11% of the country total population.

Vaccination

The vaccination process in Chile was carried out gradually and progressively, giving priority to the highest risk groups and expanding the target population according to the number of doses arriving in the country. Initially, it considered two phases. The first one began on December 24, 2020, and focused on the critical population, defined as people whose functions expose them to increased risk of infection and/or who perform functions considered critical for the maintenance of health services and essential activities for the country. The second phase corresponded to the mass vaccination plan that began on February 3, 2021. During this phase, the health authority established a timetable that began by vaccinating those aged >90 years in descending order and assigning 2 years for each day of vaccination. Based on an effective and already established public network, the governmental vaccination program aimed to

[d] This hypothesis has been validated in the recent literature. Wang et al.[12] provide evidence that GT may be a valid novel epidemiological tool to map depression prevalence. Twenge and Joiner[13] and Gianfredi et al.[14] show that the COVID-19 pandemic can be associated with a surge in Internet searches related to mental health issues.

[e] A detailed description of the questionnaire can be found in a study by Stanhope.[15] As described in Nagao et al.,[16] Google Trends is a service that shows the frequency of worldwide searches for a specific period or time interval. Similar to many of Google services, Trends is widely used to obtain information and data on Internet searches for statistical purpose.[17]

[f] While collecting data, values below 1, denoted as <1, were replaced by 1. We specify the region as CL (Chile).

[g] Available at http://observatorio.ministeriodesarrollosocial.gob.cl.

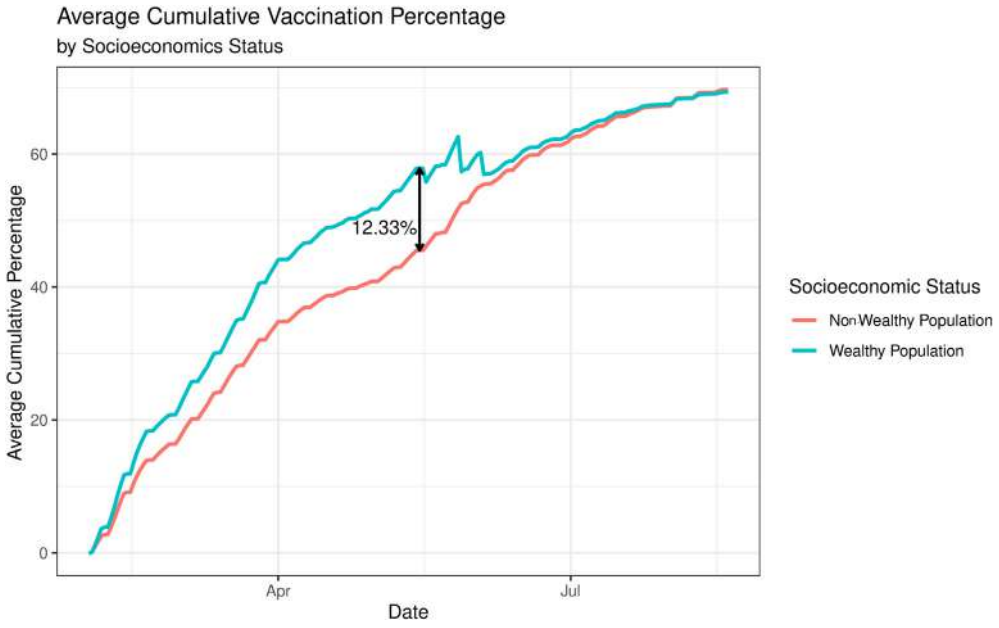

Fig. 1. Aggregated vaccination by socio-economic status: the cumulative daily percentage of vaccinated population is computed for wealthy and non-wealthy counties. Wealthy counties correspond to those belonging to the 10th percentile according to the *Poverty Index* sorting.

achieve homogeneous coverage of 80% or more of the target population. The result was outstanding: 2.7 million people were immunized in the first 15 days of the second phase, and on July 30, only six months after the beginning of the mass vaccination schedule, 80% of the target population had completed their vaccination program.[h]

Although the program achieved universal coverage of the country's entire population, in its initial phase, there were important differences in the vaccination rate in favor of people from higher socio-economic levels. As shown in Fig. 1, the difference in the cumulative percentage of inoculated persons between wealthy and non-wealthy counties increased during the first few months of the program, peaking at 12.33% in mid-May, and closing over the following weeks. As we discuss below, the existence of this gap in the early stages of the vaccination program is what allows us to statistically identify the heterogeneous effect that vaccination had on populations of different socio-economic strata.

Estimation

Event study analysis

We consider the five highly mediatized events described in Table 2 to assess the short-term performance of our measures of social care for mental health problems.[i]

To statistically evaluate the changes in our ASVA indices in the neighborhood of an event, we resort to standard tools of the event study methodology.[23–25] We consider two different event windows: the first one is the [−1;+1] window, which includes three days (the day before the event, the day of the event, and the day after the event); and the second one is the [0;+1] window, which considers the day of the event and the day after. For inference and hypothesis testing, the ASVAs for each day t are summed inside the corresponding event window to compute a Cumulative ASVA (CASVA) for that window.[j]

The Difference-in-Difference-in-Differences estimators

To analyze the dynamics of the population well-being throughout the vaccination process, we follow closely the estimation strategy in a study by Díaz et al.[8] Our approach allows us to estimate the differential effects of the mass vaccination program on social attention toward mental health disorders for different socio-economic segments of the population. In our empirical specifications, the dependent variable is the ASVA, measured for the different keywords in Table 1 at different times. As this variable is calculated from historical GT keyword searches, we can measure the public's attention to these topics daily. Two important implications follow. First, as Brodeur et al.[11] point out, to have adequate assessments of how government responses have affected the well-being of the population during the pandemic, having data before the corresponding government intervention is crucial. By using GT, we can compute the differential effect that vaccines have had on the well-being of the population between a pandemic situation without vaccines (2020) and the corresponding period but with the vaccination program in place (2021). Second, we can determine how social attention to mental health problems evolves daily, and not only on some specific dates, as occurs in studies based on surveys or online questionnaires. Therefore, we can assess whether the progress of the vaccination process induces permanent or temporary changes in the population's attention to mental health disorders.

Let i index counties and t index calendar time. Let us define a dummy variable $D_{it}(\pi)$, such that $D_{it}(\pi) = 1$ if the accumulated percentage of inhabitants inoculated in county i, at time t, is equal or greater than π, but strictly lower than $\pi + \Delta$, and $D_{it}(\pi) = 0$ otherwise. For each county, we create a total of m dummies $D_{it}(\pi)$, going from $D_{it}(0)$ (less than Δ percent of the inhabitants of county i, at time t, are inoculated), to $D_{it}(m)$ (e.g. if m = 1, it means that all the inhabitants of this county are already inoculated).

[h] For details on the logistics of the Chilean vaccination program and health system characteristics see studies by Castillo et al.[9] and Aguilera et al.[22]

[i] Although we focus our attention on the vaccination process, we consider as the first event the government's announcement of a new total lockdown for all the counties of the Santiago Metropolitan Area on July 12, 2020. Given that most of the events related to the vaccination program during our sample period can be considered good news, we considered it appropriate to test our social attention measures toward mental health problems with news that should clearly be considered bad news by the population.

[j] We also consider the [−2;+2] window in our analysis. The results are qualitative the same as with the [−1;+1] and [0;+1] windows and are thus not reported. See a study by Díaz and Henríquez[21] for a detailed explanation of the methodology.

Table 2
Events for analysis: events and announcements related to the Chilean vaccination process.

Event	Event description	Date
Event 1	Announcement of a new lockdown in every county of Santiago	12/07/2020
Event 2	Announcement of the arrival of the first 10,000 doses of Pfizer vaccines	12/24/2020
Event 3	Announcement of the official vaccination plan in Chile	01/28/2021
Event 4	Beginning of the second doses of vaccinations	03/03/2021
Event 5	First vaccinations to children aged between 12 and 15 years	07/13/2021

Let Y_{it} be the ASVA for a given keyword in county i at time t. Let W_i be a county-specific dummy variable such that $W_i = 1$ if county i is wealthy, and 0 otherwise. This dummy variable is not time varying because there are no changes in the SES of counties in the relatively short time span of our sample. Consider a longitudinal sample of n counties over T periods and the linear regression model:

$$Y_{it} =;\alpha_i + \sum_{\pi=0}^{m} \delta_\pi D_{it}(\pi) + \sum_{\pi=0}^{m} \beta_\pi W_i D_{it}(\pi) \ + \gamma W_i + \varepsilon_{it}, \quad cr \qquad (2)$$

where (β_π, δ_π) for $\pi = 0, \Delta, 2\Delta, 3\Delta, \ldots, m$ are the regression coefficients of interest, α_i is a county effect, and ε_{it} is the error term.

This setup corresponds to a *staggered DiD* model,[26,27] in which the parameters β_π are the difference-in-differences estimators: the difference in the expected ASVA for wealthy counties, before and after increasing the percentage of the inhabitants inoculated to π percent, minus the difference in the expected ASVA for non-wealthy counties, before and after increasing the percentage of the inhabitants inoculated to π percent. It should be noted that our dependent variable, ASVA, is already a difference between the volume of searches for keyword s between day t and a historical average, computed as the monthly average of the corresponding SVI index for keyword s during the corresponding month in 2020. Accordingly, the estimation we entertain is actually a triple difference estimation—Difference-in-Difference-in-Differences (DiDiD; time, vaccination progress, and SES).[28,29] The other parameters of interest, the parameters δ_π, capture the effect of increasing the percentage of inhabitants vaccinated in non-wealthy counties over the ASVA of the corresponding keyword. Using standard arguments, it is straightforward to show that the expected ASVA for the whole population, before and after increasing the percentage of the inhabitants inoculated to π percent, is given by $\tau(\pi) = \delta_\pi + \rho\beta_\pi$, where $\rho = Pr(W_i = 1)$; that is, the proportion of wealthy counties in Chile by the time of the pandemic.

Identifying the parameters (β_π, δ_π) in our setup is not straightforward. This is so because we do not observe the ASVA for each county, but rather for the entire country; in other words, we observe Y_t rather than Y_{it}. Notice, however, that Y_t can be considered as the expected value of Y_{it}, at a specific time t: $E_t[Y_{it}] = Y_t$. Therefore, Y_t corresponds to the expected value of the corresponding ASVA across all counties at any given day. Taking the conditional expectation at time t over equation (2), it is possible to show that the parameters (β_π, δ_π) are identifiable as long as W_i and $D_{it}(\pi)$ are not independent. In terms of our empirical specification, this boils down to the condition that the speed of vaccination differs between wealthy and non-wealthy counties.[k] According to the percentages of vaccination presented in Fig. 1, this seems to be indeed the case. The rate of vaccine inoculation of the population of wealthy counties differed from that of the inhabitants of non-wealthy counties during the first months of the vaccination program. This difference was sufficiently large to allow for the estimation of our DiDiD specification.

Results

Event study results

In Fig. 2, we report the z-statistics associated with the null hypothesis of no abnormal search volume intensities for each of the terms in Table 1 and each of the five events in Table 2. Panel A exhibits results for the [−1;+1] event window, and Panel B reports results for the [0;+1] event window. As the results for both event windows are generally similar, we center our discussion on the [−1;+1] window.

For the first event, the government announcement of a new lockdown for all the counties in the Metropolitan Area of Santiago on July 12, 2020, there was a high abnormal volume search for *Anguish* and *Anxiety*; the z-statistic for the corresponding CASVA results highly significant for both search terms, easily exceeding the 5% level in Fig. 2. For *Stress* and *Depression*, there are no significant effects at the 10% level.

For the rest of the events in Table 2, which should be considered as good news, our results show a reduction in social attention to mental health issues. Whenever the test statistics are statistically significant, at least at the 10% level, population reactions in terms of social care for mental health problems have the expected (negative) sign. In particular, our results are striking for the terms *Anguish* and *Anxiety*. Both keywords show abnormal searches whose direction is consistent, in all cases, with people's expected reaction to good or bad news, being almost always statistically different from zero.

For completeness, we also performed the analysis for the MHI. As the index is just an aggregation of the keywords in Table 1, the results are qualitative, the same as those presented in Fig. 2.[l]

DiDiD estimation

For the estimation of equation (2), we need to establish both the width of the bins Δ for $\pi = 0, \Delta, 2\Delta, 3\Delta, \ldots, m$ and the highest level of accumulated vaccination m, so that the identification condition holds. We consider bins of 2% width, up to an accumulated level of 70% of vaccination—that is, π = 0%, 2%, 4%, 6%, …, 70%.[m] We thus obtain 35-point estimates $(\hat{\beta}_\pi, \hat{\delta}_\pi)$, each for each bin of π, with their corresponding standard deviations. In all specifications, we include the COVID-19 reproductive number R_0 to control for the general conditions of the pandemic, the stringency of lockdown in the corresponding county was when π% of its population was vaccinated, and month dummies.[n] The abundant output of our estimations are concisely reported in Fig. 3 and in Table 3.

[k] A formal discussion and derivation of the identification condition is presented in Appendix A.

[l] For the event window [−1;+1], the CASVA for the index is positive for the first event, with a z-statistic of 1.00 but insignificantly different from zero. For the remaining events, all z-statistics are negative, and three of the four are statistically significant at the 5% level or better: z = −3.24, z = −3.74, and z = −4.68 for events 3, 4 and 5, respectively. For the [0;+1] window, the results are basically the same.

[m] We tried width lengths Δ ranging from 1% to 5% and accumulated vaccination levels m of 50%, 60%, and 80%. The results remain qualitatively unchanged.

[n] The Chilean health authorities followed an almost unique confinement strategy, known as a Dynamic Quarantine or Strategic Quarantine.[30] This strategy evolved through time, from complete and differential lockdowns imposed to the different counties of the country during the early months of the pandemic between March 24 and July 20, 2020, to a stage known as the Step by Step plan, in which the government eased the complete lockdowns imposed up to that point, implementing restrictions based on five stages or incremental steps, ranging from lockdown (phase 1) to advanced opening (phase 5). It is during this latter stage that the implementation of the mass vaccination program took place.

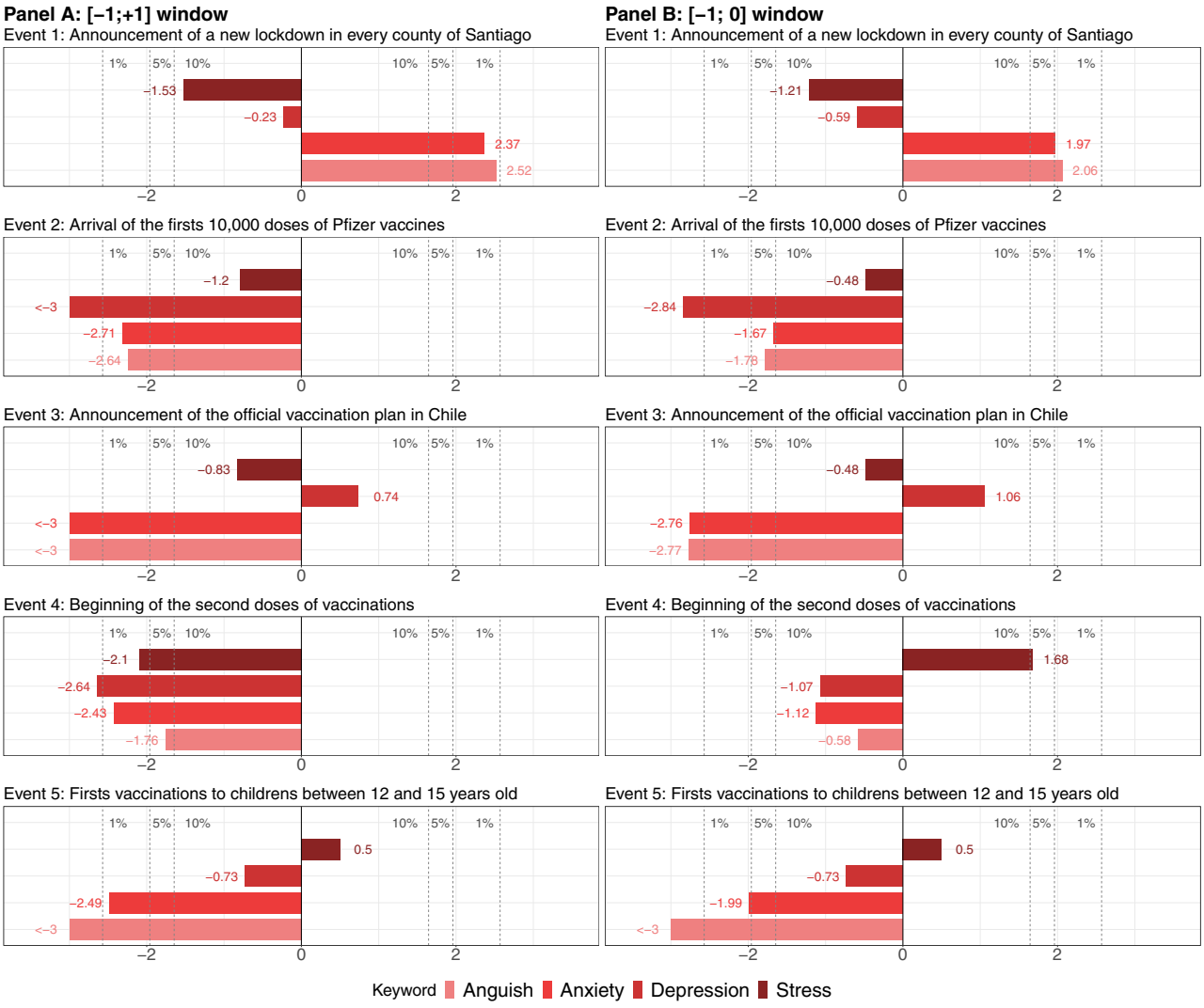

Fig. 2. Event study results. z-statistics associated with the CASVA of the corresponding keyword. Panel A reports results using the event window [−1;+1]. Panel B reports results using the event window [0;+1]. Horizontal bars correspond to the value of the z-statistics. The vertical lines indicate critical values at the 1%, 5%, and 10% levels of significance.

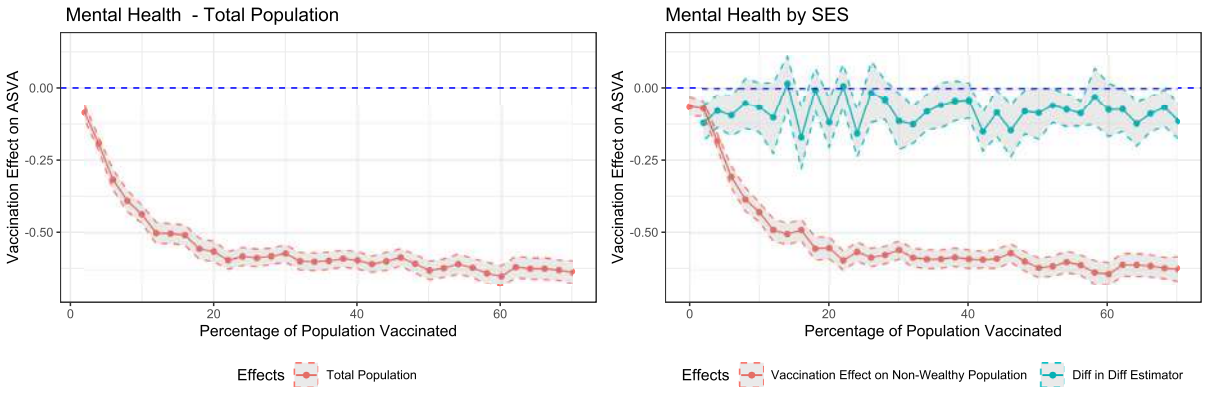

Fig. 3. (A) ASVA—Mental Health Index. Difference-in-Difference-in-Differences (DiDiD) estimation. Vaccination effects on the whole population are given by $\tau(\pi) = \delta_\pi + \rho\beta_\pi$ (left panel). Vaccination effects by SES are given by the effect in non-wealthy population (δ_π) and the *DiDiD* estimator (β_π) (right panel). Ninety percent confidence intervals are based on standard errors clustered at the county level. All regressions control for the reproductive number R_0, the corresponding month, and the stringency of the quarantine phase imposed by the health authority in the corresponding county. (B): ASVA—Anguish and Anxiety. (C) ASVA—Depression and Stress. ASVA, Abnormal Search Volume Activity; SES, socio-economic status.

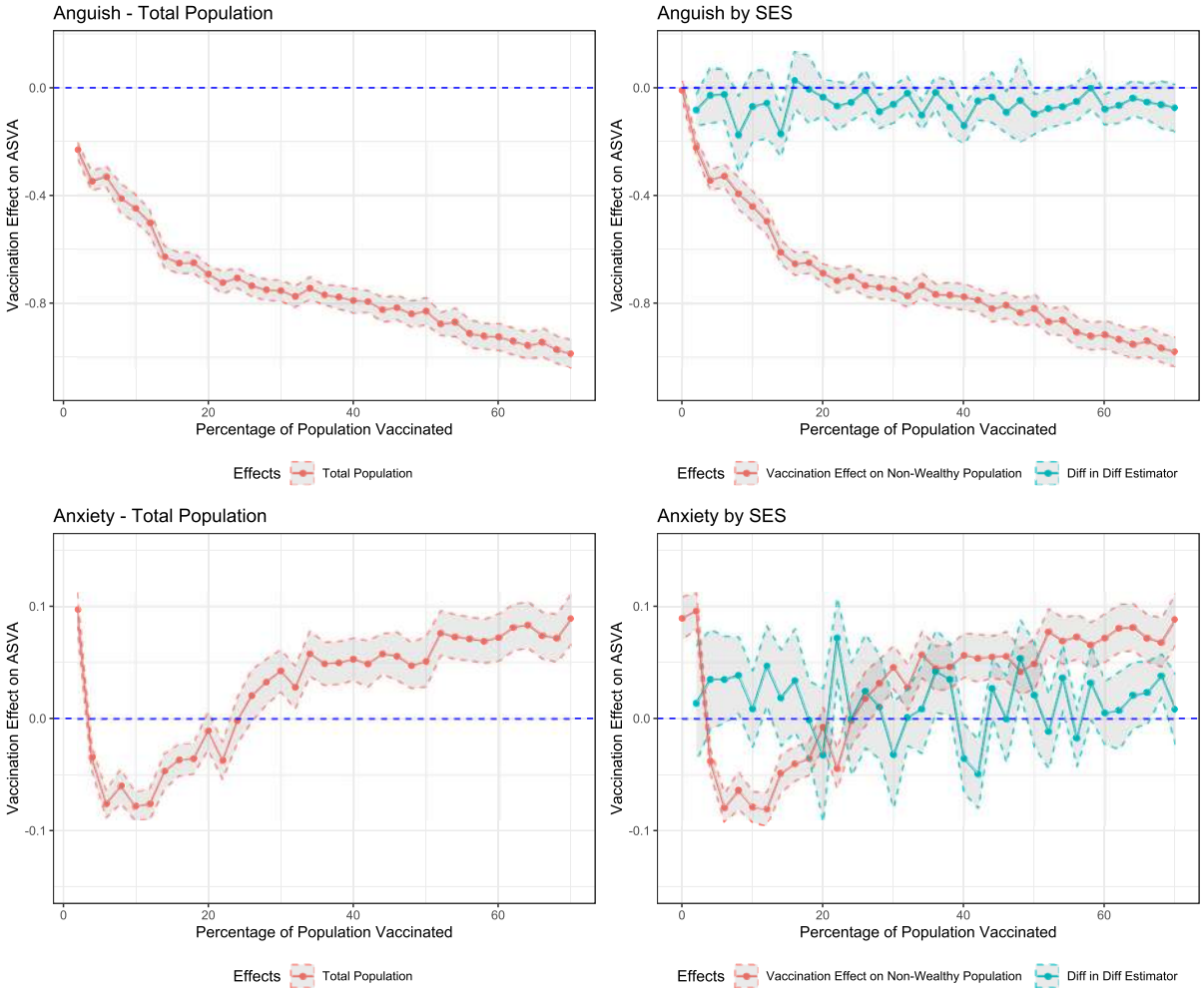

Fig. 3. (*continued*).

In Fig. 3 we present, for the *Mental Health Index* and for each of the keywords in Table 1, the estimated vaccination effect on the whole population, $\tau(\pi)$; the vaccination effects on the non-wealthy population, δ_π; and the DiDiD estimates, β_π, with their corresponding 90% confidence intervals. In Table 3 we report the average estimates of $(\hat{\beta}_\pi, \hat{\delta}_\pi)$ across π, the proportion of bins in which the effects are positive or negative, and the corresponding proportion of bins in which the effects are statistically significant at various confidence levels.

As shown in Fig. 3, there is a significant decline in public attention to mental health disorders, as reflected in the evolution of the *Mental Health Index*, as the vaccination schedule progresses. For the whole population (left panel), this reduction is sharp and persistent. From a value close to zero at the beginning of the vaccination program, the predicted coefficients $\hat{\tau}_\pi$ drop steadily with the progress of the vaccine inoculation, stabilizing at around a level of -0.6 when the percentage of vaccinated population reaches 20%. As shown in Table 3, all the estimated $\hat{\tau}_\pi$ coefficients result negative and highly significant. For the inhabitants of non-wealthy counties—90% of the population—in the right panel of Fig. 3, the series of the $\hat{\delta}_\pi$ coefficients also show a strong reduction, very similar (as expected) to the behavior of the $\hat{\tau}_\pi$ series. According to the results in Table 3, all the $\hat{\delta}_\pi$ coefficients are negative and statistically significant at any standard level of significance.

Regarding the existence of SES heterogeneity, as shown in Table 3, 94.29% of the DiDiD estimators $\hat{\beta}_\pi$ are negative. Conditional on being negative, 42.86% result significant at the 5% level, and 57.14% result statistically significant at the 10% level. That is, 54% of the DiDiD coefficients result negative and statistically different from zero at the 10% level.[o] The average value of the estimated $\hat{\beta}_\pi$ coefficients is -0.08, which compares to a value of -0.54 for the $\hat{\delta}_\pi$ coefficients. These results provide strong evidence to support the existence of SES heterogeneity in population well-being responses to the vaccination progress.

For *Anguish* and *Depression*, the series for $\hat{\beta}_\pi$, $\hat{\delta}_\pi$, and $\hat{\tau}_\pi$ in Fig. 3 shows similar dynamics to those of the Mental Health Index, with a strong and persistent effect of vaccination on the well-being of the population, and evidencing SES-induced heterogeneity.

Our results show a short-lived reduction in social attention to *Anxiety* at the beginning of the vaccination program, shortly reverting to an upward trend, with weak evidence of SES heterogeneity in the population's attention to anxiety-related issues. Regarding *Stress*, the series of $\hat{\tau}_\pi$ and $\hat{\delta}_\pi$ exhibit a signification

[o] This 54% is obtained as the product between 0.9714 (the percentage of negative βπ coefficients) and 0.5714 (the percentage of negative and significant βπ coefficients).

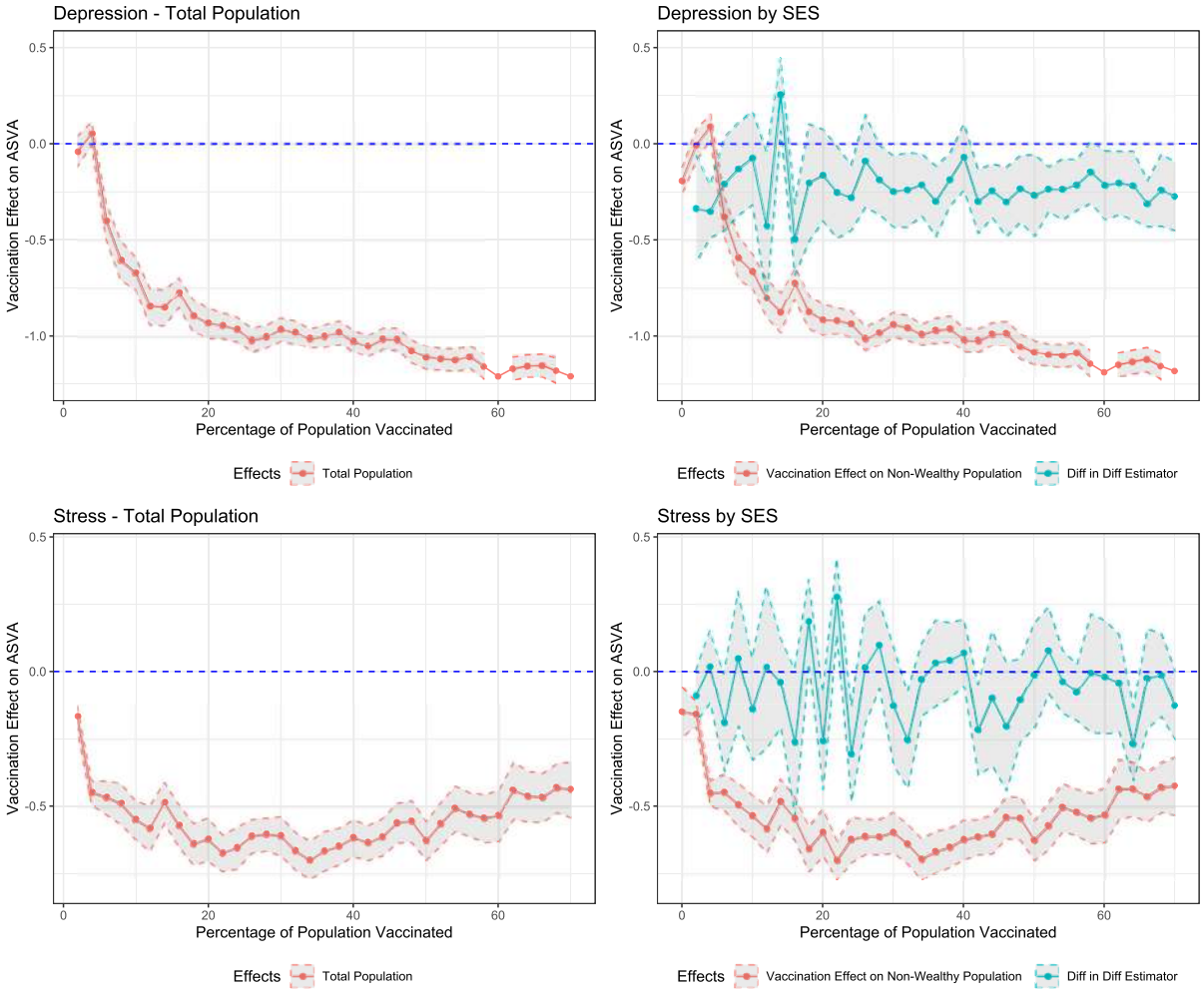

Fig. 3. (*continued*).

reduction at the early stage of the vaccination process, but with no evidence of SES-induced heterogeneity.[p]

Strengths and limitations

The use of GT data presents a number of key advantages over survey data. First, the data are not self-reported by a subsample of respondents but rather capture the impact of vaccination program on the behavior of all Google users. Furthermore, GT data do not suffer from biases such as the observer-expectation effect or interviewer bias. Third, GT data are less vulnerable to small-sample bias.

There are several limitations to the analysis. First, younger individuals are relatively more likely to use Google Search than older individuals.[21] Second, the sociodemographic characteristics of Google users are unknown. Finally, GT searches might be subject to ambiguity: some of these four terms may change, in either direction, without a direct relation with well-being of the Chilean population.

Despite the limitations mentioned earlier, recent literature supports the use of health-related Internet searches to track the evolution, incidence, and spread of different diseases. In a thorough systematic review,[14] the authors find a statistically significant increase in searches for information about mental health issues by the general public throughout the COVID-19 pandemic. Similarly, Wang et al.[12] provide evidence that GT may be a valid novel epidemiological tool to map depression prevalence. Locatelli et al.[38] find that GT data are useful for predicting outbreaks of coronavirus.[q]

Discussion

According to our results, the Chilean vaccination program has had important effects on the mental health conditions of the population. In terms of the MHI, our results indicate that such effects are statistically and economically significant, tend to persist over time, are enhanced by increased inoculation levels, and have differentiated effects according to the SES of the population. This evidence is

[p] The "U-shaped" pattern observed for Anxiety is consistent with the characteristics of the generalized anxiety disorder (GAD). According to the British National Health Service (NHS), GAD is a "long-term condition that causes people to feel anxious about a wide range of situations and issues, rather than 1 specific event … As soon as one anxious thought is resolved, another may appear about a different issue." In this sense, once vaccination anxiety is resolved, many other pandemic-related factors, such as confinement or social distancing, may be affecting the population, leading to the observed pattern. Gaitán-Rossi et al.,[31] Pera, A.,[32] Hyland et al.,[33] Shevlin et al.,[34] Bäuerle et al.,[35] Zhang et al.,[36] Lee et al.,[37] among others, provide evidence of the prevalence of GAD during the pandemic.

[q] Azzam et al.,[39] Johnson et al.,[40] and Senecal et al.[41] provide further evidence of the usefulness of online searches for the analysis of various dimensions of different diseases.

Table 3
Difference-in-Difference-in-Differences estimation: effects of vaccination on the population.

Search Topic	Parameter	Average	Positive				Negative			
			Percentage	Signif. 1%	Signif. 5%	Signif. 10%	Percentage	Signif. 1%	Signif. 5%	Signif. 10%
Aggregate	δ_π	−0.54	0.00%	0.00%	0.00%	0.00%	100.00%	100.00%	100.00%	100.00%
Mental Health Index (MHI)	β_π	−0.08	5.71%	0.00%	0.00%	0.00%	94.29%	25.71%	42.86%	57.14%
Anguish	δ_π	−0.73	0.00%	0.00%	0.00%	0.00%	100.00%	100.00%	100.00%	100.00%
	β_π	−0.06	2.86%	0.00%	0.00%	0.00%	97.14%	8.57%	22.86%	31.43%
Anxiety	δ_π	0.03	68.57%	60.00%	65.71%	65.71%	31.43%	25.71%	25.71%	25.71%
	β_π	0.01	74.29%	8.57%	14.29%	25.71%	25.71%	2.86%	2.86%	5.71%
Depression	δ_π	−0.91	2.86%	0.00%	2.86%	2.86%	97.14%	94.29%	94.29%	94.29%
	β_π	−0.22	2.86%	0.00%	2.86%	2.86%	97.14%	28.57%	65.71%	74.29%
Stress	δ_π	−0.55	0.00%	0.00%	0.00%	0.00%	100.00%	100.00%	100.00%	100.00%
	β_π	−0.06	31.43%	2.86%	5.71%	5.71%	68.57%	5.71%	14.29%	17.14%

Estimated parameters from (2). δ_π is the effect on non-wealthy population. β_π is the DiDiD estimator. Statistical significance was computed using standard errors clustered at the municipal level. All regressions control for the reproductive number R_0, month, and the stringency of the phase imposed on the corresponding county.

consistent with the results in studies by Koltai et al.[2] and Perez-Arce et al.[3] in that receiving the first dose of the vaccine is associated with declines in multiple psychological distress factors, such as depression, stress, or anguish. However, the SES-induced heterogeneity is inconsistent with the results in a study by Agrawal et al.[r] These authors find that vaccination is associated with a greater reduction in symptoms of anxiety or depression among US individuals who are more likely to be non-wealthy.[s] But these apparently contradictory results can be explained, by the differences in access to the vaccine between the Chilean and US populations.

On the one hand, the COVID-19 pandemic has exacerbated the inequalities in healthcare access that have prevailed in the United States for a long time. These inequalities have led to disparities in access to vaccines and to a proportionately greater increase in COVID-19–associated illness and death among members of racial and ethnic minority groups.[42–44] Relatedly, Siddique et al.,[45] Whitaker et al.,[46] and Anand et al.[47] find that poverty is a significant and consistent determinant of higher COVID-19 infections and fatalities in the United States. In this sense, the phenomena documented by Agrawal et al.[1] may well be reflecting the relief that vaccination brought to the lower-income population that had been experiencing high rates of infection and mortality in the early stages of the pandemic in the United States.

Chile, on the other hand, has been a world leader in its vaccination campaign, achieving universal coverage in a very short time. The difference in vaccine inoculation rates between the wealthy and non-wealthy populations in Fig. 1 cannot be attributable to socioeconomic segregation in the access to the vaccine or to the priority given to the older and high-risk individuals in the vaccination schedule.[t]

Beyond the specific factors that could be inducing different attitudes toward vaccination among the Chilean population, it is likely that people who are more accepting of the inoculation process, who therefore get vaccinated earlier, also show a more positive psychological reaction when vaccinated and experience a greater improvement in their well-being, in line with our results.

[r] This is the only other work of which we are aware that documents heterogeneous effects of vaccination on mental health in different socio-economic segments of the population.

[s] Individuals with lower education levels, who rent their housing, and who cannot telework.

[t] In (unreported) analysis, we find that controlling for the SES of the population, there is no statistical association between county densities and the number of vaccination centers, which is consistent with the claimed universal coverage of the vaccine. Furthermore, we find that there are no statistically significant differences in the distribution of age-related variables between wealthy and non-wealthy counties, so the differences in the vaccination rates in Fig. 1 cannot be attributed to the priority given to the older and high-risk individuals.

Author statements

Ethical approval

None sought as this project includes no human participants.

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Competing interests

All authors declare no conflict of interest.

Appendix A. Identification Condition

Taking the conditional expectation at time t over equation (2) yields:

$$Y_t = E_t[Y_{it}] = E_t[\alpha_i] + \sum_{\pi=0}^{m} \delta_\pi E_t[D_{it}(\pi)] + \sum_{\pi=0}^{m} \beta_\pi E_t[W_i D_{it}(\pi)]\ cr \tag{A.1}$$

It is assumed that the conditional expectation $E_t[W_i]$ is equivalent to the unconditional expectation $E[W_i] = \rho$ because the proportion of wealthy counties does not change within the time span of our sample. Accordingly, both $\bar{\alpha} = E_t[\alpha_i]$ and $\gamma\rho$ turn out to be constant in equation (A.1). Let $\lambda = \bar{\alpha} + \gamma\rho$ be the new constant term. Equation (A.1) can be written as:

$$Y_t = E_t[Y_{it}] = \lambda + \sum_{\pi=0}^{m} \delta_\pi \bar{D}_t(\pi) + \sum_{\pi=0}^{m} \beta_\pi E_t[W_i D_{it}(\pi)] \ + \bar{\varepsilon}_t \tag{A.2}$$

where $\bar{D}_t(\pi) = E_t[D_{it}(\pi)]$. In equation (A.2), it is not possible to identify (β_π, δ_π) individually if W_i and $D_{it}(\pi)$ are independent. To see this, notice that if such is the case, then $E_t[W_i D_{it}(\pi)] = E_t[W_i]E_t[D_{it}(\pi)] = \rho\bar{D}_t(\pi)$, and equation (A.2) reduces to:

$$Y_t = E_t[Y_{it}] = \lambda + \sum_{\pi=0}^{m} [\delta_\pi + \beta_\pi\rho]\bar{D}_t(\pi) + \bar{\varepsilon}_t \tag{A.3}$$

In equation (A.3), it is not possible to obtain separate estimates for β_π and δ_π but just for $\delta_\pi + \beta_\pi\rho$. Therefore, the main condition for the identification of β_π and δ_π is that W_i and $D_{it}(\pi)$ are not independent. Under dependency between W_i and $D_{it}(\pi)$, $E_t[W_{it}D_{it}(\pi)] = Cov_t[W_i; D_{it}(\pi)] + \rho\bar{D}_t(\pi)$. Letting $\Gamma_t(\pi) = Cov_t[W_i; D_{it}(\pi)]$, equation (A.2) can be written as:

$$Y_t = E_t[Y_{it}] = \lambda + \sum_{\pi=0}^{m}[\delta_\pi + \beta_\pi \rho]\bar{D}_t(\pi) + \sum_{\pi=0}^{m}\beta_\pi \Gamma_t(\pi) \ + \bar{\varepsilon}_t \qquad (A.4)$$

The effects of interest (β_π, δ_π) can be directly recovered from equation (A.4).

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Original Research

Predictors of firearm purchasing during the coronavirus pandemic in the United States: a cross-sectional study

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ABSTRACT

Objectives: This study aimed to compare determinants of firearm purchasing related to the pandemic.
Study design: This was a cross-sectional survey.
Methods: A total of 3853 online panel participants completed a survey between December 22, 2020, and January 2, 2021, to approximate a nationally representative sample of US adults (aged ≥18 years). Four firearm ownership groups were created: non-owners, a proxy for first-time COVID-19 owners, prepandemic owners with COVID-19 purchase, and prepandemic owners without COVID-19 purchase. Explanatory variables were in four domains: demographics, concern about the pandemic, actions taken in response to COVID-19, and emotional response to COVID-19. Multivariate analysis estimated the adjusted odds of the outcomes.
Results: Respondents were categorized as non-owners ($n = 2440$), pandemic-related purchasers with no other firearms ($n = 257$), pandemic-related purchasers with other firearms ($n = 350$), and those who did not purchase in response to the pandemic but have other firearms ($n = 806$). Multivariable logistic regression found that compared with non-owners, those who had firearms at home with no pandemic-related purchases are more likely to be male, live in rural settings, have higher income, and be Republican.
Conclusions: The results highlight the changing profile of American firearm owners and identify that those who purchased firearms for the first time (in response to the pandemic) should be the focus of tailored public health interventions, including provision of education about recommended firearm storage to reduce firearm violence, particularly because they are more likely to have children at home, and belong to demographic groups that may have less experience with firearm safety.

Introduction

Gun ownership in the United States is higher than in any other country with an estimated 1.2 firearms per resident.[1] During the COVID-19 pandemic, firearm purchasing is reported to have increased.[2] Firearm sales increased to approximately 2.5 million in March 2020, an estimated 85% increase compared with March 2019.[3] This increase may be because of fear and uncertainty related to the COVID-19 pandemic and stay-at-home orders enacted in some jurisdictions.[4] Similarly, firearm-related injuries and deaths increased during the pandemic, and some of these injuries, for example, domestic violence-related firearm injuries, may be associated with the increase in firearm sales.[5,6] One study reported that the primary motivations for firearm purchasing during the pandemic included protection against people, fear of an increase in crime, and concerns about supply chain disruptions, healthcare access, and the economy.[7] Another study found that compared with individuals not planning to purchase a firearm, those who were planning a purchase in the next 12 months (during the pandemic, July 2020 to June 2021) had higher economic concerns, fears of infection, and stress, as well as less tolerance for uncertainty.[8]

Before the COVID-19 pandemic, those who purchased firearms were more likely to be male, older, Republican, and live in more rural areas.[9–16] A study conducted in 2014 reported a weak relationship between firearm ownership and fear of victimization.[10]

We hypothesized that individuals purchasing firearms in the United States during the pandemic may be more likely to engage in pandemic-related behaviors prompted by fear and may have a

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higher negative emotional response to the COVID-19 pandemic compared with individuals who did not purchase firearms during the pandemic.

Methods

Study design

We approximated a nationally representative sample of US adults (aged ≥18 years) with a stratified non-probability sample to survey 3853 online panel participants between December 22, 2020, and January 2, 2021. Respondents were recruited by Climate Nexus Polling using several market research panels as described elsewhere.[17] Participants were recruited using stratified sampling methods.[17] Compensation for participants depended on the specific market research panel and respondents' preferences (e.g. cash, gift cards, reward points). Quotas were set to match the US Census Bureau's Voting and Registration Supplement to the Current Population Survey parameters for age, gender, race, educational attainment, census region, and Hispanic ethnicity. Sampling weights were used to account for small deviations from the preselected census parameters.

Outcomes

We created four firearm ownership groups from the questions, "Which, if any, of the following actions have you taken because of the spread of the coronavirus? — Purchased a gun and/or ammunition" and "Do you or anyone in your household own a gun?" as others have.[7] Groups were as follows: (1) did not purchase in response to the pandemic and has no other firearms at home ('non-owners'), (2) purchased in response to the pandemic and has no other firearms at home (a proxy for 'first-time COVID-19 owners'), (3) purchased in response to the pandemic and has other firearms at home (a proxy for 'prepandemic owners with COVID-19 purchase'), and (4) did not purchase in response to the pandemic and has firearms at home (a proxy for 'prepandemic owners without COVID-19 purchase').

Determinants

Explanatory variables were in four domains: demographics, concern about the pandemic, actions taken in response to COVID-19, and emotional response to COVID-19. Demographic determinants included gender, age, education, race/ethnicity, residence, income, and political affiliation. Other determinants included belief that the government does too much for its citizens, level of trust in the Centers for Disease Control and Prevention (CDC), actions taken in response to the pandemic (staying home, stocking up on items, keeping children at home), and worry about the impact of the pandemic on sickness, housing, crime, and martial law.

A variable that measured emotional response to the pandemic was created using the responses to the question, "How strongly do you feel each of the following emotions when you think about the coronavirus?" The 13 emotions asked about were afraid, helpless, angry, hopeful, disgusted, anxious, depressed, confused, panicked, lonely, overwhelmed, bored, and compassionate. Responses were on a 4-point scale (not at all, a little, moderately, and very). Typologies of emotional response to COVID-19 were identified by latent profile analysis based on participants' responses to the 13 emotions using common methods.[25] Four emotional response profiles emerged that primarily reflected differing intensities of negative emotions and were categorized as follows: no response, mild response, moderate response, and strong response.

Statistical analysis

We conducted bivariate analyses between the outcomes and each of the potential determinants and between pairs of determinants to assess their association and multicollinearity. None of the independent variables were highly correlated with each other defined as a correlation >0.7 for our purposes. We included variables associated with the outcomes at a *P*-value <0.05 in the bivariate analysis or reported in the literature in the final models.

Multivariable logistic regression estimated adjusted odds ratios and 95% confidence intervals between the outcomes and potential determinants. STATA version 16 (StataCorp, LP, College Station, TX) was used.

Five models were constructed to compare populations based on firearm ownership status, as follows: Model 1: prepandemic firearm owners with no COVID-19 purchase and non-owners; Model 2: first-time COVID-19 owners and non-owners; Model 3: first-time COVID-19 owners and prepandemic owners without COVID-19 purchase; Model 4: prepandemic owners with COVID-19 purchase and prepandemic owners without COVID-19 purchase; and Model 5: first-time COVID-19 owners and prepandemic owners with COVID-19 purchase.

This project was considered exempt by the George Mason University Institutional Review Board (IRB 1684418-3).

Results

The survey participation rate was 68.5%, which is considered acceptable by the American Association of Public Opinion Research standards. More than half of the respondents ($n = 2440$, 63.3%) were non-owners. Of the remaining 36.7% ($n = 1413$) reporting owning firearms, 57.0% (806/1413) were prepandemic owners who did not purchase additional firearms in response to COVID-19, 24.8% (350/1413) were prepandemic owners who purchased a firearm in response to COVID-19, and 18.2% (257/1413) were first-time owners (who purchased a firearm in response to COVID-19; Table 1).

Model 1: prepandemic firearm owners with no COVID-19 purchase and non-owners

When compared with non-owners, prepandemic owners without a COVID-19 purchase are significantly more likely to be male, have higher income, and live in rural areas. They are also more likely to identify as Republican, to strongly believe the government does too much for its citizens, and to report a high emotional response to the pandemic. There are no statistically significant differences between these two groups in actions taken in response to COVID-19, reasons for worry, and trust in the CDC (Table 2).

Model 2: first-time COVID-19 owners and non-owners

Relative to non-owners, first-time firearm owners are significantly more likely to be younger and male, more likely to believe the government does too much for its citizens, and less likely to trust the CDC. They also have greater odds of staying home, stocking up on items, and keeping their children at home. In addition, they are also more likely to be worried about losing their home but less worried about their family members or themselves getting sick from COVID-19. There are no significant differences in these two groups by political affiliation, urban/rural residence, or educational status (Table 2).

Table 1
Participant demographics, beliefs, actions, and concerns about COVID-19 by firearm ownership category.

Variable	Entire study	No ownership	First-time (COVID-19) owner	Prepandemic owners without COVID-19 purchase	Prepandemic owners with COVID-19 purchase
	n (weighted %)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Age		2440	257	806	350
18–29	750 (20.7)	440 (18.0)	80 (31.1)	157 (19.5)	73 (20.9)
30–49	1397 (35.9)	822 (33.7)	143 (55.6)	255 (31.6)	177 (50.6)
50–64	899 (23.1)	612 (25.1)	23 (9.0)	208 (25.8)	56 (16.0)
≥65	807 (20.4)	566 (23.2)	11 (4.3)	186 (23.1)	44 (12.6)
Gender					
Female	2016 (52.3)	1365 (55.9)	105 (40.9)	407 (50.5)	139 (39.7)
Male	1837 (47.7)	1075 (44.1)	152 (59.1)	399 (49.5)	211 (60.3)
Race/ethnicity					
Non-Hispanic White	2835 (70.0)	1785 (73.2)	163 (63.4)	638 (79.2)	249 (71.1)
Non-Hispanic Black	466 (10.7)	301 (12.3)	43 (16.7)	79 (9.8)	43 (12.3)
Hispanic	361 (15.9)	212 (8.7)	38 (14.8)	65 (8.1)	46 (13.1)
Other	191 (3.6)	142 (5.8)	13 (5.1)	24 (3.0)	12 (3.4)
Education					
Less than high school	241 (6.7)	164 (6.7)	21 (8.2)	39 (4.8)	17 (4.9)
High school graduate	961 (25.9)	657 (26.9)	40 (15.6)	209 (25.9)	55 (15.7)
Some college	1345 (36.1)	834 (34.2)	61 (23.7)	311 (38.6)	139 (39.7)
Bachelor's or higher	1306 (31.3)	785 (32.2)	135 (52.5)	247 (30.7)	139 (39.7)
Income					
<$20,000	808 (21.6)	575 (23.6)	55 (21.4)	125 (15.5)	53 (15.1)
$20,000–$49,999	1313 (34.1)	894 (36.6)	48 (18.7)	283 (35.1)	88 (25.1)
$50,000–$99,999	1065 (27.4)	619 (25.4)	68 (26.5)	255 (31.6)	123 (35.1)
≥$100,000	667 (16.9)	352 (14.4)	86 (33.5)	143 (17.7)	86 (24.6)
Type of residence					
Urban	1219 (32.4)	759 (31.1)	137 (53.5)	203 (25.2)	120 (34.4)
Semiurban	1748 (45.1)	1184 (48.5)	82 (31.9)	345 (42.8)	137 (39.1)
Rural	886 (22.4)	497 (20.4)	38 (14.8)	258 (32.0)	93 (26.6)
Employment					
Self or other employment	1955 (50.6)	1107 (45.4)	194 (75.5)	404 (50.1)	250 (71.4)
Unemployed	690 (18.2)	484 (19.8)	37 (14.4)	138 (17.1)	31 (8.9)
Retired	868 (22.3)	603 (24.7)	10 (3.9)	207 (25.7)	48 (13.7)
Other not working	340 (9.0)	246 (10.1)	16 (6.2)	57 (7.1)	21 (6.0)
Political affiliation					
Republican	1400 (36.5)	757 (31.0)	81 (31.5)	391 (48.5)	171 (48.9)
Democrat	1807 (46.7)	1216 (49.8)	143 (55.6)	302 (37.5)	146 (41.7)
Independent	646 (16.9)	467 (19.1)	33 (12.8)	113 (14.0)	33 (9.4)
Believe that government does too much for citizens					
Strongly disagree	969 (25.2)	691 (28.3)	47 (18.3)	170 (21.1)	61 (17.4)
Somewhat disagree	1104 (28.8)	769 (31.5)	57 (22.2)	213 (26.4)	65 (18.6)
Somewhat agree	1130 (29.2)	671 (27.5)	79 (30.7)	274 (34.0)	106 (30.3)
Strongly agree	650 (16.9)	309 (12.7)	74 (28.8)	149 (18.5)	118 (33.7)
Level of trust in CDC					
Strongly distrust	363 (9.6)	199 (8.2)	86 (33.5)	232 (28.8)	101 (28.9)
Somewhat distrust	680 (18.2)	413 (16.9)	92 (35.8)	338 (41.9)	133 (38.0)
Somewhat trust	1621 (41.7)	1058 (43.4)	46 (17.9)	149 (18.5)	72 (20.6)
Strongly trust	1189 (30.5)	770 (31.6)	33 (12.8)	87 (10.8)	44 (12.6)
Action taken					
Stay home (vs not)	2069 (53.4)	1261 (51.7)	202 (78.6)	382 (47.4)	224 (64.0)
Stocked up (vs not)	2335 (60.4)	1417 (58.1)	210 (81.7)	447 (55.5)	261 (74.6)
Kept children home (vs not)	1299 (34.2)	672 (27.5)	212 (82.5)	212 (26.3)	203 (58.0)
Worry (vs not very or not at all worry)					
Sickness	2636 (68.1)	1686 (69.1)	165 (64.2)	554 (68.7)	231 (66.0)
Losing home	1233 (33.0)	697 (28.6)	151 (58.8)	229 (28.4)	156 (44.6)
Increased crime	2193 (57.1)	1337 (54.8)	174 (67.7)	451 (56.0)	231 (66.0)
Martial law	1709 (45.1)	1028 (42.1)	157 (61.1)	330 (40.9)	194 (55.4)
Emotional response to COVID					
No response	1268 (32.6)	823 (33.7)	58 (22.6)	284 (35.2)	103 (29.4)
Mild response	1289 (33.4)	861 (35.3)	73 (28.4)	256 (31.8)	99 (28.3)
Moderate	897 (23.6)	566 (23.2)	72 (28.0)	189 (23.5)	70 (20.0)
Strongest negative	399 (10.3)	190 (7.8)	54 (21.0)	77 (9.6)	78 (22.3)

Table 2
Multivariable logistic regression models assessing relationship between demographics, beliefs, actions, and concern about COVID-19 pandemic between firearm ownership categories.

Variable	Model 1: prepandemic owners without COVID-19 purchase compared with non-owners ($n = 3246$)	Model 2: first-time owner compared with non-owners ($n = 2697$)	Model 3: first-time owner compared with prepandemic owners without COVID-19 purchase ($n = 1063$)	Model 4: prepandemic owners with COVID-19 purchase compared with prepandemic owners without COVID-19 purchase ($n = 1156$)	Model 5: first-time owner compared with prepandemic owners with COVID-19 purchase ($n = 607$)
	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Age					
18–29	Reference	Reference	Reference	Reference	Reference
30–49	**0.70 (0.54, 0.90)**	**0.62 (0.43, 0.91)**	0.75 (0.47, 1.20)	1.12 (0.75, 1.68)	**0.58 (0.36, 0.93)**
50–64	**0.74 (0.56, 0.98)**	**0.27 (0.15, 0.48)**	**0.41 (0.21, 0.81)**	**0.59 (0.36, 0.97)**	0.52 (0.26, 1.06)
≥65	**0.64 (0.45, 0.92)**	**0.32 (0.13, 0.79)**	0.43 (0.15, 1.20)	0.69 (0.36, 1.35)	0.60 (0.22, 1.66)
Gender					
Female	Reference	Reference	Reference	Reference	Reference
Male	**1.24 (1.05, 1.47)**	**1.90 (1.38, 2.63)**	**1.62 (1.09, 2.41)**	**1.42 (1.05, 1.92)**	0.97 (0.65, 1.43)
Race/ethnicity					
Non-Hispanic White	Reference	Reference	Reference	Reference	Reference
Non-Hispanic Black	1.01 (0.75, 1.35)	1.25 (0.79, 1.97)	1.50 (0.85, 2.66)	1.27 (0.77, 2.08)	0.89 (0.50, 1.58)
Hispanic	0.98 (0.72, 1.35)	1.14 (0.72, 1.81)	1.23 (0.68, 2.20)	1.25 (0.76, 2.04)	0.66 (0.38, 1.17)
Other	**0.57 (0.36, 0.91)**	0.65 (0.33, 1.28)	1.17 (0.48, 2.87)	1.09 (0.49, 2.41)	1.07 (0.42, 2.72)
Education					
Less than high school	Reference	Reference	Reference	Reference	Reference
High school graduate	1.30 (0.87, 1.30)	0.55 (0.29, 1.06)	0.89 (0.40, 2.00)	0.93 (0.45, 1.93)	0.59 (0.25, 1.39)
Some college	1.43 (0.96, 2.14)	0.69 (0.0.37, 1.29)	0.86 (0.39, 1.89)	1.52 (0.75, 3.06)	**0.40 (0.18, 0.89)**
Bachelor's or higher	1.08 (0.71, 1.65)	1.04 (0.54, 2.01)	2.00 (0.86, 4.67)	1.32 (0.63, 2.76)	0.84 (0.37, 1.93)
Income					
Under $20,000	Reference	Reference	Reference	Reference	Reference
$20,000–$49,999	**1.37 (1.07, 1.77)**	**0.51 (0.32, 0.83)**	**0.34 (0.19, 0.60)**	0.67 (0.42, 1.08)	0.55 (0.30, 1.00)
$50,000–$99,999	**1.90 (1.44, 2.50)**	0.84 (0.51, 1.40)	**0.35 (0.18, 0.66)**	0.79 (0.49, 1.29)	0.59 (0.31, 1.12)
≥$100,000	**2.16 (1.56, 2.99)**	1.10 (0.63, 1.90)	**0.42 (0.21, 0.86)**	0.78 (0.44, 1.39)	0.82 (0.41, 1.63)
Type of residence					
Urban	Reference	Reference	Reference	Reference	Reference
Semiurban	1.00 (0.81, 1.24)	0.83 (0.59, 1.18)	0.87 (0.56, 1.36)	1.14 (0.79, 1.65)	**0.63 (0.41, 0.97)**
Rural	**1.90 (1.49, 2.42)**	0.94 (0.58, 1.52)	**0.53 (0.30, 0.91)**	1.27 (0.84, 1.93)	**0.56 (0.33, 0.97)**
Employment					
Self or other employment	Reference	Reference	Reference	Reference	Reference
Unemployed	0.91 (0.71, 1.16)	0.75 (0.48, 1.19)	0.92 (0.53, 1.62)	**0.41 (0.25, 0.66)**	1.68 (0.90, 3.15)
Retired	0.99 (0.74, 1.32)	0.63 (0.27, 1.46)	0.51 (0.20, 1.31)	0.69 (0.40, 1.20)	0.69 (0.26, 1.84)
Other not working	0.76 (0.54, 1.08)	1.01 (0.53, 1.92)	1.68 (0.75, 3.80)	0.95 (0.50, 1.82)	1.58 (0.68, 3.66)
Political affiliation					
Republican	Reference	Reference	Reference	Reference	Reference
Democrat	**0.56 (0.46, 0.69)**	0.77 (0.53, 1.11)	1.29 (0.84, 2.00)	0.82 (0.57, 1.17)	**1.62 (1.05, 2.48)**
Independent	**0.53 (0.41, 0.68)**	**0.61 (0.37, 1.00)**	1.08 (0.59, 1.96)	0.71 (0.44, 1.15)	**1.89 (1.01, 3.55)**
Believe that government does too much for citizens					
Strongly disagree	Reference	Reference	Reference	Reference	Reference
Somewhat disagree	0.97 (0.77, 1.24)	1.08 (0.68, 1.72)	1.01 (0.57, 1.80)	0.90 (0.57, 1.44)	1.32 (0.73, 2.41)
Somewhat agree	**1.30 (1.02, 1.65)**	1.18 (0.76, 1.83)	1.24 (0.72, 2.15)	1.21 (0.79, 1.87)	1.07 (0.61, 1.88)
Strongly agree	**1.38 (1.04, 1.84)**	**2.17 (1.35, 3.48)**	1.50 (0.83, 2.71)	**2.16 (1.37, 3.41)**	0.89 (0.50, 1.59)
Level of trust in CDC					
Strongly distrust	Reference	Reference	Reference	Reference	Reference
Somewhat distrust	0.84 (0.60, 1.17)	**0.56 (0.31, 1.00)**	0.94 (0.46, 1.91)	1.00 (0.59, 1.70)	0.79 (0.40, 1.54)
Somewhat trust	0.83 (0.61, 1.13)	**0.40 (0.24, 0.69)**	0.64 (0.33, 1.23)	0.77 (0.47, 1.27)	0.80 (0.43, 1.51)
Strongly trust	0.87 (0.63, 1.21)	**0.40 (0.23, 0.70)**	**0.47 (0.24, 0.92)**	**0.54 (0.32, 0.93)**	0.88 (0.44, 1.77)
Action taken					
Stay home (vs not)	0.91 (0.75, 1.09)	**1.86 (1.28, 2.71)**	**2.59 (1.68, 4.00)**	**1.62 (1.18, 2.22)**	1.43 (0.91, 2.23)
Stocked up (vs not)	0.93 (0.78, 1.12)	**1.89 (1.27, 2.80)**	**2.18 (1.37, 3.46)**	**1.95 (1.41, 2.71)**	1.08 (0.67, 1.76)
Kept children home (vs not)	0.92 (0.75, 1.13)	**5.83 (3.93, 8.65)**	**6.72 (4.29, 10.55)**	**2.56 (1.84, 3.56)**	**2.28 (1.41, 3.71)**
Worry (vs not very or not at all worry)					
Sickness	1.15 (0.94, 1.41)	**0.49 (0.34, 0.71)**	**0.45 (0.28, 0.70)**	0.72 (0.51, 1.02)	0.81 (0.52, 1.27)
Losing home	1.03 (0.84, 1.28)	**2.41 (1.70, 3.43)**	**2.67 (1.70, 4.21)**	1.38 (0.96, 1.97)	**1.63 (1.03, 2.58)**
Increased crime	1.12 (0.93, 1.36)	1.18 (0.80, 1.73)	1.46 (0.92, 2.33)	**1.42 (1.01, 2.00)**	0.86 (0.53, 1.40)
Martial law	0.94 (0.77, 1.14)	1.16 (0.80, 1.67)	1.09 (0.68, 1.74)	1.11 (0.79, 1.57)	0.93 (0.58, 1.50)
Emotional response to COVID					
No response	Reference	Reference	Reference	Reference	Reference
Mild response	0.95 (0.76, 1.17)	0.84 (0.55, 1.30)	0.82 (0.48, 1.42)	0.86 (0.58, 1.27)	1.06 (0.61, 1.84)
Moderate	1.11 (0.86, 1.43)	0.93 (0.59, 1.48)	0.63 (0.35, 1.11)	**0.60 (0.38, 0.94)**	1.13 (0.63, 2.01)
Strongest negative	**1.51 (1.07, 2.14)**	1.41 (0.83, 2.41)	0.78 (0.39, 1.54)	1.06 (0.63, 1.80)	0.60 (0.32, 1.12)

CI, confidence interval; OR, odds ratio.

Model 3: first-time COVID-19 owner and prepandemic owners without COVID-19 purchase

First-time owners are more likely to be female and have a higher income and also have greater odds of staying home, stocking up on items, and keeping their children at home. They are more worried about losing their home but less worried about their family members or themselves getting sick from COVID-19 and have significantly lower odds of reporting that they strongly trust the CDC. There are no statistically significant differences by political affiliation (Table 2).

Model 4: prepandemic owners with COVID-19 purchase and prepandemic owners without COVID-19 purchase

Relative to prepandemic owners without a COVID-19 purchase, prepandemic owners with a COVID-19 purchase are younger and less likely to be unemployed. There are no differences between the two by political affiliation, educational status, or income. They are also significantly more likely to report staying at home, stocking up on items, keeping their kids at home, and worrying about crime increasing and have significantly lower odds of trusting the CDC (Table 2).

Model 5: first-time COVID-19 owner and prepandemic owners with COVID-19 purchase

More first-time owners are Democrats compared with prepandemic owners with a COVID-19 purchase. More live in urban areas and are significantly more likely to report keeping their kids at home and worrying about losing their home (Table 2).

Discussion

We found that those who purchased firearms in response to the pandemic are different in terms of demographics compared with prepandemic purchasers. Before the pandemic, American firearm owners were more likely to be male and aged ≥65 years, live in a rural setting, and be Republican.[18] We found similar associations with prior owners with no new pandemic purchase more likely to be male, live in rural settings, be Republican, and have higher income. In contrast, those with a pandemic-related purchase are younger and have lower income. Others have similarly reported that younger individuals (mean age range 34.7–40 years of age) are more likely to report plans to purchase a firearm in response to the pandemic[19,20] and that pandemic purchasers are more likely to live in urban areas.[20] Prior owners with a new COVID-19 purchase are similar in political affiliation compared with prior owners without a COVID-19 purchase; however, new firearm owners are more likely to be Democrat, which has not previously been reported.

One study of firearm purchasing during the pandemic found that firearm purchasers who had previously owned guns were similar to other firearm ownership groups in regards to key demographics, including age and whether they lived in urban or rural areas.[21] However, another study that was similar to ours in regards to sampling frame and sample size ($n = 2709$) reported that those purchasing guns *during* the pandemic were more likely to be younger, male, less educated, recently unemployed, Republican, and residents of southern states.[22] Importantly, that study's results for sex, unemployment, education, which region people lived in, and political leaning were similar to the results of studies conducted before the pandemic that looked at the demographics of firearm owners; however, the null patterns for race/ethnicity, household income, marital status, and the presence of children differed from that reported during prepandemic times.[9–16] The latter is similar to what we found, specifically, no differences by sex, race, or education were found in our adjusted models.

Pandemic-related behaviors and worries vary by firearm ownership. Prior owners with a pandemic purchase are more likely than those without one to report worry about crime increasing, similar to what has been reported previously.[7,20] Our findings parallel those from another study finding that pandemic firearm purchasers are more worried about the economy than non-purchasers.[19] We detected no association between pandemic firearm purchasing and worry about COVID-19 illness, in contrast to others reporting individuals with a pandemic-related purchase had increased fear about the danger of COVID-19 and fear of "contamination."[19] Prior owners with no pandemic purchase are more likely to report a negative emotional response to the pandemic compared with non-owners, consistent with one other study that found that individuals who already own firearms (prepandemic) had an increased fear of COVID-19 and increase the level of threat perception.[19]

Those with a pandemic purchase (regardless of prior ownership) have a greater odds of reporting stockpiling behavior, and this was also reported by others.[7] We also found keeping children at home and staying home in response to the pandemic are associated with pandemic purchasing among both prior owners and new owners, and similar associations were reported by others.[7,20] This is of concern because having children and firearms present in the same household is linked to significantly greater risk of firearm-related death.[23] Another study reported that 39% of those purchasing firearms for the first time during the pandemic reported suboptimal firearm storage.[7] Health education interventions that address recommended firearm storage may be particularly helpful for new firearm owners and for firearm owners who live with children and others.

A number of limitations are inherent in quota-based non-probability methods. First, sampling is based on the individual's propensity to respond. Second, a theoretical basis for generalizing to a source population similar to what is found for a probability-based survey does not exist. However, these methods are common in policy-related research and public polling because non-response (and non-response bias) in probability-based sampling has become extremely high. In fact, when best practices are used, non-probability–based survey results can outperform those from probability-based surveys.[24] The emotional response variable was created using the question, "when you think of the pandemic" broadly, and did not assess mental health or cognitive (e.g. threat assessment) components that could provide a more holistic view of how emotion "shows up" through actions. Firearm purchasing categories were created using two questions similar to how others have categorized this,[7] and misclassification could have occurred.

Nevertheless, this study highlights differences between those who purchase firearms in response to the pandemic by prior firearm ownership. Firearm purchasing increased significantly during the pandemic. Understanding the changing demographic of who is purchasing firearms can prepare public health, law enforcement, and other responders for a possible surge in firearm-related societal impacts.

Author statements

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Ethical approval

This project was considered exempt by the George Mason University Institutional Review Board (IRB 1684418-3).

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Competing interests

None reported.

Author contributions

A.A.R. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis and contributed to concept and design and statistical analysis. All authors contributed to acquisition, analysis, or interpretation of data, drafting of the article, and critical revision of the article for important intellectual content.

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Short Communication

SARS-CoV-2 infections in migrant populations in Germany: results from the COVID-19 snapshot monitoring survey

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ABSTRACT

Objectives: Research shows that there is an increased risk of SARS-CoV-2 infection in migrants and ethnic minorities. However, increasing evidence indicates that socio-economic factors, such as employment, education and income, contribute to the association between migrant status and SARS-CoV-2 infection. This study aimed to examine the association between migrant status and the risk of SARS-CoV-2 infection in Germany and to discuss potential explanations for these associations.
Study design: This was a cross-sectional study.
Methods: Data from the German COVID-19 Snapshot Monitoring online survey were analysed, and hierarchical multiple linear regression models were used to calculate the probabilities of self-reported SARS-CoV-2 infection. Predictor variables were integrated in a stepwise method as follows: (1) migrant status (defined by own or parental country of birth other than Germany); (2) gender, age and education; (3) household size; (4) household language; and (5) occupation in the health sector, including an interaction term of migrant status (yes) and occupation in the health sector (yes).
Results: Of 45,858 participants, 3.5% reported a SARS-CoV-2 infection, and 16% were migrants. Migrants, participants in large households, those speaking a language other than German in their household and those working in the health sector were more likely to report SARS-CoV-2 infection. The probability of reporting SARS-CoV-2 infection was 3.95 percentage points higher for migrants than non-migrants; this probability decreased when integrating further predictor variables. The strongest association of reporting a SARS-CoV-2 infection was observed for migrants working in the health sector.
Conclusions: Migrants and health sector employees, and especially migrant health workers, are at an increased risk of SARS-CoV-2 infection. The results show that the risk of SARS-CoV-2 infection is determined by living and working conditions rather than migrant status.

Introduction

In 2020, approximately 27% of the population in Germany were defined as having a statistically defined migrant background (i.e. the individual or at least one of their parents was born without German citizenship).[1] In total, 17% of the population self-migrated to Germany.[1]

International research describes a higher risk of SARS-CoV-2 infection among migrants and ethnic minorities and increased risks of severe COVID-19 disease progression, hospitalisation and death.[2] In Germany, migrants more often live below the poverty level, with an average income that is lower than that of the general population. Poverty and low socio-economic position are associated with higher rates of chronic preconditions[3] that are relevant for the severity of COVID-19 progression. In addition, factors such as crowded accommodation, limited access to health information and

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care and working in specific frontline sectors have been shown to be associated with increased risks of SARS-CoV-2 infection.[2] Migrants in Germany are often employed in low-wage, precarious jobs or jobs that are hazardous to health.[4] Furthermore, migrants frequently work and are disproportionally represented, in frontline jobs, such as those in the health care, cleaning, logistics and transportation sectors. Access to healthcare is often limited for migrants and ethnic minorities due to legal restrictions,[5] information and language barriers.[6]

The objective of this study was to examine the association between migrant status and the risk of SARS-CoV-2 infection in Germany and to discuss potential explanations for these associations.

Methods

Data collection and participants

Data from the German cross-sectional COVID-19 Snapshot Monitoring (COSMO) online survey, which started in early March 2020 and has been repeated on a weekly or bi-weekly basis, were analysed.[7] Each wave of the survey included approximately 1000 participants. Data from wave four (24 March 2020, migrant status not included before) to wave 52 (22 September 2021) were analysed.

Measures

Outcome variable

Self-reported infection status was determined by response to the following question: "Have you been infected with the novel corona virus?" coded as a dichotomous variable ('Yes', 'Yes, confirmed' and 'Yes, but already recovered' coded as yes [=1]; or 'Yes, not yet confirmed', 'I don't know' and 'No' coded as no [=0]).

Predictor variables

Migrant status was defined by own or parental country of birth (not Germany). Age groups were '18–29 years', '30–45 years', '46–60 years' and 'older than 60 years'. School education was summarised as 'Up to nine years of formal education' and 'At least 10 years of formal education (without university qualification)' vs. 'At least 10 years of formal education (with university qualification)'. Household size described the number of people permanently living in participants' households ('only me', 'two persons', 'three to four persons' or 'more than four persons'). Household language described the language mainly spoken in participants' households ('German' vs 'other'). Occupation in the health sector was always included in interviews (response options: 'yes' or 'no'); in wave 29 in-depth questions on occupational status were asked, but the differentiation in health sector yes/no was possible.

Control variables

Municipality size was categorised as '<20,000 inhabitants', '20,000 to <100,000 inhabitants' and '≥100,000 inhabitants'. Federal states were separated into regions as follows: East (federal states of the former German Democratic Republic including Berlin) and West (federal states of the former Federal Republic of Germany).

Analyses

Hierarchical multiple linear regression models were used to calculate adjusted coefficients representing the differences in the probability of self-reporting a SARS-CoV-2 infection and 95% confidence intervals. Estimates of linear probability models (LPM) were provided instead of logit or probit estimates to facilitate tracking of the coefficients' change across multiple nested models. Linear probability models prove viable for binary outcomes and categorical independent variables with interaction effects.[8] In model 1, the probability of migrants reporting an infection was calculated. In model 2, basic sociodemographic variables were integrated. Further possible predictor variables were then integrated in a stepwise manner based on theoretical considerations, as follows: household size (model 3), household language (model 4) and working in the health sector, using an interaction term with migrant status (model 5). All models were adjusted for municipality size and region to account for higher migrant proportions in cities and West Germany. Analyses were performed using Stata version 17 (StataCorp, College Station, TX, USA).

Participants who completed the survey more than once (n = 2232) and those with missing values in the analysed variables (n = 3250) were excluded from the present study, resulting in a final study population of 45,858.

Results

Study population

Among participants, 3.5% reported a SARS-CoV-2 infection, and a total of 16.0% were migrants. The median age of those ever infected was 37 years, and the median age of those never infected was 46 years. The proportion of participants reporting an infection was higher for migrants (6.8%) than non-migrants (2.9%). With increasing household size, the proportion of participants reporting an infection also increased. Participants speaking a language other than German in their household (5.8% vs 2.8%) and those working in the health sector (9.5% vs 2.9%) more often reported an infection with SARS-CoV-2.

Multiple linear regression analyses

Table 1 shows the results from the hierarchical multiple linear regression models. Coefficients for the differences in probabilities are referred to as differences in predicted proportions on a percentage point scale to facilitate interpretation. The proportion of migrants reporting an infection was 3.95 percentage points higher than among non-migrants (model 1, Table 1).

Adding basic sociodemographic variables to the model reduces the difference between migrants and non-migrants by 0.77 percentage points (model 2, Table 1).

Adding the household size variable (model 3) reduces the difference between migrants and non-migrants by a further 0.19 percentage points. Proportions for reporting an infection were higher among participants not living alone (Table 1).

When adding the household language variable (model 4), the difference between migrants and non-migrants is reduced by a further 0.52 percentage points. For participants speaking a language other than German in their household, proportions of reporting an infection were higher (Table 1).

In model 5, occupation in the health sector and an interaction term with migrant status were added. The difference between migrants and non-migrants (only valid for non-healthcare workers in this model) was 1.28 percentage points. The proportion of reporting an infection was 3.82 percentage points higher for non-migrants working in the health sector than among non-migrants in other occupations. However, for migrant workers in the health sector, this proportion was an additional 11.45 percentage points higher (Table 1).

Table 1
Results of multiple linear regression analyses, COVID-19 Snapshot Monitoring survey, Germany, n = 45,858.

Variable	Model 1			Model 2			Model 3			Model 4			Model 5		
	aCoeff	95% CI	*P* value	aCoeff	95% CI	*P* value	aCoeff	95% CI	*P* value	aCoeff	95% CI	*P* value	aCoeff	95% CI	*P* value
Migrant status															
Non-migrant (n = 38,527)	Ref.			Ref			Ref.			Ref.			Ref.		
Migrant (n = 7331)	**0.0395**	**0.0349–0.04410**	**<0.001**	**0.0318**	**0.0271–0.0364**	**<0.001**	**0.0299**	**0.0252–0.0346**	**<0.001**	**0.0247**	**0.0199–0.0295**	**<0.001**	**0.0128**	**0.0078–0.0178**	**<0.001**
Sex															
Female (n = 23,467)				**−0.0096**	**−0.0130 to −0.0063**	**<0.001**	**−0.0096**	**−0.0130 to −0.0063**	**<0.001**	**−0.0092**	**−0.0126 to −0.0059**	**<0.001**	**−0.0119**	**−0.0152 to −0.0086**	**<0.001**
Male (n = 22,391)				Ref.			Ref.			Ref.			Ref.		
Age															
18–29 years (n = 8777)				**0.0464**	**0.0410–0.0518**	**<0.001**	**0.0397**	**0.0340–0.0453**	**<0.001**	**0.0391**	**0.0335– 0.0447**	**<0.001**	**0.0351**	**0.0295–0.0407**	**<0.001**
30–45 years (n = 14,224)				**0.0336**	**0.0289–0.0384**	**<0.001**	**0.0264**	**0.0214–0.0314**	**<0.001**	**0.0257**	**0.0207–0.0307**	**<0.001**	**0.0218**	**0.0168–0.0268**	**<0.001**
46–60 years (n = 12,829)				**0.0139**	**0.0091–0.0186**	**<0.001**	**0.0105**	**0.0056–0.0153**	**<0.001**	**0.0099**	**0.0051–0.0147**	**<0.001**	**0.0076**	**0.0028–0.0125**	**0.002**
>60 years (n = 10,028)				Ref.			Ref.			Ref.			Ref.		
School education															
Up to 9 years/at least 10 years (no university qualification; n = 20,031)				**0.0041**	**0.0006–0.0076**	**0.023**	**0.00480**	**0.0013–0.0083**	**0.008**	**0.0045**	**0.0010– 0.0080**	**0.013**	**0.0037**	**0.0002–0.0072**	**0.038**
At least 10 years (university qualification; n = 25,827)				Ref.			Ref.			Ref.			Ref.		
Household size															
Living alone (n = 11,364)							Ref.			Ref.			Ref.		
2 persons (n = 18,400)							**0.0053**	**0.0010–0.0096**	**0.015**	**0.0051**	**0.0008–0.0093**	**0.020**	**0.0046**	**0.0003–0.0088**	**0.035**
3–4 persons (n = 13,649)							**0.0180**	**0.0132–0.0227**	**<0.001**	**0.0173**	**0.0125–0.0220**	**<0.001**	**0.0155**	**0.0108–0.0202**	**<0.001**
More than four persons (n = 2445)							**0.0346**	**0.0264–0.0427**	**<0.001**	**0.0327**	**0.0245–0.0408**	**<0.001**	**0.0314**	**0.0233–0.0395**	**<0.001**
Household language															
German (n = 35,039)										Ref.			Ref.		
Other language (n = 10,819)										**0.0217**	**0.0176–0.0257**	**<0.001**	**0.0205**	**0.0165–0.0245**	**<0.001**
Occupation in health sector															
No (n = 41,904)													Ref.		
Yes (n = 3954)													**0.0382**	**0.0315–0.0448**	**<0.001**
Interaction															
Migrant (yes) # occupation in health sector (yes; n = 772)													**0.1145**	**0.0995–0.1295**	**<0.001**

aCoeff, adjusted regression coefficients; 95% CI, 95% confidence interval. Bold indicates a significance level of P < 0.05.
All models were adjusted for municipality size and region (west/east).
Model 1: the probability of reporting an infection by migrant status.
Model 2: model 1 adjusted for sociodemographic variables (sex, age, school education).
Model 3: model 2 additionally adjusted for household size.
Model 4: model 3 additionally adjusted for household language.
Model 5: model 4 additionally adjusted for working in the health sector, using an interaction term with migrant status.

Discussion

The study shows that migrants in Germany are at higher risk of reporting a SARS-CoV-2 infection. However, according to the results, it is not the migrant status itself but factors such as the living situation, spoken language and workplace that increase the risk of infection. Strong effect modifications were observed for occupation in the health sector and being a migrant, which suggests that migrants working in the health sector are at particularly high risk of infection. This result can be explained by the higher exposure to the virus experienced by migrants because they often work and are disproportionally represented, in low-wage jobs, such as cleaning and individual patient care.[9] Worldwide, reported infection and mortality rates among healthcare workers were strikingly higher than those of the general population.[9]

Large household size increased the risk of infection, which is consistent with previous findings showing that the infection risk is significantly higher when living in crowded conditions.[10] Increased infection is potentially due to higher exposure to aerosols and reduced opportunities for physical distancing and isolation of infected individuals.

Speaking a language other than German at home is associated with a higher infection risk. As most of the official health information in Germany is provided in German, access barriers to reliable information sources might contribute to increased infection. Therefore, tailored risk communication and community engagement strategies are needed (e.g. using translation and interpretation services and involving community organisations).

Specific protection and prevention measures are required to address the intersecting public health risks in the pandemic and beyond. First, public health interventions need to be multilingual and community oriented to reach people in their working and living environments. Second, structural issues, such as precarious working conditions and systematic discrimination, need to be addressed. Further research is required to gain a better understanding of the role and interplay of structural and individual factors that increase infection risks, with the aim of protecting those working in and receiving health care.

Limitations

There is a potential selection bias in this study because survey participation was only available online and in the German language. Participants reported higher levels of education and were younger than the general population; thus, some population groups of interest may not be represented. In addition, own or parental history of migration was the only migration-related factor captured in the survey; therefore, other structural factors potentially affecting the risk of infection, such as legal status or discrimination, were not analysed. The effect of income on infection could not be analysed, as this variable was not included until June 2020. It should also be noted that because this study was based on a cross-sectional sample, explicit causal explanations cannot be derived.

Conclusions

Increasing evidence shows that socio-economic factors, such as employment, education and income, contribute to the association between migrant status and SARS-CoV-2 infection. The results from this study show that in Germany, migrants, health sector employees and in particular migrant health workers, appear to be at a higher risk of SARS-CoV-2 infection. Large households and language barriers also contribute to an increased risk of infection.

Author statements

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Ethical approval

Ethics approval was obtained from the University of Erfurt's IRB (#20200302/20200501).

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Competing interests

All authors declare that there is no conflict of interest.

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Short Communication

Smoking habits predict adverse effects after mRNA COVID-19 vaccine: Empirical evidence from a pilot study

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ABSTRACT

Objectives: The aim of this research was to investigate the possible association between smoking habits and the incidence of adverse effects (AEs) after mRNA COVID-19 vaccine.
Study design: A longitudinal observational study was conducted on a sample of Italian healthcare workers.
Methods: Healthcare workers who were administered the mRNA COVID-19 vaccine (either BNT162b2 or mRNA-1273) were evaluated for the occurrence of AEs after three vaccine doses. Multivariate Poisson regression analyses were fitted to predict AE risk according to smoking characteristics – such as number of tobacco cigarettes smoked per day, smoking time, and use of electronic cigarette (e-cig).
Results: Of 320 total participants, 72 (22.5%) smoked cigarettes, and 50 (15.6%) used e-cig, 49 of which being dual users. Tobacco smoking significantly increased the risks of muscle and joint pain during the primary COVID-19 vaccination cycle and of chills during the whole vaccination series. The number of cigarettes smoked per day and vaping variously predicted AE onset during the whole cycle, with a tendency to respectively reduce and increase their risks. Duration of smoking did not affect any AE, except for headache after the booster dose. Most results remained significant after Bonferroni adjustment of significance level.
Conclusion: Our pilot study indicated a possible effect of smoking habits on AE onset. Our research offers evidence that helps understanding possible predictors of the interindividual variability in COVID-19 vaccine response, serving as a reference for further studies on the effect of smoking on vaccine safety and effectiveness.

Introduction

Safety monitoring of COVID-19 vaccines is crucial to help maximize the current global vaccination campaign against COVID-19, also considering the lack of experience with the massive use of novel mRNA platforms.[1,2] Yet, to our knowledge, little or nothing has been published on the effect of smoking habits – namely, the number of cigarettes smoked per day, smoking time, and the use of electronic cigarettes (e-cig) – on the onset of vaccine-related adverse effects (AEs). Here, we present a subanalysis of the MOSAICO study ("Monitoraggio di Breakthrough infectionS dopo dose Addizionale di vaccino antI-COVID-19 a mRNA in operatori sanitari"), a longitudinal design that studied the safety and effectiveness of immunisation with the mRNA COVID-19 vaccine in the healthcare workers (HCWs) of a teaching hospital in southern Italy. This research included an analysis of the AEs after the three doses of licensed mRNA COVID-19 vaccines, in which predictive effects of selected smoking characteristics were captured.

Methods

Complete cohort assembly and study methods have been described in the MOSAICO parent papers.[1,3] Briefly, all HCWs who

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received a booster dose of an mRNA vaccine (either BNT162b or mRNA-1273) between 2 October 2021 and 15 February 2022 were asked to take part in the study. Those who accepted to participate were interviewed about their demographics and professional characteristics, as well as smoking habits and history. Data on any local (pain, redness, swelling, and itch at injection site) and systemic AE (tiredness and fatigue, headache, muscle pain, joint pain, chills, fever, swelling of lymph node, abdominal pain, nausea, vomiting, diarrhoea, breathing problems, and swelling of the face, tongue, throat, dizziness and other uncatalogued AEs that may be experienced) that occurred within seven days after vaccine administration were registered. The AEs' list aligns with the previous evidence on COVID-19 vaccine safety.[1,2,4]

The Mann–Whitney U test was used to assess differences in median daily cigarettes smoked by smokers and vapers (dual users). Chi-squared or Fisher's exact test was used when needed to assess differences in AE occurrence between current and non-smokers. Multivariate Poisson regression analyses with robust standard errors were conducted to model the association of AE after COVID-19 vaccine doses and smoking habits – smoking history (never/former, cigarette smoker, e-cig user), smoking years (continuous, in years), number of tobacco cigarettes smoked per day (categorised according to the distribution in the sample: between one and five, six and 10, 11 and 15, or >15), adjusting for possible covariates, namely, gender, age, previous SARS-CoV-2 infection, type of booster vaccine, and, for the third dose, the time interval between primary vaccination cycle and booster dose. A stepwise backward selection procedure was applied, with a significance level of <0.4 as criterion for variables to enter the final multivariate Poisson models. To ensure models' consistency, analyses were limited to those AEs that showed a cumulative incidence greater than 10% in smokers. These analyses enabled AEs' relative risks (as incidence rate ratios [RR]s) and 95% confidence intervals (95% CIs) associated with smoking habits. The significance level was set at $\alpha < .05$; however, to further test out hypotheses, a sensitivity analysis was also conducted using Bonferroni's adjustment for multiple comparisons, with significance threshold calculated $1 - (1 - \alpha)^{1/k}$, where k is the number of multiple tests on AE risk after each dose.

Results

The whole MOSAICO cohort consisted of 320 participants: complete characteristics and AE rates have been presented

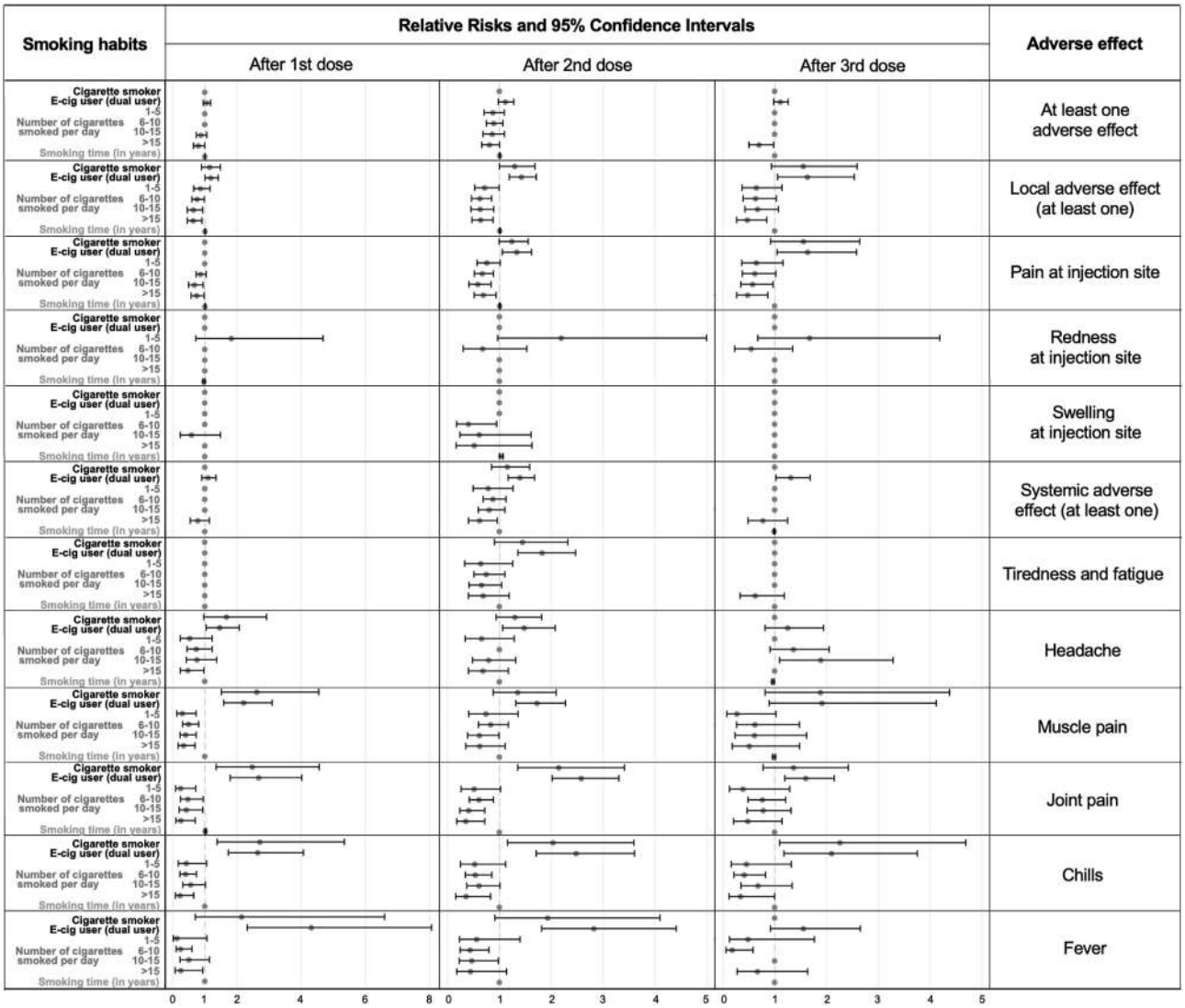

Fig. 1. Risk ratios indicating associations between the occurrence of adverse effects after COVID-19 vaccine doses and smoking habits.

elsewhere.[1,3] Overall, 198 (61.9%) HCWs were never/former smokers, 72 (22.5%) were cigarette smokers and 50 (15.6%) reported to use e-cig, 49 of which being dual users. The median time of smoking was 15 years (interquartile range, 10–20). Among 121 smokers, 16 (5.0%) HCWs smoked one to five cigarettes per day, 22 (16.3%) smoked 6–10 cigarettes per day, 25 (7.8%) smoked 11–15 cigarettes per day and 28 (8.8%) smoked more than 15 cigarettes per day. Cumulative incidence of AE in smokers is described in Table S1 (Supplementary material): no differences in AE occurrence between current and non-smokers were seen (*P*-values >0.05 for all AEs). The results are presented in Fig. 1. The number of cigarettes smoked per day and the use of e-cig variously predicted AE occurrence during the vaccination cycle, with a tendency to respectively reduce and increase their risks. Tobacco smoking alone significantly increased the RRs of muscle and joint pain during the primary vaccination cycle and of chills after each of the three doses. Duration of smoking did not show any effect on AE, except for headache after the booster dose. A complete overview of RRs and 95% CIs is presented in Table S1 (Supplementary material).

Conclusions

To the best of our knowledge, this is the first study that investigated the effect of selected smoking habits on the risk of AEs after the mRNA COVID-19 vaccine, yielding interesting results on postvaccination symptoms in smokers and e-cig users. Several pieces of research have evidenced lower antibody levels in response to the mRNA COVID-19 vaccine in smokers, although analyses according to smoking habits – including e-cig use, duration of smoking, or the number of cigarettes smoked per day – were limited or not conclusive.[5]

Although the mechanisms by which smoking affects dynamics of vaccine-elicited antibody response need to be carefully investigated, it is well known that tobacco use influences both innate and adaptive immunity, and some possible pathophysiologic bases have been suggested, which include, among others, inhibition of T cells and the ability to form memory cells, impairment of antigen-mediated signaling in adaptive immunity components.[5–7] The hallmark AEs reported in the MOSAICO sample are common signals of postvaccination response of both the innate and the adaptive arms of the immune system. Thus, the reduced AE incidence associated with the increasing number of daily cigarettes may also be the consequence of the impairment of cellular components and signaling pathways due to tobacco products that are known to reduce antibody production in response to vaccination[7] and therefore the frequency/severity of postvaccination AEs. The more individuals smoke, the most likely the antibody production is reduced and consequently diminished AEs overall.

In regards to e-cig vapers, they were all (49/50) dual users. Generally, dual usage is associated with change in smoking patterns, with a potential ancillary effect on the immune system and vaccine response. In our sample, although there was no difference in the median number of tobacco cigarettes between smokers and dual users, vapers showed narrower ranges (2–30 cigarettes smoked per day in dual users vs 1–40 in tobacco smokers). However, the results on immunologic effects of e-cig achieved hitherto are far being conclusive in human studies.[8] Furthermore, MOSAICO data set does not characterise nor quantify e-cig usage, and this point needs further investigation.

Higher risks for some systemic AEs – namely, muscle pain, joint pain, and chills – were observed in smokers. This finding seems to go against the effect of the amount of smoked cigarettes, but a possible explanation is a joint effect of the HCWs age and smoking. It is also worth noting that previous research[4] (as well as our Poisson models [data not shown]) captured that younger age predicted AE risk. In our sample, there was a correlation between older ages and an increased number of smoked cigarettes (this hypothesis was tested in a post-hoc linear regression analysis, resulting in β coefficient 0.11 [95% CI 0.10–0.12; *P*-value <0.001] per year). Similarly, we cannot exclude that the found association may be related to an effect of nicotine and other smoke components on pain reactivity.[9] Indeed, AEs and clinical pain (and thus AE perception) often covary with numerous confounding factors found in smokers (e.g. comorbidities, drug utilisation), which were precluded from analyses because they were not measured in the parent study.[3] Increase rate of joint and muscular pain is not surprising in smokers, as smoking has a well-known negative impact on the musculoskeletal system.[10] Mechanisms behind this effect of smoking are complex and only partially understood and include the role of increased oxidative stress, chronic inflammation, and endothelial inflammation with peripheral macromicrovascular, damage leading to muscle mass and strength reduction.[10] Specifically designed studies with a greater sample size could help enhancing predictive validity and improving the accuracy of estimates.

From a methodological view, it should be considered that our study may also be susceptible to small subgroup sample sizes, which may also explain the lack of significance in stratified analyses. However, most results remained significant after setting Bonferroni-adjusted alpha levels of 0.004 per test (0.05/12).

Although this was a preliminary investigation, we observed possible effects of tobacco dose–response as well as of other forms of tobacco substitution (e.g. vaping) on AE onset. The study offers interesting evidence that helps understanding possible factors that might influence the interindividual variability in vaccine response, which may increase the risk of vaccine failure in smokers as seen for other vaccination.[3] In this sense, it serves as a reference for further research on the effect smoking on vaccine response.

Author statements

Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki. The MOSAICO study was approved by the Institutional Review Board–Comitato Etico Campania Nord, with referral number CECN/1868/2022. All participants provided written informed consent before enrolment into the study.

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Competing interests

None declared.

Author contributions

D.P. participated in study designing and was responsible for data collection. L.L. analysed the data and contributed to drafting the article. D. Campagna and L.S. participated in data interpretation. R.M., A.V., D. Cacciapuoti, A.Z., M.B., and B.S. contributed to data collection and acquisition and database development. P.F. was the principal investigator of the MOSAICO project, originated the idea for the study, supervised statistical analysis, led the interpretation of the data, and wrote the article. All authors read the manuscript and gave the final approval of the version to be published.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.013.

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Original Research

Social and ideological determinants of COVID-19 vaccination status in Spain

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ABSTRACT

Objectives: This study analysed the association between social and ideological determinants with COVID-19 vaccine accessibility and hesitancy in the Spanish adult population.
Study design: This was a repeated cross-sectional study.
Methods: The data analysed are based on monthly surveys conducted by the Centre for Sociological Research between May 2021 and February 2022. Individuals were classified according to their COVID-19 vaccination status into (1) vaccinated (reference group); (2) willing to vaccinate but not vaccinated, proxy of lack of vaccine accessibility; and (3) hesitant, proxy of vaccine hesitancy. Independent variables included social (educational attainment, gender) and ideological determinants (voting in the last elections, importance attached to the health vs the economic impact of the pandemic, and political self-placement). We estimated odds ratio (OR) and 95% confidence interval (CI) conducting one age-adjusted multinomial logistic regression model for each determinant and then stratified them by gender.
Results: Both social and ideological determinants had a weak association with the lack of vaccine accessibility. Individuals with medium educational attainment had higher odds of vaccine hesitancy (OR = 1.44, CI 1.08–1.93) compared with those with high educational attainment. People self-identified as conservative (OR = 2.90; CI 2.02–4.15) and those who prioritised the economic impact (OR = 3.80; CI 2.62–5.49) and voted for parties opposed to the Government (OR = 2.00; CI 1.54–2.60) showed higher vaccine hesitancy. The stratified analysis showed a similar pattern for both men and women.
Conclusions: Considering the determinants of vaccine uptake and hesitancy could help to design strategies that increase immunisation at the population level and minimise health inequities.

Introduction

Since the beginning of the COVID-19 pandemic until October 6, 2022, more than 600,000,000 cases and 6,500,000 deaths have been notified worldwide,[1] although excess mortality attributed to COVID-19 may triple registered deaths.[2] The consequences of the pandemic have had an impact on other physical and mental health conditions, including the clinical management of non-COVID-19-related diseases,[3,4] and these consequences have not been equally distributed, affecting more the more disadvantaged social groups.[5,6] Vaccines against SARS-CoV-2 are one of the most effective tools to mitigate the consequences of the pandemic.[7,8] Furthermore, adequate coverage among socioeconomically vulnerable populations could potentially reduce COVID-19 inequalities.[9,10]

Vaccine coverage levels depend on several factors affecting vaccine availability and the willingness to get vaccinated. Related to the latter, the Strategic Advisory Group of Experts on Immunization of the World Health Organization proposed 'a model of determinants'[11] on three levels: (1) contextual influences (e.g. cultural, religious, or historical); (2) individual/social groups influences (e.g. social norms, attitudes and motivation about health and prevention); and (3)

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vaccine and vaccination-specific issues (e.g. risk/benefit profile, the introduction of a new vaccine, the role of healthcare professionals). These influences shape vaccine hesitancy, which the World Health Organization defines as 'a delay in acceptance or refusal of vaccination despite the availability of vaccination services'.[12] However, this concept raises some ambiguities because of the multiple attitudes and behaviours towards vaccination located somewhere throughout the pro/anti-vaccination spectrum.[13]

Betsch et al. proposed a '5C model' that highlights the following dimensions: (1) confidence in both vaccine safety/effectiveness, the system that delivers it and the policy-makers; (2) complacency, related to not perceiving diseases as high-risk and vaccination as necessary; (3) convenience, referred to the practical barriers affecting vaccine availability and accessibility; (4) calculation (i.e. engagement in extensive information searching); and (5) collective responsibility (i.e. willingness to protect others) to assess the psychological antecedents of vaccination.[14] In addition, the '5As taxonomy,' proposed by Thomson et al., considered four dimensions (access, affordability, awareness and acceptance) and one more related to interventions aim to facilitate people getting vaccinated.[15]

Social inequalities in both vaccine hesitancy and uptake may lead to a widening of the already existing health inequalities in COVID-19 outcomes.[16,17] For example, some research has found that having a low educational level, belonging to ethnic minority groups, or mistrusting public institutions increases the probability of vaccine hesitancy.[18–20] In terms of COVID-19 vaccines, lower vaccination rates have been found among males, migrants, young people and individuals with low income.[19,21,22] However, how social determinants of health impact vaccine hesitancy or uptake may differ across different countries.[23]

Besides social determinants, the COVID-19 pandemic has raised concerns about how political affiliations and ideology may promote or discourage vaccination.[24,25] For instance, since the beginning of the COVID-19 pandemic in the United States, people self-identified as liberal and voters of the Democratic Party had more probability to follow public health recommendations.[24,26] Thus, the study of the social and ideological determinants of vaccine hesitancy and uptake could help in designing public health strategies to overcome the barriers to vaccination experienced by the population. Therefore, the objective of this study was to analyse the social and ideological determinants of COVID-19 vaccine hesitancy and accessibility in the Spanish adult population.

Methods

Study design

We designed a repeated cross-sectional study based on secondary data from the public opinion polls elaborated by the Centre for Sociological Research (CIS, the acronym in Spanish). These surveys are conducted at the beginning of each month—except August—to estimate public opinion about political and social issues among adults. For the scope of this study, we selected the surveys conducted between May 2021, the first one including a question on vaccination status ('Are you vaccinated against COVID-19'?), and February 2022, the last survey with both questions on vaccination status and willingness.

Each survey had a sample size of 2500–4000. These surveys follow a multistage stratified with sex and age quotas and are designed to be nationally representative. More details on each survey are available on the Web site of the CIS.[25] The participants must agree to participate before the survey, and they were allowed to declinate the participation at any time during the interview. More information about the data recollection is published on the CIS Web site.[26]

Sample selection criteria

The vaccination campaign started in Spain on December 27, 2020, with two main actors: (1) the Spanish Government, which acquired the vaccines following the European Union Vaccine Strategy and designed the Spanish Vaccination Strategy;[27,28] (2) and the Regional Governments, who led the distribution and administration of vaccines through the regional healthcare system. As age is one of the most important predictor variables of clinical vulnerability to COVID-19, the Spanish Vaccination Strategy prioritised the older age groups for the early stages of the vaccine rollout. Thus, the rollout started with individuals aged ≥80 years, with the rollout for subsequent 10-year groups once all individuals in a given group had been invited to get vaccinated.

To develop a sample comprised of individuals who were eligible for vaccination at each survey moment, we designed the following criteria: individuals from each age group were selected from each survey if they reached a proportion of 50% of individuals with at least one dose of vaccine 4 weeks before the survey was conducted (Fig. S1). For example, the 30- to 39-year-old group reached a proportion of 50% of individuals with at least one dose of vaccine on July 15, 2021; thus, individuals aged 30–39 years were selected from every survey conducted since September 2021.

At the end of this process, individuals with missing information (n = 6282, 26.9% of the initial sample) related to the variables of analysis were excluded from the analytical sample. Most of the missing values correspond to the question about the vote in the 2019 election (n = 6160). Table S1 shows the sociodemographic characteristics—variables without missing values are shown—of the excluded individuals compared with the included ones. The analytical sample comprised 17,066 individuals. Fig. S2 shows the flowchart of the elaboration process of the analytical sample.

Dependent variable: vaccination status

We defined three levels of vaccination status that were operationalised as follows.

- Vaccinated: those who answered affirmatively to the question, 'Have you been vaccinated against COVID-19'. This is the reference group used in the analyses.
- Willing to vaccinate but not vaccinated: those who reported not being vaccinated at the moment of the survey and answered affirmatively ('Yes'/'Yes, depending on its origin'/'Yes, if its reliable, if it is safe'/'Yes, if there is enough information'/'Yes, following the advice of the authorities, scientific, or health workers') to the question, 'Are you willing to get vaccinated against COVID-19 as soon as possible?' This category was used as a proxy for *lack of vaccine accessibility.*
- Hesitant: those individuals who were not vaccinated at the moment of the survey and answered 'No' or 'I don't know' to the question, 'Are you willing to get vaccinated against COVID-19 as soon as possible?' This category was used as a proxy for *vaccine hesitancy.*

Independent variables

Social determinants

- Age reported as a categorical variable considering the risk of COVID-19 outcomes reported by the Carlos III Health Institute[29] (18–39, 40–59, >60 years).
- Gender as a dichotomous variable (man/woman) proxied by self-reported sex.

- Educational attainment was defined as the highest level of education reached by the respondent and categorised into three levels according to the National Education Classification of 2014:[30]
  - o Low educational attainment: 11 or fewer years of education.
  - o Medium educational attainment: from 12 to 18 years.
  - o High educational attainment (reference group): from 18 years onward.

Ideological determinants

- Vote in the last 2019 elections. Categorised as a dichotomous variable. We considered 'supporters' (reference group), those who voted for political parties that supported or abstained during the voting for the formation of the Government, and 'opposers,' those who voted for political parties that opposed the Government in 2019 (Table S2).
- Whether the respondents value more the economic or health impact of the pandemic based on the question: 'At this moment, what worries you more: the impact of this public health crisis on health, or its impact on the economy and employment?' The answers were categorised into three categories: (1) declaring more importance to the health impact (health over economy, reference group), (2) declaring more importance to the economic impact (economy over health), and (3) declaring same importance to both the economic and health impact (health as well as economy).
- Political self-placement was based on the answer to the question 'When people talk about politics usually use the terms left and right. If we had a scale from 1 to 10, being 1 "the leftmost" and 10 "the rightmost", where would you place yourself?' This variable was categorised into the following categories: (1) progressive (1–3, reference group); (2) moderate (4–7); and (3) conservative (8–10).

Because the ideological determinants might reflect similar phenomena related to vaccine accessibility or hesitancy, we performed a maximum likelihood estimation of the polychoric correlation coefficient between the three variables.[31] The results of this analysis are shown in Table S3.

Analyses

First, we conducted a descriptive analysis of the included variables by vaccination status. Second, to assess the association between social and ideological determinants and vaccination status, we estimated odds ratio (OR) and the 95% confidence interval (CI) using a multinomial logistic regression. Individuals categorised as vaccinated were the reference group, and we calculated the OR for vaccine accessibility ('willing, not vaccinated') and vaccine hesitancy ('hesitant'). We conducted one age-adjusted multinomial logistic regression model for each of the social and ideological determinants as independent variables. All analyses were stratified by gender. To consider survey weights, we used the 'svyglm' R package. All the analysis and graphics were conducted using R software (v.4.1.2).

Results

The initial sample comprised younger individuals, more proportion of women, and of people who self-identified as moderate compared with the analytical sample (Table S1). Table 1 shows the descriptive analysis of the analytical sample stratified by vaccination status. A total of 97.2% of the sample was vaccinated, 1.4% intended to get vaccinated, and 1.4% were hesitant. The median age was 55 years (interquartile range 42–66), 49.2% were women and 44.0% had the highest educational attainment, 54.2% were self-placed as political moderates, 59.8% were categorised as opposers, and the same proportion of the sample attached more importance to health than to the economy.

Fig. 1 and Table S4 show the association between the social and ideological determinants and vaccination status. Compared with people with high educational attainment, participants with medium educational attainment had higher odds of vaccine hesitancy (OR = 1.44; CI 1.08–1.93). Compared with men, women had higher odds of vaccination, but this association was not statistically significant. Gender showed no association with either accessibility or hesitancy.

Regarding political determinants, conservatives showed higher odds of lack of access and vaccine hesitancy (OR = 1.77; CI 1.16–2.69 and OR = 2.90; CI 2.01–4.15, respectively). Opposers to the government had no association with accessibility (OR = 1.17; CI 0.90–1.53) but higher odds of vaccine hesitancy (OR = 2.00; CI 1.54–2.60). We found no associations of prioritisation of health over the economy with vaccine accessibility. On the other hand, those who had no clear prioritisation had 1.86 higher odds of hesitancy (CI 1.22–2.83), and those who prioritised the economy had 3.80 higher odds of hesitancy (CI 2.62–5.49).

Fig. 2 and Table S5 show the models stratified by gender. Most associations were consistent but tended to be higher in men. The association between educational attainment and vaccine accessibility was present only in men.

Discussion

In this study exploring the social and ideological determinants of vaccine hesitancy and accessibility in Spain, we found three key findings. First, social determinants had a weak association with both vaccine outcomes, and only individuals with medium educational attainment had higher odds of vaccine hesitancy. Second, ideological determinants did not influence vaccine accessibility, but conservatives, those who prioritised economy over health, and opposers had higher odds of hesitancy. Finally, these associations showed a consistent pattern in both men and women.

We did not find major social inequalities by educational attainment in vaccine accessibility.[34,35] A study conducted in Catalonia, Spain, found that working-age individuals living in the most deprived areas had a lower vaccine coverage compared with those in the least deprived areas; but no differences were found among those aged >65 years.[9] The results on immunisation rates for non-COVID vaccines according to educational level in the Spanish context are inconsistent.[32,33] The lack of association between educational attainment and COVID-19 vaccine accessibility might reflect how the Spanish healthcare system organisation, following a Beveridge model,[34] and the design of the vaccine rollout in Spain has helped to mitigate inequities related to the educational level.[38] COVID-19 vaccines were administered in both hospitals and primary care centres and supported by habilitating other venues such as sports stadiums or parkings. At the beginning of the vaccine rollout, the entire eligible population was appointed to vaccinate by telephone by the Regional Health System. After, individuals could arrange their vaccination appointment by themselves through the internet. This organisation of the vaccination campaign might have helped to reduce the differences in vaccine accessibility, contrary to other countries such as the United States.[35] However, our definition of vaccine accessibility might reflect different barriers (e.g. healthcare-related issues, geographical dispersion, and so on), so further studies are needed to understand why individuals who were willing to vaccinate did not get vaccinated.

Table 1
Sociodemographic characteristics of the individuals included in the analysis, overall and according to their vaccination status.

Characteristics	Overall (N = 17,066)	Vaccinated (n = 16,593)	Willing, not vaccinated (n = 235)	Hesitant (n = 238)
Age (years), *n* (%)				
18–39	3588 (21.0)	3444 (20.8)	89 (38.1)	54 (22.6)
40–59	6653 (39.0)	6480 (39.0)	67 (28.4)	106 (44.4)
≥60	6825 (40.0)	6668 (40.2)	79 (33.5)	79 (33.0)
Gender, *n* (%)				
Male	8664 (50.8)	8407 (50.7)	126 (53.5)	132 (55.2)
Female	8402 (49.2)	8186 (49.3)	109 (46.5)	107 (44.8)
Educational attainment, *n* (%)				
High	7503 (44.0)	7316 (44.1)	94 (40.1)	93 (39.0)
Medium	5553 (32.5)	5367 (32.3)	88 (37.6)	98 (41.1)
Low	4010 (23.5)	3910 (23.6)	53 (22.3)	47 (19.9)
Vote in the past elections, *n* (%)				
Supporters	10,212 (59.8)	9976 (60.1)	134 (56.9)	102 (43.0)
Opposers	6854 (40.2)	6617 (39.9)	101 (43.1)	136 (57.0)
Importance attached to health vs economy, *n* (%)				
Health over economy	6283 (36.8)	6164 (37.2)	79 (33.7)	40 (16.5)
Economy over health	6135 (36.0)	5892 (35.5)	98 (41.7)	145 (60.9)
Health as well as economy	4648 (27.2)	4537 (27.3)	58 (24.6)	53 (22.6)
Political self-placement, *n* (%)				
Progressive	5813 (34.1)	5681 (34.2)	66 (28.0)	66 (27.9)
Moderate	9255 (54.2)	9012 (54.3)	132 (56.4)	111 (46.2)
Conservative	1998 (11.7)	1900 (11.5)	37 (15.6)	61 (25.9)

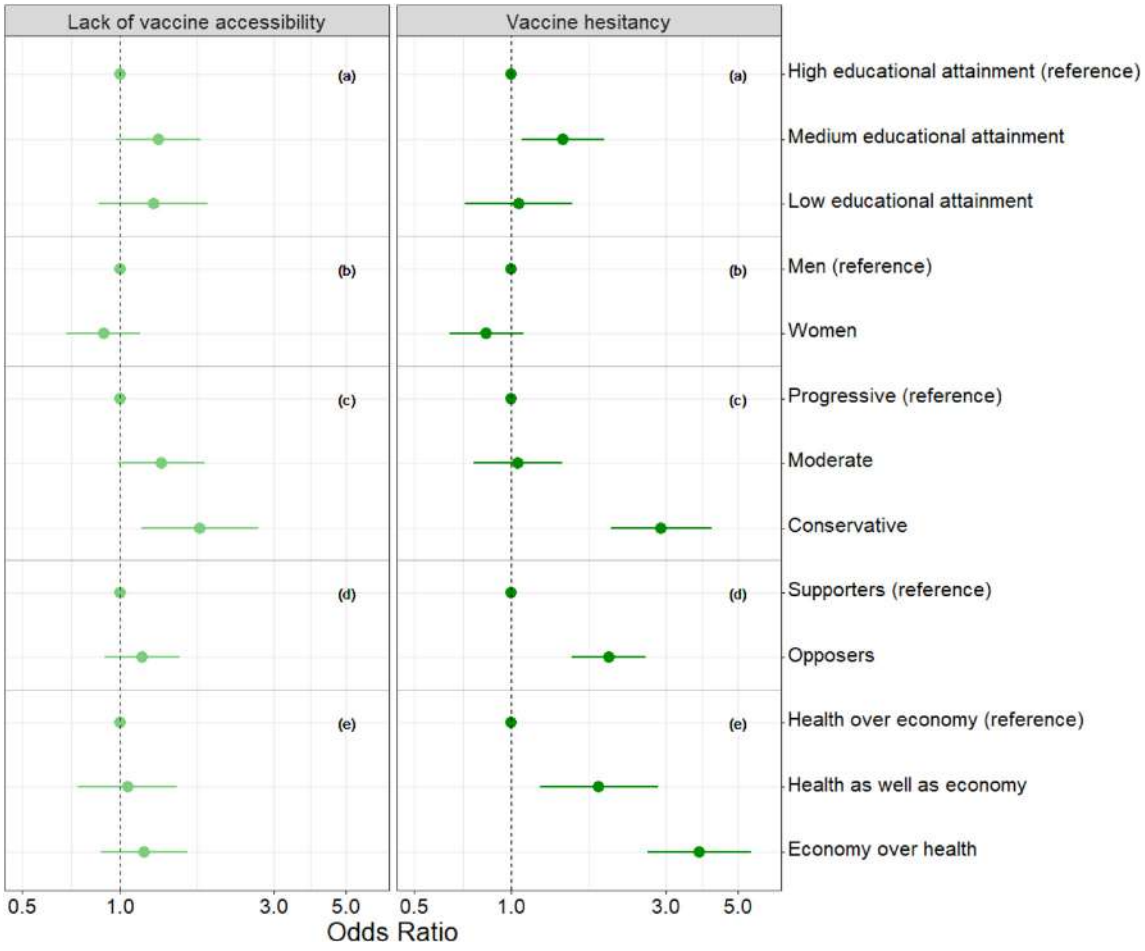

Fig. 1. Association between social and ideological determinants and vaccination status (multinomial logistic regression models, using age as an adjustment variable). (a) Model using educational attainment as dependent variable; (b) Model using gender as dependent variable; (c) Model using political self-placement as dependent variable; (d) Model using vote in the past elections as dependent variable; (e) Model using importance attached to health vs economy as dependent variable.

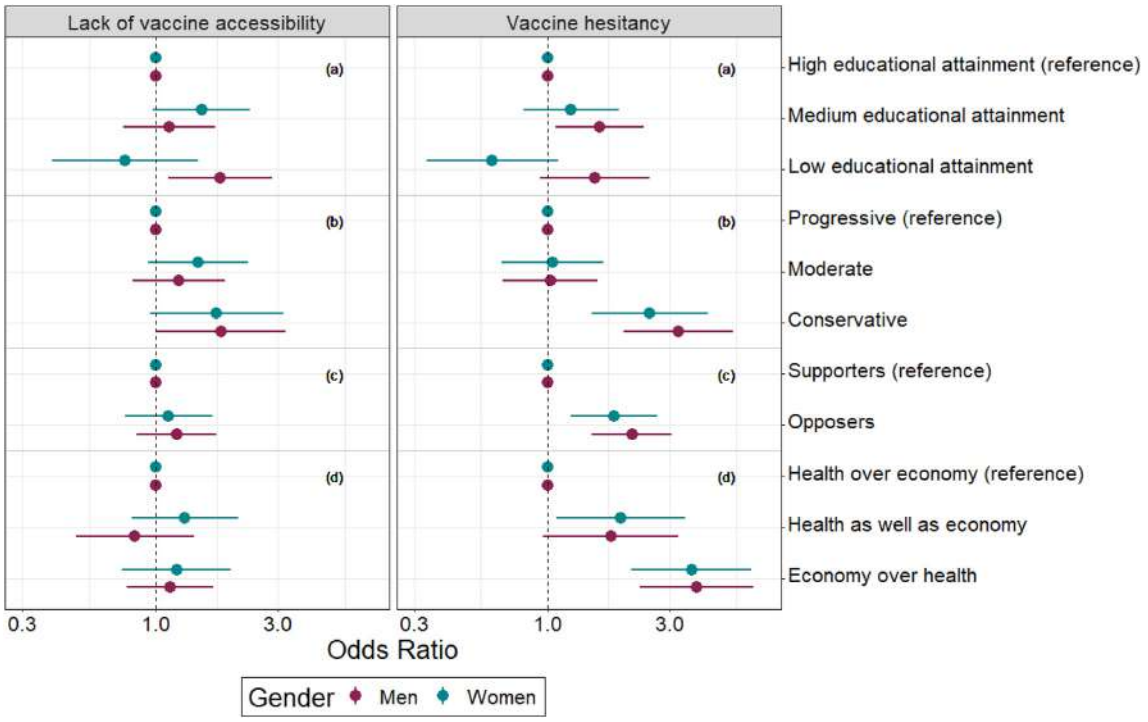

Fig. 2. Association between social and ideological determinants and vaccination status stratified by gender (multinomial logistic regression models, using age as an adjustment variable). (a) Model using educational attainment as dependent variable; (b) Model using political self-placement as dependent variable; (c) Model using vote in the past elections as dependent variable; (d) Model using importance attached to health vs economy as dependent variable.

Medium educational attainment was associated with having doubts about vaccination. Other studies have found that people with basic education had more probability to report vaccine hesitancy.[36,37] However, the higher the risk perception, the higher the vaccine acceptance.[38] In the Spanish context, people living in the most deprived areas have a higher risk of COVID-19 infection, hospitalisation, or mortality.[6,39] Thus, individuals with lower educational attainment could have a higher risk perception, hence reducing inequalities in vaccine hesitancy.

Regarding the analysis stratified by gender, the results have a similar pattern. Only one difference emerged from the analysis by gender: lower education was associated with both vaccine accessibility and hesitancy only in men. The unemployment rate among women with low educational attainment is higher compared with men in 2021 according to the National Statistics Institute,[40] and they might face fewer work-related barriers to getting the COVID-19 vaccine. Traditionally, women spent more time on unpaid care work compared with men,[40] specially dedicated to older individuals who have a higher risk of severe COVID-19, and this might enhance their vaccine acceptance.

Gender has no clear association with vaccine accessibility or vaccine hesitancy. In our study, women tended to have lower odds of both not being vaccinated and hesitancy, but this association had no statistical significance. One study conducted in the United Kingdom also found that women have higher vaccine uptake rates compared with men.[41] On the opposite, willingness to get the COVID-19 vaccine has been observed lower among women across multiple studies according to the meta-analysis of Zintel et al.[42] However, our results are consistent with the evidence that indicated that even before the beginning of the vaccine rollout, women in Spain reported a higher acceptance of the COVID-19 vaccines compared with men.[43]

Regarding ideological determinants, we found no association with vaccine accessibility while showing strong associations with hesitancy. The polychoric correlation analysis (Table S2) indicated that both vote in the last election and political self-placement were highly correlated (Maximum-likehood estimate = 0.784, *P*-value <0.01), but the prioritisation of health over the economy was not correlated with voting and political self-placement. This indicates that both partisanship and political ideology and people's values about health and the economy have relevance when we attend to consider their influence on vaccination.

Regarding vaccine accessibility, other studies in the United States context have found differences in vaccination rates related to voting in the 2020 presidential election.[44] Our results might reflect the capacity of the Spanish vaccine campaign to mitigate inequities between social groups defined by their partisanship or ideology. Another potential explanation is that vaccination has not been a partisanship issue in the Spanish context, which could be associated with a historically higher acceptance of vaccines compared to other countries.[45]

Ideology and political partisanship have been associated with vaccine hesitancy in different geographical contexts,[44] consistent with our results. A liberal conception of the economy could minimise the risk perception of COVID-19 infection and severity, perceiving the vaccine as less necessary.[46] How political partisanship shapes attitudes toward vaccination could be exacerbated during a public health emergency such as the COVID-19 pandemic.[47] The analysis stratified by gender showed a similar pattern for both men and women. Public health authorities should address the motivations that condition vaccine acceptance and how these motivations could be different depending on the context and the vaccine to design proper communications and fieldwork strategies to reduce the differences in vaccine uptake between social groups. Traditionally, community-level interventions with the participation of community leaders (i.e. healthcare staff, religious, and so on) addressing people's doubts about vaccines have improved vaccine acceptance and coverage among hesitant

individuals.[48,49] In the context of the COVID-19 pandemic, the diffusion of culturally and linguistically informational videos based on the barriers and fears related to vaccines reported by the community, in different social networks increased the odds of getting vaccinated.[50] Virtual and in-person seminars conducted by healthcare providers delivered to a military base population were able to increase vaccine acceptance among the participants.[51]

Our research has some limitations. We could not consider ethnicity because of how the survey asks this question. Several studies have observed inequities in vaccination according to race, ethnicity, or migration status, and these social groups might face administrative barriers more often, have distrust toward public institutions, or deal with institutional communication channels, which are not usually adapted to a multicultural reality.[52] Thus, further studies that focus on these types of inequities in the Spanish context are needed. Another limitation is the lack of a panel survey that allows for longitudinal analysis. However, we consider that our sample size and its representativeness allow us to study the influence of different social and ideological determinants on vaccination status. Our design was also not intended to establish causality. Finally, the question designed to define the vaccination status did not allow us to establish differences based on the number of doses, so our results may reflect the most extreme inequities in terms of vaccine uptake (fully vaccinated vs unvaccinated) instead of observing differences in terms of boosters for example.

Conclusions

We found that both social and ideological determinants had a weak association with vaccine accessibility in the Spanish population, but their influence was more consistent in terms of vaccine hesitancy: individuals with medium educational attainment, more conservative values, and who prioritised the economic impact of the pandemic tended to have more odds of vaccine hesitancy. Vaccine hesitancy and accessibility are complex and multifactorial phenomena; thus, governments and public health authorities need to address their determinants, and design vaccine rollout strategies adapted to sociopolitical contexts to facilitate vaccine uptake.

Author statements

Ethical approval

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Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Author contributions

M.F.V. and M.F. conceived the study. M.F.V. acquired the data and conducted the analysis. P.G. and U.B. contributed to the analysis. M.F.V. drafted the first version of the article, and M.F., P.G. and U.B. reviewed the article critically for important intellectual content. All the authors have approved the final version of the article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.04.007.

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Themed Paper — Original Research

‘Social’ media? How Swiss hospitals used social media platforms during the early months of the COVID-19 pandemic crisis

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ABSTRACT

Objectives: This paper about social media platforms of Swiss hospitals refers to the period between 10 February 2020 and 6 July 2020. The study included in-depth insights into the use of platforms, content analyses of posts and resonance of the posts. The study's objective was to get insights into social media post creation by and corresponding resonance in pandemic crisis.

Study design: This study included collection and analyses of posts created by a selection of Swiss hospitals during the period of study. All university hospitals and a variety of private and regional hospitals in all regions of Switzerland are represented. The data collection started before the official shutdown in Switzerland.

Methods: This study used mixed method approach and content analysis to evaluate 2,326 posts during the study period related to the COVID-19 pandemic.

Results: During the first phase of the pandemic, hospitals used social media platforms more frequently than normal. Especially in the first month, the number of posts rose disproportionally. The numbers dropped back to the initial situation after only 4 months into the COVID-19 pandemic. Most hospitals used Facebook and Twitter, whereas Instagram and YouTube's use were marginal. University hospitals used social media platforms differently than regional hospitals.

Conclusion: Most posts generated only a very low response with a median of 2. Hospitals were therefore not able to create engagement of their followers. However, hospitals that publish actively were able to build a more active community. Only a small number of posts led to heated discussions in the comments. These viral posts shared information on the illness, the vaccination, children and COVID-19.

Introduction

The coronavirus pandemic has hit world's society hard in the first half of 2020, disrupting every detail of social life. The need for information was enormous as well as the amount of information exchange on social platforms. Studies have shown that when emerging infectious diseases occur, the public often turn to social media for information.[1] This was also evident during the corona pandemic, where Instagram was one of the most important sources of information/news for young people during the (first full) lockdown in Switzerland.[2] In addition, more than 70% of Swiss respondents said they had searched for health information on the Internet and social media in the last 3 months.[3]

This mass adaptation of social media in the private sphere as a personal everyday enrichment also increases its importance as a communication channel for organisations.[4] Social media platforms are considered a fast and interactive method to provide information, set up an open channel for discussions and build trust for organisations.[5] Numerous studies demonstrate that communication plays an essential role in the management or containment of health crises.[6,7] Social networks have become established and represent important communication channels in health crises.[8,9] The (potentially) beneficial use of social media in health crisis situations is repeatedly highlighted by researchers.[10–13] Beier and Früh[14] compiled the first and only comprehensive study on the use of social media platforms through Swiss hospitals. It is largely unclear what content and interaction patterns are to be found in the communication of hospitals on social media.[14] Therefore, this study precisely addresses these points.

In social media communication, resonance is formed from the totality of user reactions to published posts. Depending on the platform, different reactions and thus participation options are

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made available.[15] On Facebook, this resonance can be seen in the number of likes, shares and comments achieved by a post. Since 2015, Facebook has offered an extended variant for the like button in the form of various emoticons, the so-called reactions such as 'Love', 'Hug', 'Haha', 'Wow', 'Sad' and 'Angry'.[16,17] Twitter also has a like function (favourite), a share function (retweet) and a comment function (reply).[18] On Instagram, it is only possible to like and comment; sharing is only possible through a private direct message to individual networked persons.[19] YouTube also has variants of the reaction options. Besides the like function, there is also the negative equivalent, the dislike button. And of course, it is possible to comment and share.[20]

Content must first attract a certain amount of attention from users in order for them to interact with posts via the basic reactions of likes, shares and comments. The three types of reactions can be differentiated based on their varying degrees of activation[21] and different intentions for action behind the reactions. A like is considered the simplest form of reaction and minimally active, as it only requires a single click but goes beyond passive reading. Sharing a post already requires a stronger activation of the users than a like[21] because the users make the post their own to a certain extent, possibly add to or change it and publish and disseminate the content themselves a second time in their own community.[22] A comment creates the possibility of a dialogue,[23] which enables a kind of self-expression by expressing one's own opinion and interacting with other users.[24] In summary, it can be said that likes are easier to achieve, whereas a high level of engagement must be present for both sharing and commenting. A higher number of shares and comments is more difficult for an organisation to obtain.

Furthermore, user reactions play a central component in the visibility of posts. Studies show that posts that are frequently liked, commented on or shared can reach a much larger circle of users.[25,26] Through the user reactions of the 'primary audience', the subscribers/followers of the profile, the post becomes visible in their user circles, the so-called 'secondary audience', who in the best case also react to it to make the post visible again in further user circles[25] see also 'first-degree followers' and 'second-degree followers' according to Jacobs and Spierings.[26] A like gives the content creator the 'advantage' that the content is spread beyond his or her circle of followers. A like does not open up a new interaction channel but expands the existing one by increasing the visibility and responsiveness of non-followers.[24] Sharing, in turn, opens new channels of interaction and can also gain a much wider reach through chains of sharing. Shared content can be liked and commented on by new audiences in a new 'space'. Sharing thus represents the most important means of resonance and visibility.[24] The comment can be seen by the commenting user's community in their news feed, making the original post visible and 'responsive' to non-followers. A comment under the post can be commented on and liked by the audience it reaches. From the point of view of information dissemination, a great advantage of the comment function is that it can be done repeatedly. Each individual comment increases the chance of visibility so that a heated debate between users under a post can be useful for information dissemination.[24]

In summary, it can be said that an overall high resonance within the various audiences increases the probability for the post owner, here the hospitals, to reach the broadest possible audience on social media.[16] This is related to the algorithmic control/selection of the social media platforms. Not all posts are shown to users in the feed with the same priority. For example, it is not always the most recent posts that appear at the top. Whether a post is visible depends, among other things, on user interests, friendships or the number of user reactions to the posts.[27] However, the algorithms are constantly being changed and are not accessible to the public.

Hospitals are considered opinion leaders and are viewed as acknowledged experts.[28] They occupy an important role in spreading credible and reliable information about medical issue, for example, during the current coronavirus pandemic. Hospitals could now use social media channels as a crisis communication tools to connect with their followers and provide facts and information for patients, staff, media and other stakeholders. Social media platforms are often faster in distributing information than traditional news media. They could be installed for early detection, raise awareness of outbreaks and incidences, timely news feed, syndromic surveillance and validate behaviour and attitude relevant for the crisis.[29] Almost all age categories are widely represented on social media platforms making it easy for hospitals to reach their most important stakeholders.[30] For example, in Switzerland in particular, journalists and politicians are reached on Twitter in addition to private individuals.[31] Thus, especially in times of a pandemic, the public visibility that can be achieved through social media is a relevant component for healthcare organisations such as hospitals and will be investigated in this study. Therefore, the following questions will be investigated.

RQ1: How did different Swiss hospitals use social media during the important first phase of the corona pandemic?

RQ2: Were hospitals able to achieve mobilisation of the public, indicated by the resonance of their posts as a proxy for user engagement?

RQ3: Which content of Swiss hospitals' posts achieved the most resonance with the public?

Methods

Data collection

The hospitals' social media posts and the associated metadata were collected by a specialised media monitoring tool. Unicepta Technologies enables users to continuously monitor relevant topics on the Web, for example, social media. The social media content is initially rendered as a mention ('snippet'). Structured and unstructured data are recorded that enable access to the content. All metadata provided by the social media platforms are included in the data export, enabling ordering. Excluded sources are private news and non-public communication; password-protected forums or Web sites; Web sites that take technical precautions to avoid being searched. The German law on ancillary copyright applies. In compliance with the law, in terms of content, only a snippet is initially specified. The full text is accessed via the original link. Ubermetrics Technologies GmbH (later Unicepta Technologies), founded in spring 2011, is a spin-off of the Humboldt University of Berlin (https://www.humboldt-innovation.de/de/spinoffs/Ubermetrics-36.html), which is follow-up financed by the High-Tech Gründerfonds.

All posts published on the social media profiles of the selected hospitals were collected in the period from the week beginning 10 February 2020 until (and including) the week beginning 6 July 2020. The following social media platforms were considered: Facebook, Twitter, Instagram and YouTube. Unfortunately, LinkedIn, although an important platform for hospitals, could not be considered, as it does not make data from professionals that it does not own accessible via its Business API. The period was deliberately chosen before the first corona case in Switzerland reported by the Federal Office of Public Health (FOPH) on 25 February 2020.

The first data set consisted of a total of 4,979 entries. The data set was filtered in the tool according to the following keywords: Coron* OR Covi* OR Covid-19 OR Sars* OR Virus OR Pandem* OR Pandém*. This ensures that only posts that deal directly with the corona topic are analysed. This resulted in the final data set of 2,326 contributions on social media from Swiss hospitals.

Hospital selection

To evaluate the social media platforms of the hospitals, the authors decided on the following selection: first, all five hospitals associated with a university were included in this study. The following main selection is based on the seven major regions of Switzerland according to the Federal Statistical Office.[32] The hospitals of the major regions were further subdivided into the categories of private hospital and regional hospital, analogous to the classification of the members of the industry association H+ and the Bundesamt für Gesundheit.[33] In each region, one large, medium and small general and acute care hospital or cantonal hospital (if available) and one large, medium and small private hospital (if available) were selected. The large, medium and small hospitals were equally divided across all 26 cantons of Switzerland, if possible. If this was not the case, the hospital with the most followers on Facebook or Twitter was chosen. A detailed overview of the hospitals by type can be found below and in Table 1.

a) University hospitals (all): Universitätsspital Zürich (USZ), Universitätsspital Basel (USB), Inselspital Bern (Insel), Hôpitaux Universitaires Genève (HUG), Centre hospitalier universitaire vaudois (CHUV)
b) Switzerland-wide private hospitals: Hirslanden and Swiss Medical Network
c) Hospitals in major regions
   - Geneva region: Hôpital de La Tour, Hôpital Riviera-Chablais, Hôpital du Valais.
   - Central Plateau region: Solothurner Spitäler, Réseau hospitalier neuchâtelois, Michel Gruppe AG, freiburger spital (HFR).
   - Region of Northwestern Switzerland: Kantonsspital Aarau, Claraspital.
   - Zurich region: Spital Zollikerberg, Stadtspital Zürich (formerly Stadtspital Waid und Triemli), Kantonsspital Winterthur, Kantonsspital Baden.
   - Region of Eastern Switzerland: Kantonsspital St. Gallen (KSSG), Kantonsspital Graubünden (KSGR), Spital Oberengadin, Spital Linth.
   - Region of Central Switzerland: Kantonsspital Obwalden, Luzerner Kantonsspital.
   - Ticino: Ente Ospedaliero Cantonale.

Categories

For the qualitative analysis of the 37 most resonant or viral posts, the first step was a categorisation. The content of the posts in the social media was categorised following the Thematic Analysis Approach of Clarke and Braun.[34] Posts could also be assigned to multiple categories. The following categories were identified. 'Recognition of work' is found in social media posts where hospitals thank their collaborators for their immense extra work. 'Information' means all posts that provide medical (in a broad sense) information about the virus, the illness and the vaccine. Within the category 'Call to Action', all posts with a request were categorised. This could be a call to get tested or a call to stay at home during the shutdown. 'Solidarity' were posts that expressed the solidarity between healthcare workers and the general population. Under the category 'Reassurance', one will find posts that reassure the public, visitors and patients. Posts that may have information but with humour are labelled 'Infotainment'. The last two categories are 'Call for donations' and 'Job offers, call for support'.

Data preparation

The data set was prepared and visualised with analytical methods via Jupyter notebooks, running the programming language Python. The majority of posts had zero or very little resonance, leading to the creation of a subset of the most viral posts (2%), which is explained below.

Table 1
Number of posts across different platforms and total resonance per hospital.

Name of Swiss hospital	Type of hospital	Total posts	Posts				Total resonance	Average resonance per post
			Facebook	Twitter	YouTube	Instagram		
Hôpitaux Universitaires Genève (HUG)	University hospital	913	107	585	163	58	87,330	95.7
Hôpital du Valais	Regional hospital	290	147	104	0	39	17,818	61.4
Inselspital Bern (Insel)	University hospital	145	55	90	0	0	5753	39.7
Ente Ospedaliero Cantonale	Regional hospital	144	103	41	0	0	15,645	108.6
Centre hospitalier universitaire vaudois (CHUV)	University hospital	110	69	41	0	0	31,594	287.2
Universitätsspital Zürich (USZ)	University hospital	100	37	39	8	16	27,428	274.3
Swiss Medical Network	Private hospital	79	47	0	16	16	1897	24.0
Hirslanden-Gruppe	Private hospital	75	42	24	5	4	4563	60.8
Réseau hospitalier neuchâtelois	Regional hospital	64	63	1	0	0	8350	130.5
L'Hôpital de La Tour	Private hospital	58	35	4	5	14	2033	35.1
Kantonsspital Baden	Regional hospital	47	33	0	0	14	11,014	234.3
Stadtspital Zürich	Regional hospital	36	36	0	0	0	10,482	291.2
Universitätsspital Basel (USB)	University hospital	35	0	23	7	5	736	21.0
Kantonsspital Aarau	Regional hospital	26	18	5	2	1	1288	49.5
Kantonsspital Obwalden	Regional hospital	25	12	6	0	7	799	32.0
Claraspital	Private hospital	25	23	2	0	0	3847	153.9
Kantonsspital Graubünden	Regional hospital	24	13	11	0	0	3533	147.2
Kantonsspital Winterthur	Regional hospital	23	22	0	1	0	7717	335.5
Hôpital Riviera-Chablais	Regional hospital	20	20	0	0	0	3293	164.7
freiburger spital (HFR)	Regional hospital	20	0	20	0	0	9	0.5
Kantonsspital St.Gallen	Regional hospital	17	17	0	0	0	1686	99.2
Spital Linth	Regional hospital	17	13	0	0	4	1181	69.5
Solothurner Spitälern	Regional hospital	14	10	2	2	0	796	56.9
Spital Oberengadin	Regional hospital	7	5	0	0	2	346	49.4
Michel Gruppe	Private hospital	6	3	2	0	1	216	36.0
Luzerner Kantonsspital	Regional hospital	5	0	0	2	3	0	0.0
Spital Zollikerberg	Regional hospital	1	1	0	0	0	230	230.0
Total		2326	931	1000	211	184	249,584	107.3

Results

The 2,326 posts from 27 hospitals across Switzerland were analysed between 10 February 2020 and 6 July 2020. In this study period, the authors found posts quantity between 1 and 913 between all hospitals. Likewise, the achieved resonance, between 87,330 and 0, as well as the average of resonance and contributions show great differences.

Twitter and Facebook are the most used

A simple breakdown by platforms shows that Twitter accounted for almost half of the posts made during this period. Facebook was also heavily used. Twitter and Facebook together shared 83.0% of all posts.

Fig. 1 shows that university hospitals in particular are significantly more active on social media than other hospitals in other categories. Their posts account for 56.0% of all posts. In contrast, regional hospitals accounted for 33.5% of posts and private hospitals for only 10.4%.

In the evaluation of the posts in the category of university hospitals, HUG comes out on top. The HUG has produced 70.0% of the posts in the specified period. The USB on the other hand is far behind with 2.7%, as are all the other university hospitals. The Insel has produced 11.1% of the posts.

University hospitals prefer the Twitter platform to Facebook (see Fig. 2). Twitter accounted for 59.7% of all posts or tweets. The university hospitals thus produced an above-average amount of content for this social media platform in contrast to the other hospital types.

While university hospitals mainly use Twitter, regional hospitals tend to use Facebook (65.8%). The use of Instagram is similarly low in all hospital categories.

Number of posts peaked around early April

On 25 February 2020, the first case of the novel coronavirus is confirmed in Switzerland. As expected, the number of posts across all hospitals increased strongly at the start of the pandemic. On 16 March, the Federal Council placed the country in an unprecedented lockdown by declaring an 'extraordinary situation'. Subsequently, the number of contributions from Swiss hospitals increased rapidly, reaching a peak at the end of March, and then falling steadily, especially from the end of April onwards (see Fig. 3). The resonance (not shown) across all posts shows a similar shape and peak in April and a relatively rapid decline thereafter.

A closer analysis of 913 posts of HUG (who contributed 39% of all posts) over time shows that in the week beginning 6 April, almost 160 posts were released, with a total resonance of almost 20,000. The weekly posts are shown in Fig. 3 for all hospitals (blue) and for HUG (orange).

Results of the 37 most viral posts

Most posts have very little resonance, with a median of around 2 (mean of 107.0) across all 2,326 posts. Thirty-seven of these posts were evaluated as being viral, which corresponds to approximately 2% of all posts. Here, viral was defined as resonance of over 1,000 in the observed weeks from February to July 2020.

Focusing on the viral posts, 37 posts by nine different hospitals have been identified, with the majority being Facebook posts (31) with the rest being Instagram (see Fig. 4). No Twitter nor YouTube posts have created any high resonance.

For a qualitative evaluation of the 37 viral posts in the study, the following categories were identified:

Recognition of work (17 posts out of 37 with resonance >1'000): Example by HUG (originally in French, translated by authors).

https://www.instagram.com/p/B-g_WyEH0P8/

Teams — Masks, gloves, protective gowns and even respirators delivered by the Swiss Army would not reach doctors and frontline caregivers without the Transportation, Distribution and Warehouse Service (TDWS). "To deliver meals, our distributors must now enter covid-19 units. Often with fear in their stomachs. But they don't back down. What amazes me the most? The speed with which we have adapted to this crisis. Everyone, at all levels, is finding solutions. Sometimes within hours. The HUG liner has been transformed into a formula 1," says Marie-Paule Kellner, head of the sector.

The TDWS transports patients between its various sites and ensures the distribution of consumables and goods for the entire HUG. The team of the HUG Transport, Distribution and Warehouse Service thanks the population for its support and generosity during this time of crisis.

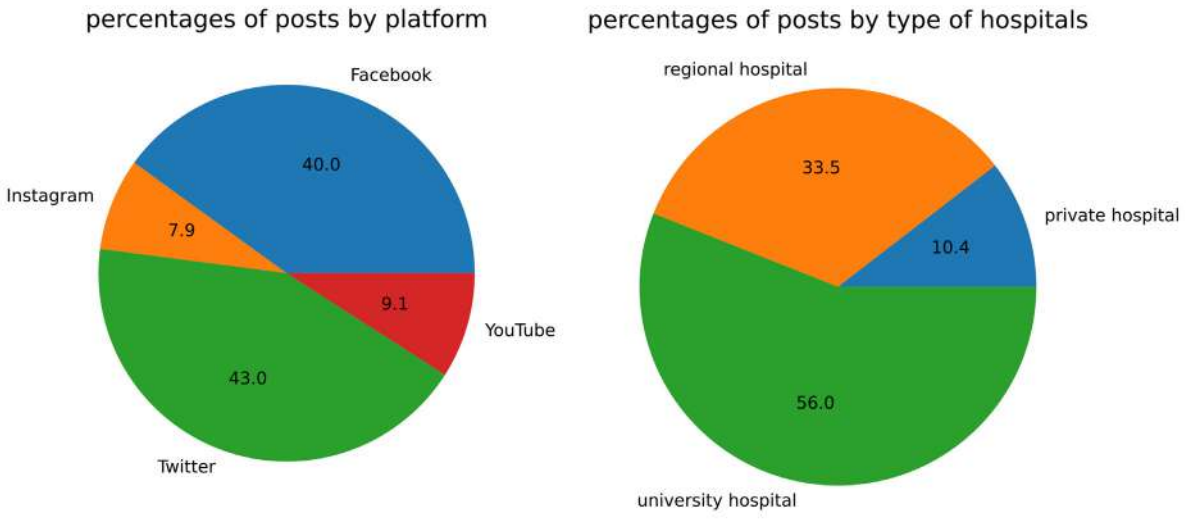

Fig. 1. Percentage of posts across different social media platforms and across different hospital types.

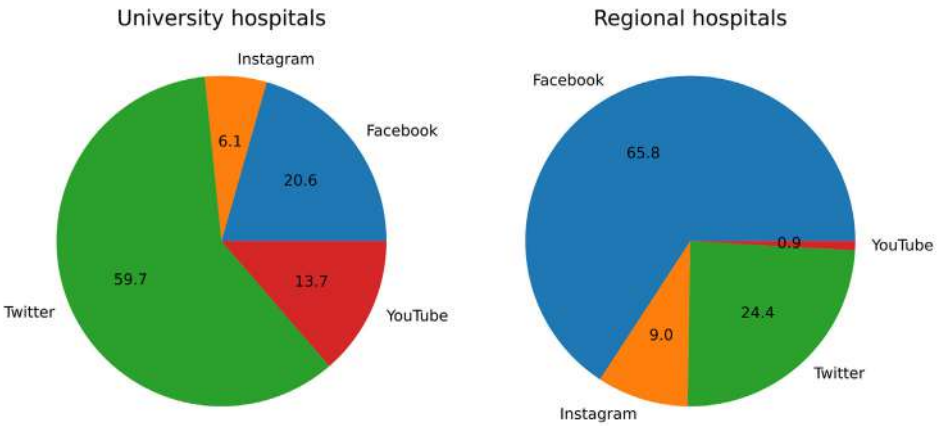

Fig. 2. Percentage of posts across different social media platforms, split by type of hospital.

Information (12 of 37): Example by CHUV

https://www.facebook.com/watch/?v=2601664790107083.

■ *CORONAVIRUS* ■ *What does it mean to be cured of COVID-19? Is one then immune or can one be infected a second time?*

Answers from Prof. Thierry Calandra, Head of the Infectious Diseases Department of the CHUV/Centre hospitalier universitaire vaudois 📸: @louisbrissetphotographer.

Call to action (5 of 37): Kantonsspital Winterthur

https://www.facebook.com/141348992583972/posts/3031108733607969.

Stay at home. The KSW remains there for you. ❤️.

Solidarity (4 of 37): Example by Ente Ospedaliero Cantonale

https://www.facebook.com/52581576779/posts/10156756992531780.

It is certainly a special May 1 that we experience today. From Locarno Hospital, which has been on the front lines of the COVID emergency for weeks, we send a virtual hug to the staff, patients, their families and all the people who have felt the need to make a gesture, even a small one, of solidarity during these difficult times. A heartfelt thank you to everyone for the great humanity shown!

Reassurance (2 of 37): Example by HUG

https://www.facebook.com/206413169374157/posts/3391876200827822.

🏥 As of March 17, 2020, the HUG is increasing its emergency capacity for people suffering from acute respiratory problems of recent onset (cough, fever, etc.). A 200 m^2 tent has been set up behind the hospital to ensure an initial triage of people coming for outpatient consultations and to carry out a screening test, if necessary. Gradually, the HUG are adapting their system according to the needs identified. Several specialized units are already dedicated to the care of patients suffering from COVID-19. Non-urgent operations are being postponed to avoid overloading the intensive care and recovery rooms and to be able to accommodate more patients. The HUG is also preparing to double its capacity in intensive care and acute care, notably by increasing the density of rooms. Since the end of January, the HUG have been working on several scenarios to be able to respond to an overload linked to the COVID-19 epidemic and to continue to ensure the care of all patients.

Infotainment (2 of 37): Example by USZ

https://www.facebook.com/514569845343656/posts/1959958967471396.

"How much longer?"

Want to know what it's really like in a USZ emergency and why we haven't lost our laughter despite Covid-19? This funny video will show you. Have fun!

Call for donations (1 of 37): Example by CHUV

https://www.facebook.com/975855452425631/posts/3501013153243169.

■ *CORONAVIRUS* ■ 👨‍⚕️👩‍⚕️ *United and united because without them, we can do nothing. Donate to the Mutual Aid Fund*

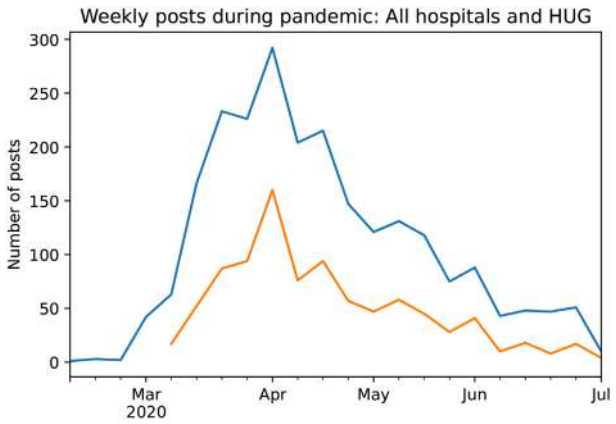

Fig. 3. Number of weekly posts during the study period, or all hospitals (blue) and HUG (orange). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

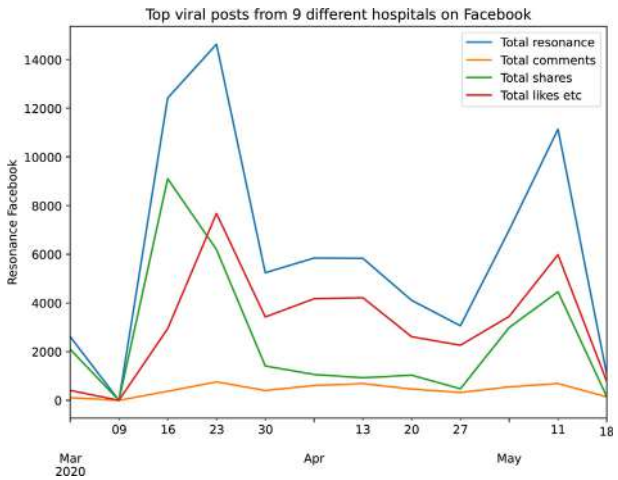

Fig. 4. Resonance of top viral posts.

which supports CHUV staff in precarious situations due to the COVID-19 crisis. Online at www.fondationchuv.ch or by SMS at 488. Just send CHUV with the amount of the donation to 488. Here is an example: CHUV 100 to 488 (For a donation of CHF 100.-). Created by the CHUV Foundation, the COVID-19 Mutual Aid Fund aims to help CHUV employees who are facing particularly complicated situations in this period of crisis.

For the past 6 weeks, the need for psychological, family, social and financial assistance has been mounting. These needs range from simple childcare in a department that operates 7 days a week, 24 h a day, to housing needs due to living with an elderly person, to complex travel arrangements. The staff, who play an essential role in the pandemic, are facing difficult situations to take care of the community. Thank you for your solidarity and generosity ❤️.

Job offer, call for help (1 of 37): Example by Kantonsspital Graubünden

https://www.facebook.com/104000326349557/posts/2870566709692891.

You are a qualified nurse? You have time capacities and are flexible? We are looking for you to support us during the Corona crisis. Please apply with your CV, last certificate, diploma or SRK recognition at hrcorona@ksgr.ch.

Comments and reactions varied between 11,133 from the Facebook video of USZ to 1,001 from the Hôpital du Valais. Interestingly, the most liked, shared and commented post of the USZ was also the post that made the least reference to corona. The video, which entertainingly recreated everyday life in the emergency ward, makes no reference to corona at all in the video and only writes in the accompanying text: "[…] why we haven't lost our laughter despite Covid-19?[…]". All other posts refer directly to the pandemic event or the COVID-19 disease itself.

Seven of the 37 posts led to discussion in the comments. Three of the 37 posts received a majority of positive responses in the comments, whereas the remaining 27 posts received exclusively positive responses. Here, a correlation with the date of the posts is less apparent than a correlation with the category. All posts that led to discussions with different opinions in the comments were assigned to the category Information. The exception was the CHUV's appeal for donations, which promoted the aid fund for employees in need and also led to discussions in the comments. Examples of posts with more pro/contra discussions than others in the comments:

Example 1. CHUV, Facebook https://www.facebook.com/975855452425631/posts/3472148106129674: Link to the newly launched Web site of the CHUV with correct information (vs misinformation). This resulted in a discussion regarding ibuprofen during corona. The post was assigned to the category Information.

Example 2: CHUV, Facebook https://www.facebook.com/975855452425631/posts/3586503361360814: Interview with Dr. Sandra Asne (paediatric infectiologist) on the topic of children and corona. The post was assigned to the Information category and led to discussions regarding whether children were drivers or not of the pandemic.

Posts in the appreciation category received a particularly large number of positive comments. This category included posts in which the hospital or clinic thanked its employees for their extra effort during the pandemic. These were particularly frequently recorded with 'thumbs up', 'likes' and hearts in the comments.

Example 1. Stadtspital Zürich, Facebook https://www.facebook.com/watch/?v=224939602208563: video of the people clapping as a thank you to the healthcare workers.

Example 2. HUG, Instagram https://www.instagram.com/p/B-g_WyEH0P8/

The HUG would like to thank the employees in the transport and magazine departments for the extra work they did during the pandemic.

The four posts in the solidarity category also received only positive comments, as the example of the Hôpital de Valais shows.

Example Hôpital du Valais, Facebook https://www.facebook.com/150564764978991/posts/2877908865577887.

On behalf of the staff, the hospital would like to thank the population for a banner that says 'thank you' to the hospital's healthcare staff. The banner was apparently created by someone from the public.

HUG and CHUV with most viral posts

Within the 37 viral posts, two hospitals stand out: HUG with 17 posts and CHUV with 8. Other hospitals were represented significantly less frequently such as USZ,[4] Kantonsspital Winterthur[2] and 4 hospitals with one viral post each (Hirslanden, Hôpital du Valais, Stadtspital Zürich, Kantonsspital Graubünden and Ente Ospedaliero Cantonale (EOC)). The other 18 hospitals did not manage to post anything with significant resonance.

At both HUG and CHUV, the category of most viral posts showed a certain regularity of information. For example, CHUV made regular posts with medical information on the pandemic and on COVID-19 with interviews with professionals. HUG's most viral posts were all from the appreciation category. These posts followed the same structure, similar types of pictures and length of text.

Discussion

RQ1: How did different Swiss hospitals use social media during the important first phase of the corona pandemic?

As the study shows, Swiss hospitals used social media very differently during the first phase of the pandemic. This is shown by the total number of posts during the study period (see Table 1) and the different use of the various social media platforms (see Fig. 1).

Larger hospitals or hospital groups in particular had considerably more posts. This is probably because of the resources of the communication departments but cannot be confirmed by this study and requires further investigation.

It is not surprising that much less was published on YouTube because it always requires video production, which means a certain amount of effort. The frequent use of the versatile, established and widespread platform Facebook can also be explained. As in Switzerland, in particular, journalists and politicians can be reached via Twitter in addition to private individuals, the use here is also obvious. However, it is surprising that the very interactive and easy-to-use platform Instagram was used so little. Especially because Facebook and Twitter are integrated into the publication process via Instagram. It is particularly noticeable that university hospitals published much more on Twitter than on the other platforms, whereas regional hospitals relied mainly on Facebook. This could be because of usage habits or differently defined target groups. This also needs to be investigated further.

Commonalities can be found at the time of publication (see Fig. 4). All hospitals posted a lot, especially in the first month. At the end of the study period, just 4 months after the start of the pandemic, the number of weekly posts fell back almost to the normal level before the pandemic occurred. Hospitals thus saw a need to use social media much more than usual, especially in the first month.

RQ2: Were hospitals able to achieve mobilisation of the public, indicated by the resonance of their posts as a proxy for user engagement?

As the majority of posts generated only a very low response with a median of 2 (mean of 107.0), the answer to the second research question must unfortunately be negated. Looking at the average of response and post (Table 1) also confirms this picture.

If we look at the type of user reactions for the most viral posts using the example of Facebook (Fig. 4), it is noticeable that apart from the simplest and minimally active form, the like, the posts were mainly shared. Very few comments were made regularly. This shows that for the community, the focus was less on dialogue and more on disseminating the content.

It is interesting to note that of the nine hospitals that had the most viral posts all except two are also in the top 10 by number of posts as per Table 1. Hospitals that published a lot have thus also been able to build up a very active community. Exceptions are the Kantonsspital Graubünden (24 posts) and the Kantonsspital Winterthur (23 posts), which published a below average number of posts, but were able to trigger a high user response with individual posts that turned viral.

RQ3: Which content of Swiss hospitals' posts achieved the most resonance with the public?

Posts that were published as expressions of appreciation towards employees received a particularly high response. So-called hard facts, such as medical information about the pandemic, practical rules of conduct for the population or even organisational information such as opening hours and examination locations, did not meet with a high response and thus did not receive much visibility on social media.

The posts that received a lot of engagement by the users were mostly found in the category of 'appreciation of work'. The comments were practically exclusively positive comments, short videos with clapping hands and heart symbols.

Only a small number of posts led to discussion in the comments. All these posts were from the category 'information' and included information on the nature of the illness, the vaccination and COVID-19 in children. It is surprising how rarely users engaged in discussions on the social media platforms of hospitals in Switzerland during the study period.

This study shows the lack of engagement in most hospitals' posts generated in the early month of the pandemic crisis in Switzerland. Our study was not designed to identify the causes of this lack of response. Nevertheless, certain statements can be made about the relationship between volume and resonance. First, hospitals, especially HUG, that posted more than average also tended to achieve a higher response. Furthermore, posts that were dedicated to the category of 'appreciation' achieved more resonance. It could be that hospitals with fewer followers before the pandemic also received less response for their posts during the pandemic. However, this would be a circumstance for another, more detailed study.

Author statements

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Original Research

Socio-economic inequality and healthcare costs over the life course — A dynamic microsimulation approach

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ABSTRACT

Objectives: Although there is well-established evidence for the existence of socio-economic inequalities in virtually all dimensions of health, little is known about the implications of these socio-economic disparities for healthcare costs from a cumulative life course perspective. Accounting for differentials in healthcare use patterns and mortality, we assess how lifetime costs differ between socio-economic groups.

Study design: This study used dynamic microsimulation modelling.

Methods: Combining price weights for healthcare services with information on healthcare consumption from the 2014 Austrian Health Interview Survey (n = 15,771), we calculated average cost profiles by gender, age and education consistent with aggregate System of Health Accounts. A dynamic microsimulation model was used to project cumulative healthcare costs over the entire lifecycle for the 2019 birth cohort in four different scenarios to illustrate the influence of the different cost determinants on lifetime costs.

Results: Before considering social inequalities in mortality, men with compulsory education have close to 66% higher lifetime costs than men with tertiary education; for women, the difference is close to 20%. Accounting for longevity differentials reduces this gap to approximately 40% for men and 10% for women. Closing the gap in healthcare use and in longevity between socio-economic groups would reduce lifetime healthcare expenditure by 4.1% in the 2019 birth cohort and by 19% in the whole population.

Conclusions: Accounting for mortality differentials between socio-economic groups has a large impact on estimated lifetime healthcare costs. Reducing social inequalities in health can contribute to containing healthcare expenditures against the backdrop of rising life expectancy.

Introduction

There is well-established evidence for the existence of socio-economic inequalities in virtually all dimensions of health.[1–3] Little is known about the implications of these socio-economic disparities for healthcare costs, especially from a cumulative life course perspective. Differences in health status by socio-economic group do not necessarily translate into corresponding differences in lifetime healthcare costs for two reasons. First, socio-economic status impacts access to and use of healthcare services, with substantial variation by country and type of service.[4–7] Second, pronounced socio-economic inequalities in life expectancy affect the lifetime use of the healthcare system and the resulting cumulative costs.

A marked social gradient has been observed concerning specialist doctor visits (particularly dentists) and the utilisation of preventive services.[1,4,8,9] In contrast, in most industrialised countries, needs-adjusted social inequalities are much lower for general practitioner (GP) visits and not significant for hospitalisations. Available studies indicate that socio-economic inequalities in health status translate into higher healthcare costs for more vulnerable social groups, at least within health systems that provide universal or nearly universal publicly financed coverage for health services. A recent analysis for the Netherlands shows that total healthcare expenditure for people with lower socio-economic status is between 50% and 150% higher than for people with high socio-economic status, depending on the age group.[10] These results

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are consistent with results from other studies for England, Sweden and Canada.[11–14]

These studies, however, analyse healthcare costs at specific points in time and may thus overstate the extent to which more vulnerable socio-economic groups use the health system over their lifetime. From a life course perspective, the lower life expectancy of these groups tends to offset the higher costs associated with their lower health status. In contrast, earlier onset of diseases and chronic conditions may shift the healthcare costs to younger ages. The extent to which these differential effects impact the social gradient in lifetime health costs must ultimately be determined empirically. This question is of interest to improve our understanding of the distributional effects associated with the healthcare system and gain a fuller picture of economic costs resulting from social inequalities in health.

There is very limited evidence on the link between socio-economic inequality and healthcare costs over the life course. Asaria et al.[15] investigate lifetime hospital costs by level of neighbourhood deprivation in England. Combining data on hospital admissions by age, sex and place of residence with average costs and data on survival, they find that people living in the most affluent areas had lower lifetime hospital costs than those living in more deprived areas. This pattern was more pronounced for women than men and emergency admissions than elective admissions.

We examine lifetime healthcare costs by socio-economic status in Austria using a novel approach that combines survey data and aggregate information from register data to model the healthcare costs with a dynamic microsimulation model. This approach allows us to provide estimates that are consistent with the System of Health Accounts (SHA)[16] for aggregate health costs and with official demographic projections while isolating the effects resulting from different cost determinants, most notably age-related healthcare use patterns, socio-economic differences in mortality and increases in life expectancy. In Austria, health insurance coverage is nearly universal (99.9% in 2018), granting access to a wide range of services and ensuring a comparatively low level of unmet medical needs.[17,18]

We approximate socio-economic status with the educational level, which has a particularly strong correlation with health and is also associated with large differences in mortality.[19,20] On average, across Organisation for Economic Co-operation and Development (OECD) countries, people without a high-school diploma have a life expectancy 6 years shorter than those with tertiary education; the difference is more pronounced for men than for women.[7,18]

Methods

Data on healthcare consumption and healthcare costs

Information on the use of healthcare services was gathered using microdata from the Austrian Health Survey (ATHIS) for 2014. This representative population survey, covering all age groups (N = 15,771), documents the number of inpatient hospital stays (except for stays related to childbirth), daycare stays, as well as the number of visits to GPs and specialist doctors (including hospital outpatient visits). Respondents' educational attainment is coded according to the International Standard Classification of Education (ISCED).

Statistics Austria provides official statistics for aggregate healthcare spending in 2014 by gender and 5-year age groups. These data follow the SHA classification covering the healthcare functions HC.1 to HC.5, representing total healthcare costs for services and goods excluding investments. Our analysis focused on inpatient, outpatient and daycare services. Among these categories, inpatient services are the largest cost item (61%), followed by outpatient services (37%) and daycare services (<2%). Together these services account for 90% of personal healthcare service costs and 71% of total expenditure according to SHA healthcare functions HC.1 to HC.5. In Austria, close to 90% of costs for hospital care and almost 80% of outpatient medical care are covered by government and compulsory insurance schemes.[7] Because hospital stays related to childbirth are not covered by the ATHIS survey, we detract the aggregate childbirth inpatient costs from the healthcare spending data of women in the corresponding age groups. We calculated average healthcare costs by gender and age group using population data.

Based on the information provided by the Austrian Ministry for Work, Social Affairs, Health and Consumer Protection and by the Austrian National Public Health Institute, we determined price weights for the different healthcare service categories under scrutiny. Inpatient hospitalisations have by far the highest average unit cost (856 Euro per day) and are the most important determining factor in cost estimation. GP and specialist doctor visits were assigned a price weight of 57 Euro and 76 Euro, respectively. For daycare, which is not used very often and for which no price reference was available, we assumed a unit cost of 600 Euro.

Estimation of cost profiles

In the first step, we analysed the use of healthcare services with the ATHIS data, calculating how the consumption of doctor and hospital visits is distributed by gender, age and education. We distinguished three levels of education: low (at most compulsory schooling, ISCED 0–2), medium (lower and upper secondary education and apprenticeship, ISCED 3–4) and high (tertiary education, ISCED 5+). The disaggregation by education level was limited to ages 20–85 years: For the under-20-year-olds, a differentiation according to education categories is not meaningful. For ages >85 years, differentiation by education level would be problematic because of the low number of observations in some groups, particularly women with higher education. Although this is a limitation, previous findings indicate that socio-economic differences in health tend to decrease at higher ages.[21–23] Thus, for individuals aged < 20 years and those aged >85 years, healthcare utilisation was assumed to be independent of educational attainment.

In the second step, we used the healthcare price weights to determine individual healthcare costs. To ensure correspondence to the average SHA expenditure profiles by gender and age group, we calibrated the average healthcare costs by gender, age group and education.

Microsimulation of costs over the life course

To calculate healthcare expenditure over the entire lifecycle, we used the dynamic microsimulation model microWELT.[24] Based on European Union Statistics on Income and Living Conditions data, microWELT provides a representative cross-section of the Austrian population regarding gender, age and education structure in the baseline year. The model consists of several interconnected family demographic, health and socio-economic modules and models the further development of the Austrian population.

Following Asaria et al.,[15] we assumed that the healthcare cost profiles by gender, age and education remain constant. We estimated cumulative lifetime costs by combining these profiles with mortality information for different socio-economic groups. Each individual in the microWELT population was attributed the average healthcare costs according to gender, age and education. To apply gender- and education-specific survival probabilities for each age, we combined data on remaining life expectancy by education for 25- and 65-year-olds[25] with the actuarial life tables.[26] The model

reflects population projections by Statistics Austria by reproducing changing age-specific mortality rates and accounts for the overall increase in life expectancy. Relative differences in mortality between education groups were kept constant throughout the simulation.

Our approach allowed for calculating yearly healthcare costs for the total population consistent with SHA aggregates and determining lifetime costs for a specific population cohort. We focused on the cohort of newborns in 2019, summing the costs over ages to obtain the cumulative lifetime costs by gender and education group. Exploiting the flexibility of our model, we separated and quantified the effects that different assumptions, such as changes in life expectancy, have on cumulative lifetime costs. The analyses were performed using the open-source software R (version 4.2.2) and the open-source dynamic microsimulation programming technology Modgen.[27] All codes and the model can be downloaded from the project website www.microWELT.eu.

Results

Healthcare cost profiles by gender, age and education

Fig. 1 shows the cost profiles for men and women by age and education. While the cost profiles increase significantly with age, the costs of persons with higher education tend to be lower than those of the other education groups at all ages. While women show larger differences by education above 40, men display larger differences in younger groups. According to the calculations provided by Statistics Austria, there is a large gap in absolute expenditure levels by gender in the highest age group, with women aged ≥90 years reporting, on average, 57% higher costs than men. This large gap can be traced back primarily to inpatient services, where average expenditures are approximately 17,000 Euro for women but only close to 11,000 Euro for men. This sizeable difference can probably be explained by hospitalisations connected to long-term care needs, which affect women more than men.

Assuming constant age-specific mortality and unchanged relative differences in mortality between education groups, the life expectancy of men born in 2019 ranges from 76 years (low education) to 83 years (higher education). In contrast, women show smaller education-specific differences, with life expectancy varying between 83 years (low education) and 86 years (higher education). Fig. 2 shows the corresponding survival curves. A steeper educational gradient in mortality for men than for women has been documented in previous studies for European countries as well as for the United States.[28,29] The causes for this gender difference, however, are not yet fully understood and might include, *inter alia*, behavioural factors and differences in the distribution across hazardous workplaces by gender and education.

When considering forecasts of increasing life expectancy, the average life expectancy of those born in 2019 ranges between 85 and 93 years, depending on education and gender (see Figure A1 in Appendix 1).

Healthcare cohort cost profiles

The microsimulation projection combines data on survival and healthcare costs by gender, age and education. Fig. 3 displays the age-specific costs for the 2019 birth cohort with constant age-specific mortality. The data reflect average expenditure levels per cohort member, that is, costs at each age applied to the share of individuals of the birth cohort still alive. For both genders, at older ages, the combination of different survival probabilities and age-specific costs leads to decreasing average costs in all three education groups.

Socio-economic differences in mortality lead to a reversal of the cost ratios between education groups along the age dimension. Those with lower education have higher average health costs at younger ages but lower costs at older ages. The pattern is less pronounced for women, where expected healthcare expenditures for those with lower education are slightly higher than for the other

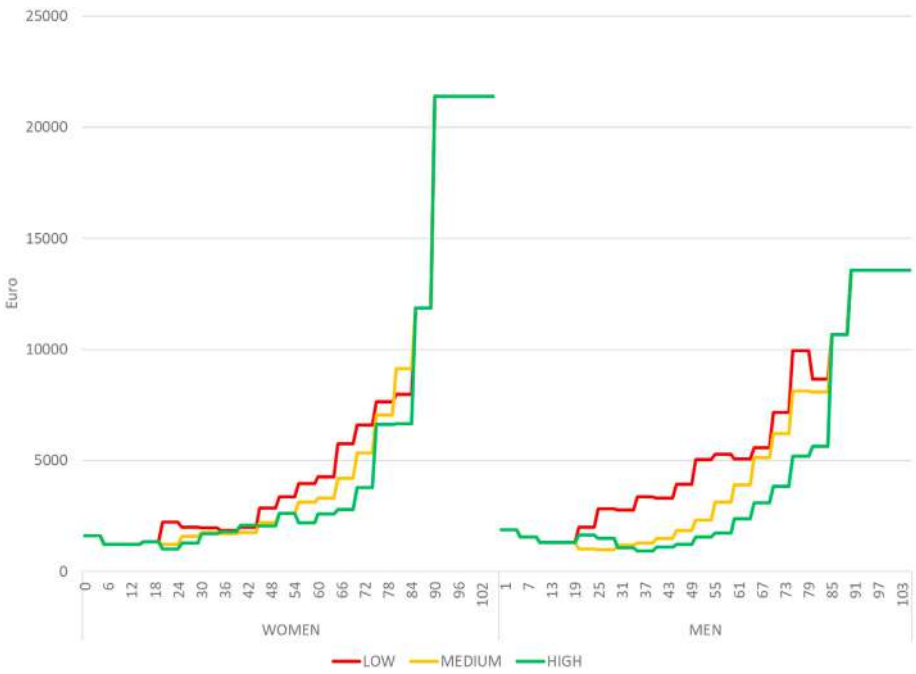

Fig. 1. Age profile of public health expenditures by gender and education. On average, the expenditure levels correspond to official statistics for public healthcare spending in 2014 covering inpatient, outpatient and daycare services, provided by Statistics Austria by gender and age (in 5-year groups) following the System of Health Accounts (SHA) classification. 2019 prices.

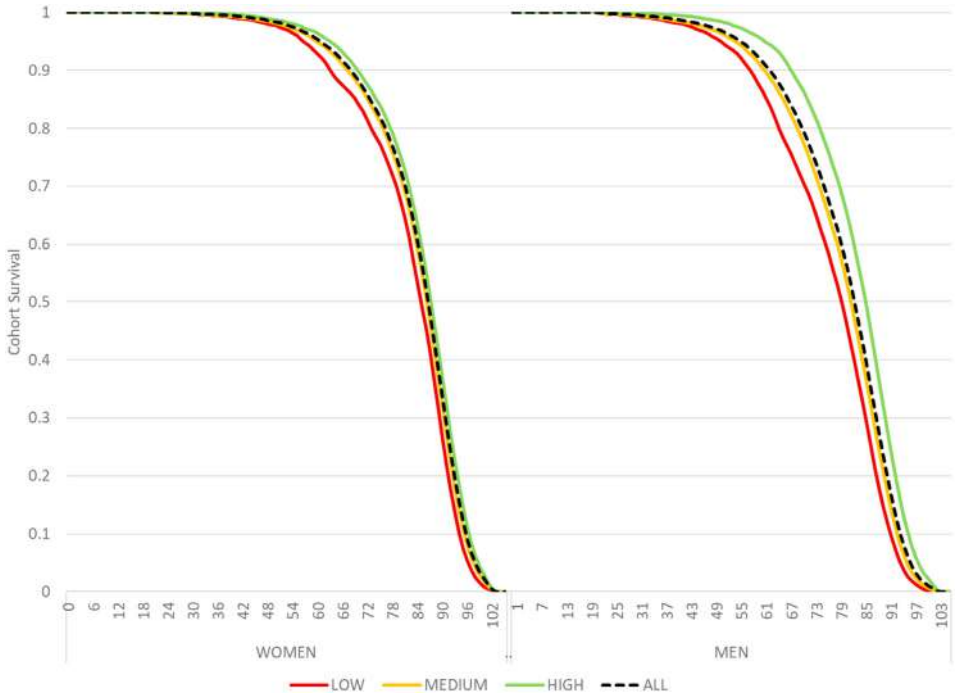

Fig. 2. Survival curves without mortality improvements. Survival curves for the 2019 birth cohort based on remaining life expectancy by education for 25- and 65-year-olds by Murtin et al. and actuarial life tables provided by Statistics Austria (2019), assuming constant age-specific mortality.

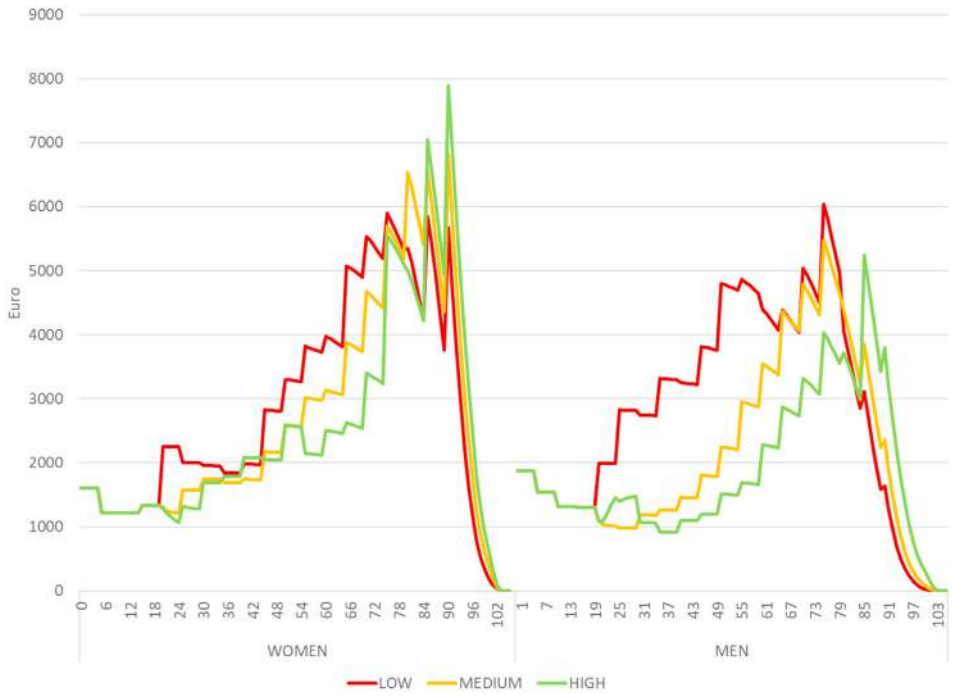

Fig. 3. Cohort profile of healthcare expenditures. Microsimulation results for the 2019 birth cohort combining healthcare costs by gender, age and education (Fig. 1) and survival curves by gender and education (Fig. 2). The data reflect average expenditure levels per member of the birth cohort, assuming constant age-specific mortality. 2019 prices.

education groups up to age 75 years. For men, those with low education have significantly higher expenditure levels between the ages of 20 and 65 years. After that point, higher mortality in the lower education group leads costs first to converge to the level of those with medium education and then to fall significantly below the level for men with high education.

Figure A2 in Appendix 1 shows the results for the cohort cost profiles taking into account increasing life expectancy to reflect population projections. The cost curves shift to the right, with higher expenditures at older ages. The increase in healthcare costs is particularly strong for men aged >70 years and women aged >80 years.

Life course healthcare costs by gender and education

Total healthcare costs over the life course by gender and education result from the sum of the age-specific per-capita values in Fig. 3. To illustrate the influence of the different cost determinants, Table 1 presents the results in four steps. The first column shows what the healthcare costs of the cohort born in 2019 would be if life expectancy remained unchanged and if there were no differences in life expectancy by education group. In this scenario, the lifetime costs of men with lower education are >80% higher than those with high education, and for women, the difference amounts to 25%. The second column displays the results for constant life expectancy but considers education-specific differences in mortality. Here, the differences in costs across education groups are reduced to approximately 50% for men and 13% for women.

The third and fourth columns present the results of scenarios where increasing life expectancy, consistent with the official population projections, is considered. The third column displays calculations neglecting differences in education-specific mortality, whereas the fourth column incorporates the social gradient in life expectancy. In both cases, lifetime healthcare costs rise by nearly 40% for women and approximately 35% for men. Differences between education groups are smaller than in the first two scenarios, where life expectancy was kept constant. Higher life expectancy increases lifetime healthcare costs for all groups, thus reducing the relative impact of socio-economic differences. Without education-specific differences in mortality, the healthcare costs of people with low educational attainment are close to 66% higher for men and 20% higher for women with high education. Including education-specific life expectancy in the model narrows the differences to 40% and 10%, respectively. Shorter life expectancy accounts for a reduction in lifetime costs of the lower education group by approximately 8% for men and 6% for women. On the other hand, lower mortality leads to an increase in the estimated lifetime healthcare costs of the higher education group by about 8% for men and 3% for women.

Whether we consider increasing life expectancy or not, considering the social gradient in mortality reduces the expenditure gap across education groups by approximately 40% for men and almost 50% for women.

Discussion

Main findings

In line with previous research, our estimates indicate that in a longitudinal perspective, lower life expectancy reduces but does not outweigh the higher average healthcare costs that we observe for vulnerable socio-economic groups from a cross-sectional perspective.[15] Using education as an indicator of socio-economic status, we find that inequalities in healthcare expenditure are larger for men than for women. Before accounting for the social gradient in mortality, the lifetime costs of men and women with compulsory education are about two-thirds and one-fifth higher, respectively, than those of men and women with tertiary education. Taking education-specific differences in mortality into account, which are more pronounced for men than for women, this difference is reduced to approximately 40% for men and 10% for women. These values refer to projections for the cohort born in 2019 and include an increase in life expectancy consistent with population projections.

If the population groups with lower and medium education had the sex- and age-specific healthcare costs associated with those with higher education, the total healthcare expenditure for the 2019 birth cohort would be approximately 4.1% lower. This difference can be interpreted as the low long-term benchmark for the costs associated with socio-economic inequalities in health, as the 2019 cohort – with a projected share of 38% with high and below 10% with low education – has a far more favourable educational composition than the current population. In contrast, current health expenditures would be 19% lower if the average age-specific costs of the high education group would apply to the whole population. While out of the scope of this article, our microsimulation approach is specifically powerful in projecting the evolution of period costs under various scenarios.

Strengths and limitations

Our study contributes to filling the research gap concerning the link between socio-economic inequality and healthcare system use from a life course perspective. The results provide an interesting benchmark for other countries with a comprehensive public healthcare system. Using a dynamic microsimulation model in this context is novel and has several advantages. It produces results that are consistent with aggregate SHA statistics as well as with the official population projections. Covering different healthcare services, we can account for a large share of expenditures in the healthcare system. The method allows isolating effects resulting from different cost determinants, most notably age-related healthcare use patterns, socio-economic differences in life expectancy and increasing life expectancy.

These strengths notwithstanding our study are subject to several limitations, which will have to be addressed in future research. First, for our cohort analysis and lifetime projections, we

Table 1
Lifetime healthcare costs by gender and education.

Gender and education		Constant age-specific mortality; no differential mortality by education	Constant age-specific mortality; differential mortality by education	Decreasing mortality; no differential mortality by education	Decreasing mortality; differential mortality by education
		In Euro per person (in 2019 prices)			
Female	Low	318,375	298,010	430,535	406,092
	Medium	284,084	279,038	395,095	389,068
	High	253,602	262,478	359,492	369,443
	All	274,462	273,710	383,368	382,532
Male	Low	324,712	295,842	414,295	379,937
	Medium	232,284	224,706	312,595	304,810
	High	176,683	197,951	249,856	270,006
	All	222,703	222,054	301,514	300,261
Total	Low	321,835	296,795	421,493	391,138
	Medium	256,173	249,702	350,629	343,823
	High	220,778	235,095	312,762	327,050
	All	248,455	247,702	342,211	341,152

Total healthcare costs over the life course by gender and education resulting from the sum of the age-specific per-capita values in Fig. 3. Costs based on 2014 SHA figures by Statistics Austria.

had to rely on the simplifying assumption that the age profiles of healthcare costs remain constant and can be used for cohort analysis. Second, we did not control for needs-adjusted inequalities in healthcare use. If disadvantaged social groups face barriers in accessing the healthcare system or are less likely than more advantaged groups to seek healthcare services when they need them, our results (that are based on data for actual use) might underestimate the impact of socio-economic health differences. Available studies indicate that socio-economic inequalities in healthcare use in Austria are pronounced concerning specialist doctor visits, but that hospital stays (which account for the largest share of health costs) and GP visits are equitably distributed.[4,30] Third, we did not account for end-of-life healthcare costs. A study for England shows that end-of-life healthcare costs are higher among patients with lower socio-economic status, even after being controlled for patient-level characteristics.[31] In this respect, too, our projections may underestimate social inequalities in using the health system. Finally, in our study, we use educational attainment to approximate socio-economic status without investigating the mechanisms that determine the relationship between education, health and mortality. As highlighted by the gender difference that we observe in the educational mortality gradient, educational attainment may be operating differently across population subgroups to influence health and mortality.[32] To gain a more comprehensive picture of the impact that socio-economic inequalities have on lifetime healthcare costs, more studies using different indicators for socio-economic status will be needed.

Author statements

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Ethical approval

No ethical approval was applicable. This study did not involve human participants or animal subjects. The manuscript does not contain personal and/or medical information about an identifiable individual and/or a case report/case history.

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Competing interests

None declared.

Data availability

Microdata used for this research cannot be made available because of legal restrictions: Microdata from the Austrian Health Survey (ATHIS) and the European Union Statistics on Income and Living Conditions (EU-SILC) can be requested free of charge from Statistics Austria for scientific analysis by members of a university or a relevant scientific institution (email: forschungundlehre@statistik.gv.at). Users are not allowed to pass on the data to third parties. (http://www.statistik.at/web_de/services/mikrodaten_fuer_forschung_und_lehre/datenzugang/antrag_fuer_sds/index.html). All codes and the model can be downloaded from https://www.microwelt.eu/Model/Model-Index.html.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.04.001.

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Review Paper

The relationship between parental adverse childhood experiences and the health, well-being and development outcomes of their children: a systematic review

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ABSTRACT

Objectives: A growing body of research is emerging regarding the relationship between parental adverse childhood experiences (ACEs) and negative health, well-being and developmental outcomes in their children. This systematic review seeks to understand the relationship between parental ACEs and the health, well-being and developmental outcomes of their children and whether the relationships differ according to the number and type of parental ACEs.
Study design: Systematic review.
Method: The review includes articles published between 2000 and 2021 from studies using quantitative longitudinal methods and multivariate analysis to investigate the relationship between parental ACEs and their offspring's outcomes. Relevant studies were identified through a systematic search of five databases and findings synthesised using a narrative synthesis. This review was registered on PROSPERO (CRD42021274068).
Results: Nineteen studies met the inclusion criteria and were included in the review. This resulted in a combined population sample of 124,043 parents and 128,400 children. Diversity in measurement of parental ACE exposure and in the type of ACEs measured within the studies precluded a meta-analysis. Offspring of parents exposed to ACEs had a higher risk of a range of negative health, well-being and developmental outcomes. This relationship differs according to the number and type of parental ACEs, with a positive relationship observed between the number of parental ACEs and the risk of negative health, well-being and development outcomes in their children.
Conclusions: These findings indicate that screening for parental ACEs by health visitors, midwives and other health or social care staff may identify an at-risk population of infants, children and adolescents and improve child outcomes.

Introduction

Adverse childhood experiences (ACEs) are defined as harmful or distressing childhood events, which occur in a child's family or social environment before the age of 18 years.[1,2] It is well recognised that ACEs have a negative long-term impact on health outcomes and behaviours for the individual.[1,3–7] Less is known about the intergenerational effect of parental ACEs exposure. Whilst there is evidence that parental ACEs have a negative impact on their children's health, development and well-being, no systematic review on this topic has yet been conducted.

Reported prevalence of ACEs varies, but approximately one-fourth of people report exposure to one to three ACEs, and around 10% report four or more.[8] Prevalence varies according to classification. The most widely used classification of ACEs is from the original ACE study by Felitti et al.[9] and comprised 10 ACEs, categorised into abuse, neglect and household challenges (Table 1). More recently, literature[10–13] has argued for the need to expand on the original ACE classification to include additional and more contextual measures such as community violence, peer

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Table 1
The original list of 10 ACEs.[9]

Main categories of ACEs	Subcategories of ACEs
Abuse	Physical abuse
	Sexual abuse
	Emotional abuse
Neglect	Physical neglect
	Emotional neglect
Household challenges	Parental substance abuse, *including drugs, alcohol and smoking*
	Domestic violence
	Parental separation/divorce
	Parental mental health difficulties
	Parental imprisonment

ACEs, adverse childhood experiences.

victimisation, low socio-economic status and separation from migrant parents. ACE classifications are fluid and likely to change further in the future as research adds to our knowledge of ACEs.

For the individual, ACEs have a negative long-term impact on health outcomes and behaviours. ACEs have been associated with alcoholism, drug use, smoking-related diseases, coronary heart disease and obesity in adulthood.[1,3–6,9,14,15] It is also known that the more ACEs an individual faces during childhood, the greater the likelihood of negative outcomes.[4,6,7,9,16,17]

ACEs affecting a parent may also have consequences for their children. A number of articles have suggested that parental ACEs have a negative impact on their children's health, development and well-being.[2,17,18] Several mechanisms have been proposed, including an increased risk of maternal depression in those with ACEs, which in turn is associated with impaired parenting behavioural mechanisms,[2,19–21] and an increased risk of prenatal exposure to alcohol or other substances, affecting the healthy development of offspring;[21–24] impaired maternal-infant dyadic functioning[25] or through altered gene expression (epigenetics).[26–28] Other studies suggest that the impacts of parental ACEs on the outcomes of their offspring are sensitive to the type and timing of ACE exposure.[24,26,29,30]

A multigenerational approach to improve child health outcomes would address both the prevalence of ACEs and the impact of parental ACEs on their children. Antenatal or early childhood screening for parental ACEs may identify children at risk and better target supportive interventions and community health service provision.

This systematic review, to the best of our knowledge, is the first to synthesise evidence from quantitative longitudinal studies to address two questions.

1. What is the relationship between parental ACEs and the health, well-being and developmental outcomes of their children (up to the age of 18 years)?
2. Does this relationship differ according to the number and type of parental ACEs?

The review focused on the 10 original ACEs (Table 1). This is because this review is looking at previous publications, the vast majority of which use this widely accepted classification.

Methods

We conducted this review in accordance with the 'Preferred Reporting in Systematic Reviews and Meta-Analysis' (PRISMA) guidelines[31,32] and used narrative synthesis.[33] This review was registered on the PROSPERO database (registration number: CRD42021274068).[31,32]

Eligibility criteria

Inclusion and exclusion criteria are detailed in Table 2. There was no language exclusion, but the review was restricted to quantitative longitudinal studies to provide understanding regarding the strength, direction and size of relationships and to papers using multivariate analysis in which maternal age, parental education and other variables affecting child outcomes were controlled for.

Search strategy

Seven broad categories of outcomes were selected for investigation following a scoping search of over 50,000 papers. Database search terms were constructed around these concepts and combined with the Boolean operator 'AND'. The search strategy was tested in MEDLINE and then expanded to CINAHL, PsycINFO, SocINDEX and Academic Search Ultimate. Databases were searched up to 31 January 2022. The search strategy in all databases was limited to studies published between 2000 and 2022. The bibliography and reference lists of all relevant studies were searched for additional relevant studies. The MEDLINE search strategy is presented in Appendix 1.

Selection process

Screening consisted of title, abstract and full-text screening. Two reviewers (R.A. and F.A.) screened half of the study titles

Table 2
Criteria for inclusion or exclusion of studies.

Criteria	Inclusion criteria	Exclusion criteria
Focus	Papers focussing on the impact of parental ACEs on offspring's development, health and socio-economic outcomes	Papers focussing on the impact of ACEs on the individual's own subsequent health, well-being and development outcomes
Exposure of interest	Papers that have explored the impact of having at least one parent who has experienced at least one ACE, on offspring's outcomes	NA
Methodology	Quantitative design Longitudinal design Multivariate analyses	• Qualitative design • Cross-sectional • Descriptive/bivariate analyses only
Date	Publication date of 2000–2022	Publication date of earlier than 2000
Setting	Global literature	N/A
Type of publication	Academic peer-reviewed published articles describing primary research	• Publications that are not peer-reviewed • Reviews • Editorials • Letters • PhD theses

ACE, adverse childhood experience; N/A, not available.

independently identifying studies as relevant, irrelevant or 'unsure' based on the title indicating the study examined the impact of parental ACEs on offspring's outcomes, or not. The 'unsure' category was then rescreened into either the relevant or irrelevant group. Both reviewers independently reviewed the abstracts of studies identified as relevant from the title screening process and determined their relevance. The full text of all potentially relevant studies was screened by R.A. against the inclusion and exclusion criteria (Table 2). Where relevancy was unclear, the second reviewer was consulted.

Data collection process

R.A. independently extracted data using the JBI Manual for Evidence Synthesis guidance.[34] Data relevant to the study characteristics (author, year, journal and aim), study design, subject characteristics, exposure, outcome and independent variables, and key findings were extracted into a Microsoft Excel Spreadsheet.[35]

Critical appraisal

Quality of individual studies was assessed using the Critical Appraisal Skills Programme (CASP) checklist for cohort studies,[36] where a study's maximum score was 24. Although there is no agreed way of summarising the scores for the CASP tool, we followed Njau et al.[37] (where a total score of $\geq$20 = high quality; 16–19 = moderate quality; $\leq$15 low quality) and reviewed each of the individual quality items to support the analysis and data synthesis process. Quality was screened by R.A. and double screened by P.H. and F.A. Appendix 5 provides CASP critical appraisal of included studies.

Data synthesis

Meta-analysis was precluded because of methodological diversity within the studies, including diversity in the range of outcomes reported, the age at which the outcomes were assessed, and the type of ACEs studied. A narrative synthesis was conducted using the Cochrane's guidance on narrative synthesis.[33] First, included studies were grouped and analysed by outcome category measure, exploring findings related to review question 1. Outcome categories were defined by reviewer 1 to ensure replicability.

- Cognitive development was defined as the development of knowledge, skills, problem-solving, perception and language.[38]
- Childhood growth outcomes related to the growth of the offspring, such as preterm delivery and low birth weight.
- Emotional development was defined as how children notice, express and manage emotions.[39]
- Risk-taking behaviour outcomes were defined as any conscious or unconscious actions where there is uncertainty surrounding the outcome, such as smoking, drug use and risky sexual behaviour.[40]
- Receipt of child protection support/social work intervention was defined as measures and structures put in place to prevent and respond to child abuse, neglect, exploitation and violence.[41]
- The definitions of physical and mental health outcomes and educational attainment were determined to be implicit, including illnesses, such as obesity, depression and anxiety,[42] and outcomes relating to children's learning.

Next, studies that investigated associations specific to the number or type of ACEs were grouped to answer the second review question. Studies were sorted according to whether they were investigating how the number and/or the type of ACEs impacts the relationship between parental ACE and offspring health, well-being and developmental outcomes. Findings were compared within the subgroups, but when making comparisons, reviewer 1 considered the ACE measure used and outcomes explored.

Results

Characteristics of included studies

An overview of the characteristics of included studies can be viewed in Table 3. A more detailed description can be seen in Appendix 2.

Setting

The 21 studies included in this review were published between 2007 and 2022 (see Fig. 1) and scored high quality on the CASP (Appendix 2 and Appendix 5). Most (n = 14) were conducted in the United States.[17,43–55] Three studies were conducted in the United Kingdom[56–58] and in Canada[59–61] and one (5.3%) study was conducted in Norway.[62] None were conducted in low- or middle-income countries.

Table 3
Overview of included studies.

Study Characteristics	Studies (n)	Studies %
ACE measured		
Sexual abuse	20	95.2
Physical abuse	19	90.5
Emotional abuse	13	61.9
Physical neglect	10	47.6
Emotional neglect	10	47.6
Parental separation/divorce	9	42.9
Domestic violence	9	42.9
Parental substance abuse	8	38.1
Parental mental health difficulties	8	38.1
Parental imprisonment	6	28.6
Scales to measure ACEs		
Original ACE Questionnaire	8	38.1
Childhood Trauma Questionnaire	5	23.8
Traumatic Life Events Questionnaire	3	14.3
Unvalidated measure	2	9.5
NorVold Abuse Questionnaire	1	4.8
Trauma History Questionnaire	1	4.8
Prospective measure	1	4.8
Country study was conducted in		
USA	14	66.7
UK	3	14.3
Canada	3	14.3
Norway	1	4.8
Outcome category investigated		
Emotional development	10	47.6
Physical/mental health	6	28.6
Cognitive development	3	14.3
Risk-taking behaviours	2	9.5
Childhood growth	2	9.5
Educational attainment	1	4.8
Receipt of child protection support	0	0.0
Setting		
Large diverse population	8	38.1
Urban	8	38.1
Other/unspecified	4	19
Low income	2	14.3
Critical Appraisal Skills Programme (CASP) overall rating		
High quality	20	95
Moderate quality	1	5
Low quality	0	0

ACE, adverse childhood experience

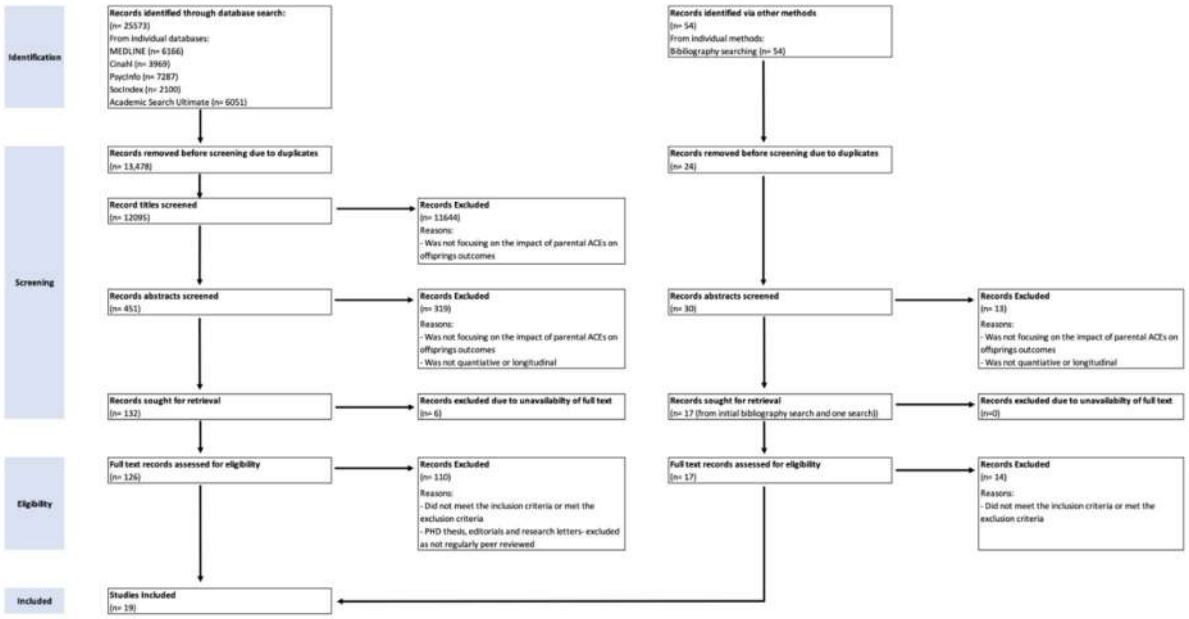

Fig. 1. PRISMA flow diagram of ACE review. Adapted from: Page et al.[31]; Page et al.(B).[32]

Participants

Most studies (n = 18) included mother-infant dyads exclusively, with only three studies also including father-infant dyads.[17,46,59] Age of the offspring when outcomes were investigated ranged from birth[44,48–50] to 18 years of age.[59] Prevalence in the parent population of exposure to at least one type of ACE during childhood ranged from 17.1%[57] to 68.2%.[59]

Study design

All studies, apart from Noll et al.,[50] collected ACE exposure data retrospectively using questionnaires, most commonly using the Original ACE Questionnaire[15,17,44,46,47,51,59–61,63] and the Childhood Trauma Questionnaire.[48,49,52,53,56,64] Noll et al.[50] collected ACE data prospectively, identifying young girls who had reported exposure to sexual abuse to child protection services in the last 6 months and following them through until motherhood. The average number of types of ACEs examined was 5.2, with the range of 1–10. Sexual abuse (95.2%) and physical abuse (90.5%) were the two most common types of ACEs investigated, with parental imprisonment being the least common (28.6%).

Emotional development was the most common outcome category investigated (n = 10), followed by physical and mental health (n = 6), cognitive development (n = 3), risk-taking behaviours (n = 2), childhood growth (n = 2) and educational attainment (n = 1). No studies were included that investigated the outcome category of receipt of child protection support.

Review question 1: what is the relationship between parental ACEs and the health, well-being and developmental outcomes of their offspring (up to the age of 18 years)?

Cognitive development

Three studies explored the association between parental ACE exposure and offspring cognitive development outcomes.[17,48,49] Folger et al.[17] found for each additional maternal ACE reported, there was an 18% increase in the risk of suspected developmental delay in communication, fine and gross motor skills, personal-social function and problem-solving at age 2 years (risk ratio = 1.18, 95% confidence interval [CI]: 1.08–1.29). Mothers who reported at least three ACEs were 2.23 times more likely to have a child with a suspected developmental delay. Hendrix et al.[48] found that maternal emotional abuse was significantly associated with stronger functioning coupling between the amygdala and the medial prefrontal cortex. This accelerated development can increase the risk for certain neuropsychiatric disorders[65] and decrease neural plasticity.[66,67] Moog et al.[49] observed a significant association between maternal childhood abuse or neglect and newborn grey matter volume. These studies indicate that maternal childhood experiences of abuse and neglect can negatively affect the cognitive development of offspring through impaired brain development and suspected developmental delay.

Childhood growth

Two studies explored the association between parental ACE exposure and offspring growth.[44,50] Noll et al.[50] found offspring of mothers who had been sexually abused in childhood were 2.8 times more likely to be born preterm (odds ratio [OR]: 2.8 ± 1.44, 95% CI = ±0.37; $P < 0.05$). Ciciolla et al.[44] found infants of mothers with exposure to six ACEs were four times more likely to be born preterm, have a low birthweight or be admitted to a newborn intensive care unit during the first 6 weeks (OR = 4.33, 95% CI: 1.02, 18.39). When investigated as a separate outcome, infants of mothers with high ACE exposure were almost nine times more likely to be admitted to newborn intensive care unit (OR = 8.7, 95% CI: 1.34, 56.65).

Physical and mental health

Five studies explored the association between parental ACE exposure and offspring physical health outcomes.[43,46,52,53,59] None examined mental health outcomes in children.

Children of mothers exposed to childhood physical, sexual and emotional abuse or domestic violence were significantly more likely to be either overweight or obese[52] or diagnosed as autistic by age 3 years[53] and at increased risk of infant bronchiolitis diagnosis after adjusting for maternal smoking, asthma and social support.[43] Beveridge et al.[59] found parental ACE exposure was not a significant predictor of youth pain intensity but did predict parent chronic pain status. Eismann et al.[46] found higher maternal exposure to ACEs was significantly associated with an increased risk of missed well-child

visits (routine check-ups) by age 2 years. For each additional maternal ACE exposure, there was a 12% increased incidence rate of missed well-child visits (OR = 1.12, 95% CI 1.03, 1.22).

These studies indicate that maternal ACEs can negatively impact the physical health outcomes of their offspring and early use of health care.

Emotional development

Seven studies[45,47,54,56,58,60,61] examined the association between parental ACEs and their children's internalising behaviour, specifically emotion disorder, anxiety, depression, somatisation, separation anxiety and peer problems. Five studies found a small but significant association,[45,54,56,58,61] and two studies found a non-significant but trending association[48,60] between maternal ACEs and offspring internalising behaviour. Fenerci and Allen[45] found that there was a positive association between maternal childhood experience of physical abuse and domestic violence, but not sexual abuse. Interestingly, the two studies that found evidence of a lack of association were the only two to use all 10 maternal ACEs as exposure variables in their analysis, collected through the Original ACE Questionnaire. This suggests it is plausible that only specific types of maternal ACEs may be a risk factor for offspring's internalising behaviour and that the association is diluted because of the inclusion of other unrelated maternal ACEs in these studies.

Seven studies[45,47,56,58,60–62] observed a significant association between maternal ACEs and children's externalising behaviour (hyperactivity, aggression, disruptive behaviour disorder and conduct problems). Fenerci and Allen,[45] the only study to explore the associations between specific types of ACEs and offspring externalising behaviours at 12 years of age, observed a significant association with physical, but not sexual, abuse.

Other studies observed a significant association between maternal ACEs and surgency/extraversion temperament and/or negative affectivity[61]; maternal childhood sexual abuse and oppositional, peer and conduct problems[55]; and maternal physical, sexual and emotional abuse and their children's adjustment problems at age 4 and 7 years (parent-reported adjustment).[57]

These studies suggest that maternal ACEs can negatively impact the emotional development outcomes of their offspring. Impaired emotional development can have significant implications on the health, well-being and developmental outcomes of the child, such as through poor educational attainment and later psychopathology.

Educational attainment

One study explored the association between maternal childhood sexual abuse and educational attainment of offspring up to age 7 years,[55] observing that children of mothers with a history of childhood sexual abuse had significantly lower scores on picture vocabulary tests used to assess expressive language skills compared with children of mothers with no history of childhood sexual abuse.

Risk-taking behaviours

Two studies investigated the relationship between parental ACEs and offspring's smoking.[51,52] Pear et al.[51] found a maternal childhood history of physical abuse and parental substance abuse was significantly associated with a 20% and 17% increased risk level of offspring smoking, respectively. Roberts et al.[52] reported that mothers' exposure to childhood abuse was a significant predictor of her offspring smoking. In addition, offspring of mothers who reported the most severe level of childhood abuse were at the greatest risk of smoking.

Review question 2: does this relationship differ according to the number and type of parental ACEs?

Eight studies included in the review investigated how the observed association between parental ACEs and offspring outcome differed according to the number of ACEs the parent was exposed to; all observed an increase in the number of parental ACEs increased the risk to the offspring of experiencing a negative outcome in their cognitive development,[17,48,49] physical health[43,46,53] or emotional development.[47,57]

Seven studies investigated how the relationship differed according to the type of parental ACEs.[48,51–53,56,57] Five studies, with the exception of Collishaw et al.[57] and Myhre et al.,[62] found that the associations observed between overall ACE score and offspring outcomes differed when specific ACE types were examined. For example, maternal childhood physical and emotional, but not sexual, abuse were risk factors of offspring's autism diagnosis.[53] Pear et al.[51] found that a mother's experience of parental mental illness in her childhood was not associated with her offspring smoking, but maternal childhood physical abuse and parental substance abuse during her childhood was.

Discussion

To our knowledge, this is the first systematic review to examine the relationship between parental ACEs and the health, well-being and developmental outcomes of their children. Significant associations were observed between parental ACEs and offspring outcomes, with the exception of offspring pain intensity. When parents were exposed to ACEs, their children were significantly more likely to have impaired brain development, developmental delay and learning difficulties; be born preterm; be more likely to be diagnosed with bronchiolitis, obesity, or autism; miss routine health check-ups; demonstrate externalising behaviours or a suboptimal temperament (defined as extraversion or negative affectivity); have adjustment or socioemotional development problems; and smoke. Overall findings suggest that parental exposure to ACEs negatively impacts the health, well-being and developmental outcomes of their offspring. It is possible that the impact of parental ACEs on child health, well-being and development extends beyond the outcomes examined in the studies included in this review.

A consistent finding was that as the number of ACEs a parent was exposed to increased, the greater the negative effect on their children, indicating that children of parents who experienced many ACEs are more at risk of negative health, well-being and developmental outcomes. The studies also suggest the relationship between parental ACEs and offspring outcome is type dependent, although inconsistency in the outcomes studied precludes reaching a clear understanding of which types of parental ACEs pose a greater risk to children's health, well-being and development outcomes. Overall, the results indicate that the relationship between parental ACEs and offspring outcomes differs according to the number and type of parental ACEs.

Policy and practice implications

These findings support interventions aimed at reducing the occurrence of ACEs and underpin the need to take a 'multigenerational' approach in addressing the effects of ACEs. A conventional method used by front-line health and other community workers to identify children at risk is to examine the child's environmental, sociodemographic or economic characteristics. Whilst this review does not provide evidence against this method of identification, it suggests screening for parental ACEs might lead to earlier identification of potentially at-risk children and enable community teams to more accurately target interventions for children at risk of negative

health, well-being and developmental outcomes. The design and delivery of interventions may also be better informed and bespoke in response to ACE-related information. In addition, evidence that babies of mothers who were exposed to ACEs had a significantly higher risk of being born preterm and/or with impaired brain development[44,48–50] indicates that screening for parental ACEs should be conducted early in pregnancy if interventions implemented before birth can reduce this risk. The included studies indicated some mediating variables between parental ACEs and offspring outcomes, such as maternal physical and mental health, smoking and alcohol use and offspring and maternal telomere length. This is another important avenue for further investigation.

Limitations

Criteria for classifying ACEs have been debated since Felitti et al.'s[9] initial work in this area. However, to conduct a systematic review of the literature, it was necessary to use a focused classification of ACEs. As the 10 categories of ACEs described by Felitti et al.[9] are the most widely used classification of ACEs, they were the focus of our review. This may have excluded studies that use other classifications of ACEs.

Methodological limitations within the included papers reduced the ability to draw firm conclusions. They included mostly retrospective examination of parental ACEs, variability in the methods used to measure parental ACE exposure and type and number of ACEs measured, lack of continuity over the age at which a child's outcomes were investigated and a lack of studies investigating child outcomes past the age of 13 years. This diversity precluded a meta-analysis.

All studies were conducted in high-income countries, limiting the generalisability of findings to middle- and low-income countries or to humanitarian settings where the population may have greater exposure to ACEs. This disparity may have been exacerbated by the inclusion only of (expensive) longitudinal studies.

Some studies included in this review used data from pre-existing cohorts. Four pre-existing cohorts were used in more than one study, and it is possible that the data from individual patients may have been used more than once. Whilst this has the potential to introduce bias, the narrative synthesis approach of this review will limit the potential for any bias.

Within a systematic review, it is possible to define the search terms used both narrowly and widely. Defining the search term widely will inflate the number of papers identified, and it is important to maintain a focus consistent with the scope of the research question. The search terms we used identified more than 13,000 unique papers, which were manually screened by the authors. It is possible that in the area of defining 'parental mental health difficulties', too narrow an approach was taken. However, during an initial scoping exercise, it was found that widening this term led to the inclusion of a large number of papers outside of the scope: in particular, those concerning maternal depression during pregnancy. We therefore believe our focused approach allowed us to explore the comprehensive literature on the topic within the scope of our review.

Recommendations for future research

A notable research gap is the effect of paternal ACEs on offspring outcomes. Only two of the 19 studies included fathers in their population sample, and even in these studies, a smaller number of fathers participated than mothers.

Second, no studies investigated outcomes beyond the age 13 of years. Following up children to at least the age of 18 years would increase the number of studies investigating outcomes, such as receipt of child protection support, mental health outcomes or educational attainment, which were largely unexplored.

Third, the lack of studies conducted in low- or middle-income countries and humanitarian settings is an important gap because parental resilience to provide protective and nurturing care may come under strain. Further research using current tools or contextually modified ACEs that better reflect adversities in those settings may enable better targeting of limited resources on infants and households most at risk in populations experiencing widespread acute need.

Fourth, more research is needed to investigate the association between maternal ACEs and offspring internalising behaviour, with types of ACEs separated to measure specific effects before forming a conclusive statement regarding the association.

Finally, seeking agreement on definitions of ACEs and outcomes of particular interest would allow collaboration across longitudinal studies, creating a valuable resource to increase the potential from future research investigating the relationship between parental ACEs and offspring outcomes. Future research, including primary research, should be conducted to examine the impact of specific types of ACEs, including wider definitions as proposed by Cronholm et al.[68] and Finkelhor et al.[69]

Conclusions

Findings suggest that offspring of parents who have been exposed to ACEs are at greater risk of a variety of negative health, well-being and developmental outcomes. In addition, this relationship differs with the number and type of parental ACE exposures, with a positive relationship being observed between the number of parental ACEs and risk of negative outcomes in their offspring. These findings have implications for policy and practice, including the recommendation that screening for parental ACEs by health or community workers may be an effective way to identify at-risk infants, children and adolescents, enabling earlier or bespoke interventions. Overall, this review provides a comprehensive overview of available literature on this relationship and highlights the important implications that accounting for parental ACEs may have towards efforts to improve child outcomes.

Author statements

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Competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.03.025.

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The role of Medical Officers of Health in Civil Defence and how they influenced modern emergency medical practice

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ABSTRACT

Objectives: The article will examine the role of the Medical Officer of Health within United Kingdom Local Authorities in the period preceding the Second World War, the war itself, the residual impact of their work on emergency medical and public health practice and lessons that can be learned to improve.
Study design: The article uses archival and secondary source analysis of documents related to the work of the Medical Officer of Health, their staff, and associated organisations.
Methods and results: The Medical Officer of Health performed a key role in the Civil Defence of the United Kingdom, ensuring that the victims of aerial bombardment were treated quickly. They also worked to ensure the public health of the population was maintained, especially those covering areas receiving evacuees, and worked to improve conditions within deep shelters and other areas with displaced individuals.
Conclusions: The work of the Medical Officer of Health created the forerunner of modern emergency medical practice in the United Kingdom, often through local innovation, and embedded the work on health promotion and protection fulfilled by Directors of Public Health.

Introduction

Amid the plethora of films and popular culture related to the Second World War, there is one group of individuals who are very rarely featured: the staff of the Civil Defence Casualty Service. This organisation was responsible for immediate life-saving response to the various forms of aerial bombardment that threatened the United Kingdom. At its heart, coordinating prewar planning and wartime response was the Medical Officer of Health (MOH). Their role was instrumental in forging the Service, and they were vital in allowing innovation to thrive and be adopted locally, regionally, and nationally. The Medical Officers of Health (MOsH) had to continue their peacetime role of providing public health leadership for their locality, a role exacerbated by the evacuation of individuals during the conflict and conditions forged through bombing.

This article will explore the role of MOsH prewar, their significant role in creating their local Civil Defence Casualty Service, their wartime role and their impact on modern emergency medical and public health practice. The article will comprise a historical review, with a conclusion to explain the implications and importance of the study for modern practitioners, both in understanding the history and recognising modern parallels.

Prewar activities

The MOH, in the period before Air Raid Precautions (ARP), was already a role with significant and ever-increasing responsibilities. The MOH predated the Ministry of Health and had their origins in the Sanitary Boards that were amongst the first examples of Local Authority control in urban areas. Their duties encompassed the modern roles of Public Health and Environmental Health and were responsible for the health of the inhabitants of their locality. This included their physical health, mental health, and the wider sanitary conditions in which their area was based. Within many areas, infectious diseases were endemic, and the MOH had to ensure the provision of hospitals for treatment, alongside vaccination and public education. MOsH had the unenviable task of trying to coordinate the various medical establishments within their area. These included any hospitals run by the local authority, isolation hospitals for infectious diseases and voluntary and private hospitals. Following the Local Government Act 1931, the MOsH gained the duties of the Poor Law guardians and their eponymous

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workhouses, which most transformed into municipal hospitals. Alongside these duties, the MOH's department coordinated general practice, midwifery and community nursing. The MOH was born of a period where the idea of universal health provision was alien and that health care was the preserve of local authorities and the private sector; central government became involved only in emergencies. There was little direction from the Ministry of Health on most areas of responsibility, a situation that had changed little from the Ministry's predecessors in the Local Government Board despite the lessons of the Flu Pandemic of 1918–1920.

In the period immediately after the First World War, there was disagreement within Whitehall over who had primacy of future ARP, with the War Office and Home Office both believing that it should be the other. It was agreed, because of the civilian areas that it would cover, that the Home Office and Local Authorities should be responsible for ARP, rather than local military commanders and their subordinates. By placing much of the responsibility for ARP onto Local Authorities, the government also recognised both the need for local knowledge and the difference in trust levels between central and local government amongst the population. It also demonstrated that expertise in directly running services still sat at the local level during this period rather than centrally.

The ARP department, founded in 1935, created a series of memoranda for the various services Local Authorities would need to create. The first of these memoranda, published in 1935, formed the Casualty Service. The service, created with little input from the Ministry of Health, was to be coordinated by the MOH in each scheme-making authority; these were to be upper tier and unitary authorities across the country in the same manner of Directors of Public Health today.[1] The service consolidated existing health provision within a local authority area to report to the MOH and created new wartime services; an enlarged ambulance service, a first aid party service, first aid posts and gas decontamination centres and emergency arrangements for war dead. It was assumed that the Voluntary Aid Societies, St John Ambulance, the British Red Cross and St Andrews would provide the bulk of the staffing for these new services, with the MOH liaising closely with the local units. In addition, it was expected that all hospitals within the Local Authority would be categorised into those that would receive casualties and those that were specialist or too small, with plans on each category's use.[2]

The MOH was to find themselves with significant extra work in creating these services. Their role involved considerable diplomacy, as many of the existing services were not under their direct control but under other council-aligned services, such as the Police, Fire Brigade or Voluntary Sector for Ambulances,[3] and private and voluntary bodies that ran hospitals. They also found themselves having to deal with the Home Office in regard to their compliance with the ARP requirements and attend the ARP Committee of the Local Authority, where they were a standing member and had to explain the necessities of health. Many MOsH, rather than carrying the full burden of this work alone, requested a deputy to fulfil the demands of the ARP work.[3] A number of these staff became experts in their own right, with Dr John Chapel completing a PhD thesis on Casualty Services in Leicester in 1937[4] and Dr Gerald Shirlaw, Deputy MOH for Battersea, writing two books on the subject in 1940[5] and 1941.[6]

For MOsH in rural areas, they had the additional difficulty of planning for potential evacuees and refugees to be placed in their area, including the need to respond to communicable diseases that, although endemic in the cities, were relatively unknown in their locality.[7] These needs, when balanced against national requirements, meant that MOsH would on occasion push back against directives to convert hospitals. In one particular case, the Cardiganshire MOH, Dr Jones, successfully argued that the County Maternity Home should remain as a specialist centre because of the expected numbers of refugees and evacuees that would be arriving in the area and the resulting need for specialist maternity care.[8]

Post-1938, the MOH gained the additional workload that resulted from a change in ARP oversight. Half of their service, Hospitals, Ambulances and First Aid Posts were now overseen by the Ministry of Health; the rest of their work stayed with the Home Office.[9] The Ministry of Health changed the requirements for First Aid Posts, reducing gas attack preparedness and increasing their ability to treat minor injuries resulting from high explosive and incendiary attack; consequently, the MOH had to adapt their operating model, staffing needs, and protections afforded to the buildings. The new arrangements meant that Medical Officers were serving two government departments with competing priorities, as well as being accountable to their local authority colleagues. The increased workload with the Ministry of Health also impacted workload through the co-location within their hospitals of Emergency Medical Service beds. This was the Ministry's first foray into directly running medical services on a nationwide level, and their local officers built up effective working relationships with the MOsH of which they were residing. This split between various departments can still be seen to this day, with Directors of Public Health having to provide support and assurance to their Local Authority (LA) colleagues and elected members, to their NHS Partners and to two central government departments.

The MOH also needed to respond to an issue not envisaged when planning ARP. The Voluntary Aid Societies, expected to provide the personnel for Casualty Services, informed the Government that they were committed to provide volunteers to the War Office and Admiralty and that their most able-bodied volunteers would be unavailable.[10] This resulted in MOsH actively recruiting staff they had not planned for and identifying where women would be best deployed as part of Casualty Services. In many cases, the role of ambulance attendant and driver was adjusted to become a female role, allowing male volunteers to be diverted to the first aid and rescue parties.

Wartime work

The wartime roles of the MOH were dependent on the location they covered. For officers who covered remote areas, their wartime work began earlier and aligned to their traditional responsibilities. These areas were the first to receive evacuees. This evacuation brought challenges for their receiving areas; in Cardiganshire, the MOH found that his staff were so inundated with infectious diseases and wider poor health that two dedicated medical facilities were established to provide treatment to the new residents. These medical facilities were to operate for the duration of the conflict and were adapted as the war continued from providing infectious disease response and health protection work to wider health promotion, including dentistry, optometry and dietary support.[7]

The rural MOH had to be more inventive than their urban colleagues when planning for aerial bombardment. As these areas did not have the wealth of resources of their urban colleagues, the MOH adapted their plans and made greater use of smaller, community-based response. Their creation, the First Aid Point, was built on the premise that a focal point within a village could be used to store equipment and provide a location for training and a deployment point for volunteers. The rural MOH also made greater use of combined mobile first aid post and ambulance units based at the main hospitals within their locality so that the volunteers within the First Aid Point would stabilise patients until definitive care arrived on scene before onward transport.[11]

For the MOsH covering areas at higher risk of aerial bombardment, their war was to prove exceptionally challenging. The

predicted gas attacks, which resulted in detailed planning by ARP, did not materialise and were replaced by widespread use of high-explosive and incendiary bombs. This resulted in the repurposing of many buildings by MOsH, as the need for significant numbers of gas decontamination centres reduced and First Aid Posts and hospitals increased. The creation of deep shelters, where it was hoped that high-explosive bombs would not reach, created issues for MOsH when considering the public health of those using them. The lack of sanitation, especially in the case of London Underground stations and deep caverns, meant that MOsH had to mandate that toilets and running water were provided in these locations and that their status was recognised and made official. Once this had been done, additional resources were created until each shelter had access to dedicated medical personnel, full sanitation including showers, and staff from the MOH's department to monitor them.[12]

At the height of the invasion risk to the United Kingdom, MOsH also began close liaison with their colleagues in the Regular Army and Home Guard. As the latter did not have medical staff of its own at this point, the MOH was to provide First Aid Parties to fighting forces in their area. In return, there was considerable cooperation between both services throughout the conflict, including joint training and exercising.[13] This cooperation occurred without many of the MOsH and their military colleagues being aware that, had the War Office been given primacy for ARP, it would have been the military in charge of Casualty Services and the MOsH operating in a supporting role.

As the conflict continued, the MOH had to grapple with the convergence of their wartime work and peacetime responsibilities in a similar way to their modern counterparts during the COVID-19 pandemic. During the period of the Second World War in the United Kingdom, only doctors and midwives were allowed by law to assist a woman in childbirth.[14] This in peacetime did not cause concern, but in wartime was proving difficult, as midwives could not reach patients and mothers could not reach maternity hospitals during air raids. A number of MOsH, alongside their Association and the Central Midwives Board, successfully lobbied the Ministry of Health for a position statement on the response needed for midwifery cases across the country during air raids; within London, this ensured that a midwife would be on duty each night within deep shelters in case of deliveries during raids.[15]

As the conflict continued, the MOH was often found at the heart of local innovation. This was in part because of the lack of clear guidance from government, and the independence and authority MOsH still had within their locality. With no national formulary in 1939, many MOsH were experimental in what they allowed doctors within their posts to administer. In Southampton, the MOH issued cocaine in liquid form to all First Aid Posts as a treatment for eye injuries.[16] The MOsH also adapted mandated services to suit the realities of the conflict. The Ministry of Health had instructed all local authorities to have mobile first aid posts available to deploy to incidents. Designed around vans or lorries, they were not designed to be treated on in the majority of cases but merely to transport significant amounts of equipment and personnel to the incident scene. These mobile units were heavily criticised in urban areas, as they were slow, unable to pass bomb craters, and rarely needed in the role envisaged. Many MOsH adapted the concept by placing the doctor, the element most needed, and a number of nurses in a car with equipment.[17] This adaptation, providing first aid staff at the scene with advanced medical support, was adopted by central government as a Light Mobile First Aid Post. In those areas where local medical practitioners had offered to join an Incident Doctor rota, there is also evidence of local uniformity of practice and equipment. Wolverhampton's MOH, Dr Jolly, ensured that his Incident Doctors were issued standardised haversack bags with equipment. This ensured that any doctor responding off the rota was trained and equipped to the same standard in a comparable way to the first aid and ambulance staff they would be responding alongside.[3]

Postwar legacy

The impact of MOsH and their wartime work can be seen across multiple areas. Their work helped to create the modern emergency medical system in the United Kingdom, albeit at different rates of adoption. The ambulance service was in many respects the earliest success story, as the wartime work it had undertaken showed that it could be more than just a patient transport service but a fully functioning emergency response service too.[18] It was unfortunate that as the Casualty Service had been run as part of the Local Authority rather than the Ministry-led Emergency Medical Service, many of the innovations highlighted through the Casualty Service were not included within the National Health Service but instead lay forgotten until being ‘re-invented’ in subsequent decades.

Within the field of public health, the wartime experience of MOsH showed that a balance between health protection and health promotion was vital and that these areas were closely intertwined. The work of MOsH in regard to evacuees also highlighted the stark nature of health inequalities within the United Kingdom and the urgent need to tackle it across the country. The wartime activities of MOsH in health protection and promotion linked closely with the findings of the Beveridge Report and helped cultivate the need for a National Health Service to respond to the issue of Squalor, as Beveridge worded it.

Conclusion

To conclude, it is of real importance to understand the wartime work of the MOH, both in its historic context and its wider impact on current Public Health practice. The ability of the MOsH to respond quickly to changing circumstances, and work alongside nascent services founded in crisis, has been reflected in modern practice during health protection incidents, larger incidents such as COVID and other incidents related to emergency preparedness, resilience and response.

By understanding the work of predecessors, public health practitioners can recognise parallels in their present work but also identify areas of innovation historically that can be adopted today. It is also important and timely to understand the historic foundations of public health practice to show that it is a field with a strong and ever-evolving foundation and that it is a field that has made a real difference to the health and well-being of the United Kingdom.

Author statements

Ethical approval

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Competing interests

There are no competing interests.

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Editorial

The roots of the healthcare crisis in England

For many years, the National Health Service (NHS) in England has been vaunted as one of the best healthcare systems in the world, delivering good healthcare outcomes at relatively low cost per capita amongst the leading industrialised nations.[1] However, the winter of 2022/2023 has been the most challenging winter faced by the NHS, and it has struggled to cope with high patient demand for health care, with long delays to Accident & Emergency (A&E) care, delayed hospital admissions and postponed outpatient appointments.

One barometer for the acuity of the demand is the number of patients on waiting lists for NHS treatment. Compared to 2008, when there were around 2 million patients on its waiting lists, the waiting lists had risen to over 7 million patients by the end of 2022.[2] Whilst the COVID-19 pandemic has undoubtedly led to increased healthcare demand and had a negative impact on waiting lists, only 2 million of the waiting list occurred during the recent pandemic period. The crisis therefore is not just a manifestation of pandemic impacts on the system but has been brewing for several years and has now come to a head.

Whilst the crisis is the result of a complex mix of factors, the main driver is chronic underfunding of the NHS since the financial crisis of 2008. As with many other developed nations, England has an ageing population – more people are living longer and increasingly with multiple comorbidities. This trend is projected to increase yet further over the next two decades.[3] This directly translates to ever greater demand for health and social care for the elderly. Government funding of the NHS over the past decade has simply failed to keep pace with the rising demand for health care, let alone inflationary costs of delivering that care.

This under-resourcing of the NHS has led to worsening hospital staffing and bed shortages, a situation that is expected to worsen in future years.[4] This is against the backdrop of the United Kingdom already having a relatively low bed to population ratio compared with many of its European neighbours. In part, this was due to a policy shift to move more patient care delivery into the community, but there has been insufficient investment to build up the community care needed. There has also been significant social care underresourcing, which means there are insufficient social care home beds, staff and domiciliary care services. Consequently, elderly patients who need these social care beds or care packages are not able to access them in a timely fashion and end up stuck in hospitals (i.e. the proverbial “bed blockers”).

The NHS is in dire need of a long-term workforce strategy and sustained investment. In recent years, there have not been enough doctors and nurses trained, and their pay has been stagnant at a time when the costs of living have risen significantly. Worsening working terms and conditions leads to disgruntled staff leaving prematurely – in other words, the health service is haemorrhaging staff as fast as it is training them. One in 13 posts in hospital and community services were vacant. In particular, there has been a decline in the number of primary care doctors and community nurses.[5] Neither can the NHS recruit its way out of this crisis, as it has done so in the past by drawing on international health staff, due to the worsening global health workforce crisis.[6] Overstretched staff also increases the likelihood of less good care being delivered and errors being made – a serious patient safety risk.

Some may argue that this is evidence that the English model of healthcare delivery does not work and that radical solutions, including reorganisation or a different model of delivery (e.g. insurance based or greater privatisation) may be the solution. That would, however, be a naïve conclusion to draw. The root cause of the problem is not system failure, but underfunding, so reorganisations won't help. Indeed, any system of healthcare delivery that is underfunded will fail to deliver care to meet patient demands and expectations. Greater privatisation would likely worsen health inequalities in the country and drive up healthcare costs, and all insurance-based systems suffer the problem of moral hazard.

If the UK system is sufficiently resourced in the longer term (i.e. with sustained investment), it can deliver good care fairly efficiently, but this will require greater government expenditure and therefore likely taxation that the public may not find palatable. Indeed, one problem with publicly financed health services such as the NHS where health care is delivered free at the point of access is that the public may not fully appreciate the true costs of health care, which could influence their willingness (or lack of) to pay for health services. Perhaps the singer Joni Mitchell summed it up best, “you don't know what you've got till it's gone”.

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Review Paper

Water, sanitation, and hygiene vulnerability in child stunting in developing countries: a systematic review with meta-analysis

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ABSTRACT

Objectives: This study aimed to perform a systematic review and meta-analysis to assess the scientific evidence of the relationship between vulnerability to access to safe drinking water, sanitation, and hygiene (WASH) practices on stunting in children aged <5 years in developing countries.
Study design: This is a systematic review and meta-analysis article to assess the relationship between under-five stunting and WASH vulnerability in developing countries.
Methods: The systematic review with meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol methodology. The following databases were used: LILACS, MEDLINE (via PubMed), SciELO, Web of Science, ScienceDirect, SCOPUS, and Embase. All original studies identified that related WASH vulnerability to stunting in children aged <5 years in developing countries was included. Three authors performed independently the selection and extraction of data from the articles. The statistical software STATA version 11 was used. Cochran's Q test and Chi-square test (I^2) with 95% significance were used to assess the heterogeneity of the studies.
Results: The search resulted in the initial identification of 2047 articles; after reading the abstracts, followed by the full articles, 14 articles were included in the systematic review and eight articles were included in the meta-analysis. The studies selected for the systematic review were published between the years 1992 and 2021 and conducted in eight countries, namely, Ethiopia, India, Indonesia, Bangladesh, Tanzania, Peru, China, and Lesotho. The studies assessed vulnerability to access to WASH on the growth of children aged <5 years. There was a significant difference when relating WASH vulnerability to children's height. The meta-analysis of this study showed that the impact of WASH on child stunting is significant when it comes to lack of sanitation in 72% of the studies.
Conclusions: The study found that WASH vulnerability contributes to stunting in children aged <5 years in developing countries. Based on our findings, we recommend incorporating WASH strategies, especially sanitation, into the formulation of interventions integrating with health promotion policies for healthy early childhood development.

Introduction

It is estimated that approximately 149 million preschool children aged up to 5 years, mostly from low- and middle-income countries, are stunted.[1] Child growth stunting is when a child's height is below the average height-for-age (Score Z) of the World Health Organization (WHO) Child Growth Standards.[2] In addition to being directly associated with food and nutrition insecurity in these populations, stunting is also related to several other social, economic, and environmental determinants of health. These include local environmental factors, such as deficiency in access to safe drinking water, sanitation facilities, and hygiene practices (WASH), which is responsible for diarrheal diseases and enteric infections during childhood.[3,4] The high incidence of waterborne diseases during childhood could interrupt healthy growth trajectories, contributing to undernutrition.[5]

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0033-3506/

The lack of access to WASH is a global health crisis that is especially more prevalent in developing countries as well as they are considered in the Organization for Economic Co-operation and Development (OECD) DAC 2022 and 2023 list ranking.[6] The vulnerability of WASH in these contexts is therefore neglected risk factor in child development.[7]

Child stunting is a public health problem for under-fives in developing countries, and a better understanding of the impacts of WASH vulnerability on child development is needed. According to WHO and United Nations International Children's Emergency Fund (UNICEF), stunting is more common in places with low access to improved sanitation.[8] This issue motivated researchers to the following research questions: (1) Does WASH vulnerability generates a growth deficit in children aged <5 years? (2) Which components of WASH are most significant in generating child growth deficit?

In this regard, this systematic review (SR) and meta-analysis (MA) aimed to assess the scientific evidence of the relationship between vulnerability to stunting in young children aged <5 years in developing countries and access to safe drinking water, improved sanitation, and hygiene practices in stunting of children aged <5 years in developing countries. The study hypothesizes is that the lack of access to WASH leads to more diarrheal diseases that affect children's growth.

Methods

Study design

This is a SR and MA article to assess the relationship between under-five stunting and WASH vulnerability in developing countries.

Protocol and registration

This SR of published scientific literature used the recommendations proposed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[9] for its design. It was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under protocol number 326671.

Search and research sources

For the selection of studies used in this review, a literature search was performed of articles published in the following databases: Latin American and Caribbean Literature (LILACS), MEDLINE (via PubMed), SciELO, Web of Science, ScienceDirect, SCOPUS, and Embase. The search was carried out by three authors (A.R.M.A., J.R.M.S., and L.L.V.) independently. In the databases, the search was conducted using the following descriptors: (“sanitation” OR “water” OR “hygiene” OR “wash”) AND (“children” OR “child”) AND (“stunting” OR “growth curve” OR “height” OR “weight”) AND (“low-and middle-income countries” OR “social vulnerability” OR “developing countries”). In the ScienceDirect database, it was possible to search for only eight descriptors, namely, ((sanitation) OR (wash)) AND ((children) OR (child)) AND ((stunting) OR (height) OR (weight)) AND (developing countries)). The search date was April 26, 2022. The studies were identified by systematic search and used Rayyan - Intelligent Systematic Review software to retrieve and manage them.

Eligibility criteria

The inclusion criteria for the studies were (1) original articles; (2) date performed: until April 26, 2022; (3) study in developing countries; (4) study with children aged <5 years; and (5) study that related WASH vulnerability with child stunting. The exclusion criteria were as follows: (1) repeated or duplicate articles, (2) SR and MAs articles, (3) articles that did not correspond to the age range of the children, and (4) studies that did not conclude the relationship of interest to the present study.

Screening process

The three authors (A.R.M.A., J.R.M.S., and L.L.V.) screened the articles and added them to Rayyan's platform and used the "blind off" method, following the following steps to screen the articles: (1) reading the titles, (2) reading the abstracts, and (3) reading the full article for data extraction. Discrepancies were resolved after a discussion among the three authors to decide which articles were included or not in the study.

Data extraction process

The following information was extracted from the articles for the systematic review: (1) reference with authors, year of publication, title, and periodical; (2) year of data collection; (3) country; (4) classification of the OECD; (5) type of study; (6) sample size (n); and (7) age (months). The height-for-age values for performing the MA were considered according to (8) statistical values used for the odds ratio (OR); (9) confidence interval (95% CI). In addition, it considered only data concerning those of children "with WASH vulnerability." Data extraction from the selected studies was conducted using the MicrosoftTM Excel program.

Conceptually, the components of WASH were defined as (1) access to safe drinking water ("improved" water), such as treated, boiled, or filtered water, piped or from the tap;[10,11,12] and (2) access to improved sanitation, such as facilities (toilet, plumbing, and treatment) that ensure hygienic separation of human excreta from human contacts, such as the case of populations that do not practice open defecation,[7,13,14] and improved hygienic practices, such as households that have handwashing facilities with availability of soap and other detergents near the toilet.[15]

Evaluation of the quality of studies

To measure the methodological quality of the articles included in the SR, the Joanna Briggs Institute assessment tool[16] was used. The results were calculated as a percentage, scoring 1 point for "yes", 0.5 points for "not clear," and 0 points for "no."

Statistical analysis

MA was performed using a random effect model. Heterogeneity was assessed by Cochran's Q test with a significance level of $P < 0.10$, and its magnitude was assessed by I-squared (I^2).[17]

The analyses were performed with the Metan command of the Stata program (version 11.0). The associations between WASH vulnerability and children's growth patterns were assessed by the OR and its CI. In the studies that did not present this measure, we used the mean Z-score and its respective CIs.

Subgroup analysis was performed to investigate the differences in risk among the different components of WASH vulnerability. The existence of the small study effect was also assessed by visual inspection of the funnel plot and Egger's test.

Results

Searches and selection of studies

The search resulted in the initial identification of 2047 articles, and after the exclusion of duplicates, 1452 remained. After applying the inclusion criteria, the first step of reading the titles resulted in 39 studies. In the second stage of reading the abstracts, 25 articles were selected. In the third stage of reading the full articles, 14 articles were included in the SR and eight articles were included in the MA (Fig. 1).

Characteristics of the studies

The studies selected for SR were published between the years 1992 and 2021 and conducted in eight countries: Ethiopia, India, Indonesia, Bangladesh, Tanzania, Peru, China, and Lesotho. According to the OECD classification, of the eight countries studied, 43% are considered as "least developed countries", 43% are considered as "lower middle-income countries", and 14% are considered as upper middle-income countries. The studies assessed access to WASH on the growth of children aged <5 years (Table 1). As for the association of the components present in WASH, 72% of the studies included access to water, 86% of the studies included sanitation, and 29% of the studies included hygiene in the assessment.

For the evaluation of child growth for the MA, the height-for-age data (Z-score) were considered by the values of (1) OR and (2) mean with the CIs. For the evaluation of the studies that did not enter the MA, the main results, in percentages and the differences between means, were considered. WASH vulnerability was assessed through the information on access to water, sanitation, and hygiene in each study (Table 2).

Quality of the studies

Of the 14 studies selected for the SR, 13 studies, or 93%, were scored with excellent quality according to the criteria adopted for quality assessment in this study.

Meta-analysis

As OR values and mean with CIs of height-for-age (Z-score) were extracted from the articles, two MAs were performed. Five articles were eligible for analysis of the OR values. In Fig. 2, they appear grouped by WASH components (water, sanitation, and hygiene) in order of publication and have the weighted mean of value of the increase or decrease in children's height, with CI and the weight that varies according to the sample of the articles in question. It is observed that although two of these studies have a small sample size, there was a significant difference when relating WASH vulnerability to children's height, OR 1.23 (95% CI 1.05-1.41) with an emphasis on sanitation, OR 1.56 (95% CI 1.28−1.84).

Three studies were eligible for the analysis of children's height Z-score values and the CI. In Fig. 3, these are in order of publication and have a height-for-age value that varies according to the sample of articles from these authors. Most of the studies indicate that there was a significant reduction in children's height when compared with the WASH vulnerability.

The funnel plot, a test performed to investigate the risk of publication bias, is shown in Fig. 4. In our analysis, although most of the studies fall within the boundaries of the funnel, we still obtained studies that indicated the risk of publication bias. Egger's test was also performed, and this in turn indicated a significant risk of publication bias ($P = 0.018$), as did the results found by the Meta Funnel test.

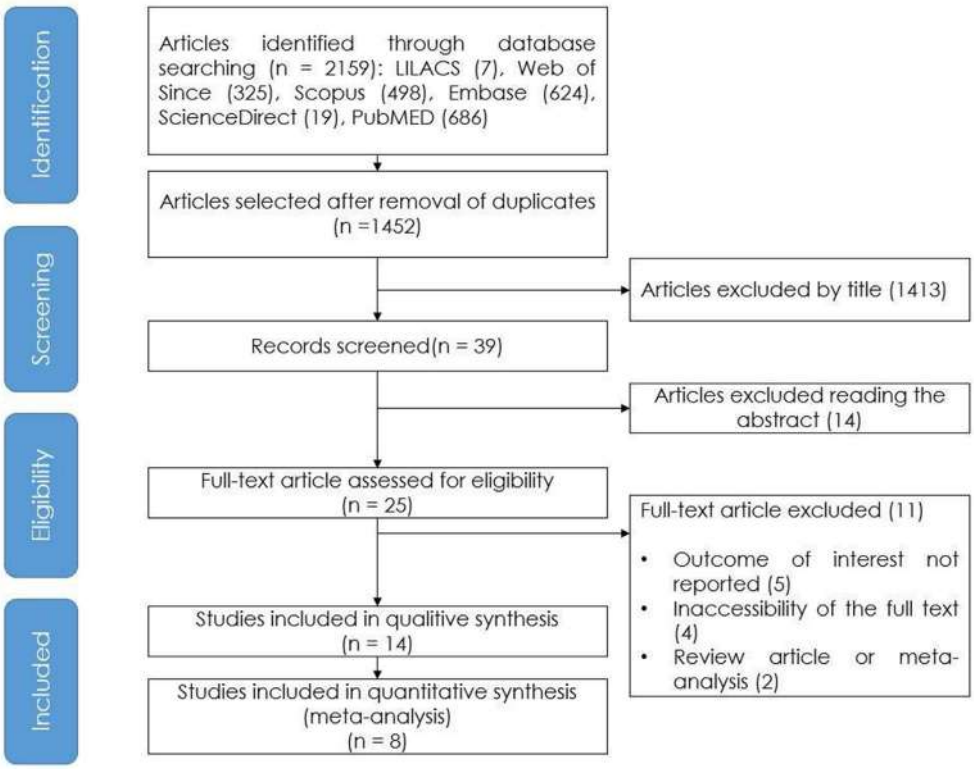

Fig. 1. Flowchart of identification and selection of articles for systematic review and meta-analysis.

Table 1
Information from selected articles on the vulnerability of WASH on child growth used in the systematic review.

Nº	Reference	Data collection year	Country	OECD classification	Type of study	Sample size	Age (months)
1.	Ademas et al., 2021	2019	Ethiopia	Least developed countries	Longitudinal studies	630	0–5
2.	Bekele et al., 2021	2000, 2005, 2011, and 2016	Ethiopia	Least developed countries	Cross-sectional studies	33,744	0–59
3.	Choudhary et al., 2021	2015 and 2016	India	Lower middle-income countries	Longitudinal studies	58,038	6–23
4.	Diana et al., 2021	2014 and 2015	Indonesia	Lower middle-income countries	Cross-sectional studies	622	6, 9, and 12
5.	Berendes et al., 2020	2015	Bangladesh	Least developed countries	Longitudinal studies and cross-sectional studies	516	0–59
6.	Cameron et al., 2020	1997, 2000, 2007, and 2014	Indonesia	Lower middle-income countries	Cross-sectional studies	6365	0–59
7.	Chakrabarti et al., 2020	2019	India	Lower middle-income countries	Longitudinal studies	722	0–12
8.	Rah et al., 2020	2014	Indonesia	Lower middle-income countries	Longitudinal studies	1450	6–35
9.	Augsburg et al., 2018	2011, 2013, and 2014	India	Lower middle-income countries	Longitudinal studies	964	0–59
10.	Mshida et al., 2018	2009	Tanzania	Least developed countries	Longitudinal studies	310	0–59
11.	Assefa et al., 2017	2013 and 2014	Ethiopia	Least developed countries	Longitudinal studies	597	24–59
12.	Checkley et al., 2004	1995–1998	Peru	Upper middle-income countries	Cross-sectional studies	230	0–24
13.	Cheung, Y.B., 1999	1991	China	Upper middle-income countries	Longitudinal studies	1045	0–60
14.	Esrey et al., 1992	1984 and 1985	Lesotho	Least developed countries	Cross-sectional studies	119	0–59

OECD, Organization for Economic Co-operation and Development.

The MA of this study also shows that the impact of WASH on child stunting is significant when it comes to lack of sanitation. Sanitation vulnerability was found to be significant to child stunting in 72% of the studies included in the SR. The studies reviewed concluded that children living in homes that have access to improved sanitation are less likely (10 percentage points;[7] 29%;[18] and 46%[19]) to be stunted compared with children in homes without improved sanitation and who defecate in the open.[7,18,19]

Discussion

This study shows that there is a deficit in the height growth of children aged <5 years in locations with higher WASH vulnerability in developing countries. The results of this study are consistent with data published by WHO and UNICEF from 1997 to 2020, such as the case of Ethiopia, which shows that under-five stunting (36.8%) is greater when access to improved sanitation is low (17.7%).[2] Considering the data published by these organizations (WHO and UNICEF), all countries in the studies included in this review have made positive progress in access to improved sanitation over time (1997–2020) while reducing the prevalence of stunting in children. Thus, sanitation improvements may benefit growth among children and adolescents aged >5 years,[11] which confirms the hypothesis of this study that lack access to WASH leads to more diarrheal diseases affecting children's growth.

Repeated exposure to fecal pathogens can thus cause malabsorption and loss of nutrients through diarrheal diseases developing into malnutrition and growth retardation, effects with negative impacts over the life span.[7,20] Sanitation, therefore, is an indispensable element of disease prevention and primary health care programs.[14] Therefore, good sanitation practices are responsible for boosting better health conditions in communities as well as in the nutritional status of children.[13]

Some studies found that a better water source alone did not provide complete health benefits. Children from households with access to piped water without adequate sanitation were 1.8 cm (0.1–3.6) shorter than children in households with sewerage.[21] This is associated with the need to improve sanitation in developing

Table 2
Information from selected articles for the meta-analysis of WASH vulnerability in child growth.

Reference	OR (95% CI)	Mean	WASH component	Total group size
Ademas et al., 2021[15]	3.85 (2.13–6.97)	–	Water	630
Ademas et al., 2021[15]	1.71 (1.23–2.38)	–	Sanitation	630
Ademas et al., 2021[15]	2.43 (1.74–3.40)	–	Hygiene	630
Bekele et al., 2021[19]	1.01 (0.80–1.28)	–	Water	33,744
Bekele et al., 2021[19]	1.33 (0.92–1.92)	–	Sanitation	33,744
Bekele et al., 2021[19]	1.02 (0.86–1.20)	–	Hygiene	33,744
Chakrabarti et al., 2020[11]	1.30 (1.07–1.57)	–	Water girls[a]	722
Chakrabarti et al., 2020[11]	1.21 (1.03–1.42)	–	Water boys[a]	722
Chakrabarti et al., 2020[11]	0.78 (0.57–1.07)	–	Sanitation girls[a]	722
Chakrabarti et al., 2020[11]	0.89 (0.66–1.19)	–	Sanitation boys[a]	722
Rah et al., 2020[18]	1.22 (0.96–1.53)	–	Water	1450
Rah et al., 2020[18]	1.63 (1.26–2.08)	–	Sanitation	1450
Mshida et al., 2018[10]	13.00 (5.80–30.00)	–	Water	310
Choudhary et al., 2021[28]	–	−1.49 (−1.50 to 1.47)	Water	58,038
Choudhary et al., 2021[28]	–	1.04 (1.02 to 1.07)	Sanitation	58,038
Checkley et al., 2004[21]	–	0.60 (−0.10 to 1.40)	Water	230
Checkley et al., 2004[21]	–	0.90 (0.20 to 1.70)	Sanitation	230
Diana et al., 2021[12]	–	−0.31 (−0.57 to 0.04)	Water	622
Diana et al., 2021[12]	–	−0.02 (−0.39 to 0.35)	Sanitation	622
Diana et al., 2021[12]	–	0.06 (−0.03 to 0.15)	Hygiene	622

CI, confidence interval; OR, odds ratio; WASH, water, sanitation, and hygiene.
[a] The authors Chakrabarti et al., 2020 extracted the results by gender, so we present the results with the terms “Water girls,” "Water boys," “Sanitation girls,” and “Sanitation boys.”

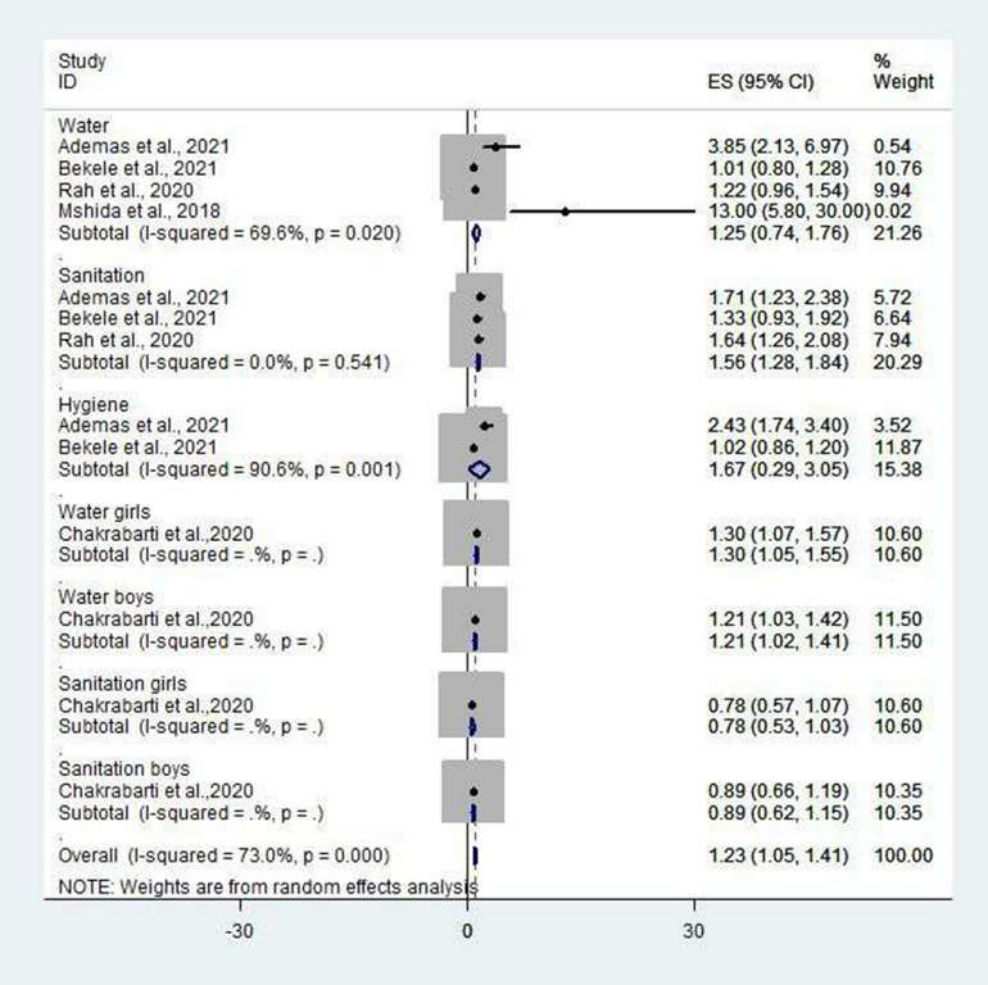

Fig. 2. Meta-analysis of the relationship between stunting and access to WASH using random effects analyses. I-squared = 73.0%, $P = 0.000$. Ademas et al., 2021,[15] Bekele et al., 2021,[19] Rah et al., 2020,[18] Mshida et al., 2018,[10] Chakrabarti et al., 2020.[11]

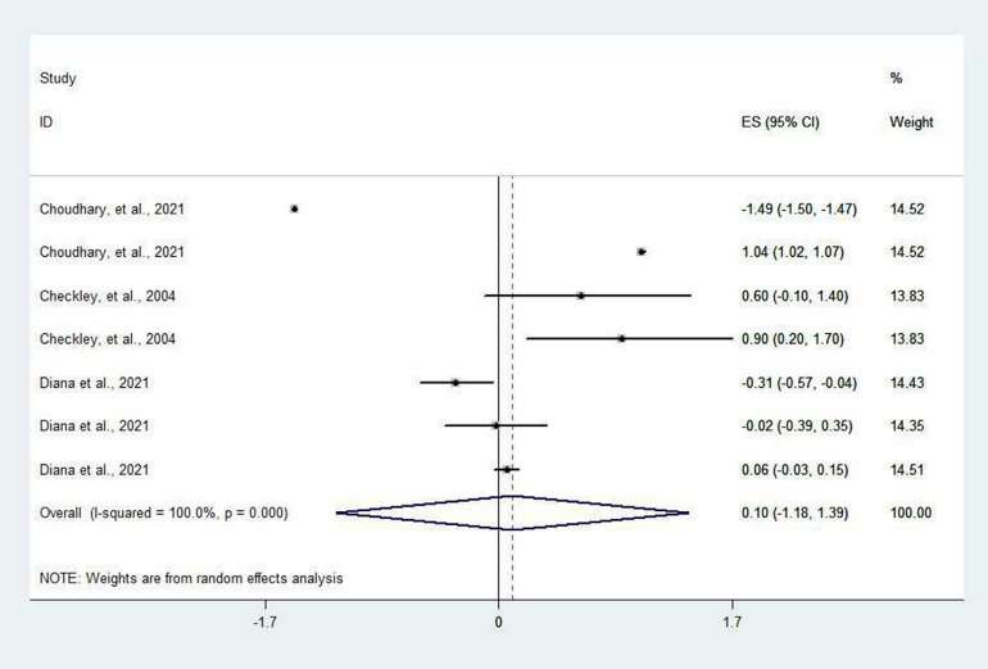

Fig. 3. Meta-analysis of the mean and confidence interval of height-for-age value varying by the sample of articles using random effects. I-squared = 100%, $P = 0.000$. Choudhary et al., 2021,[28] Checkley et al., 2004,[21] Diana et al., 2021.[12]

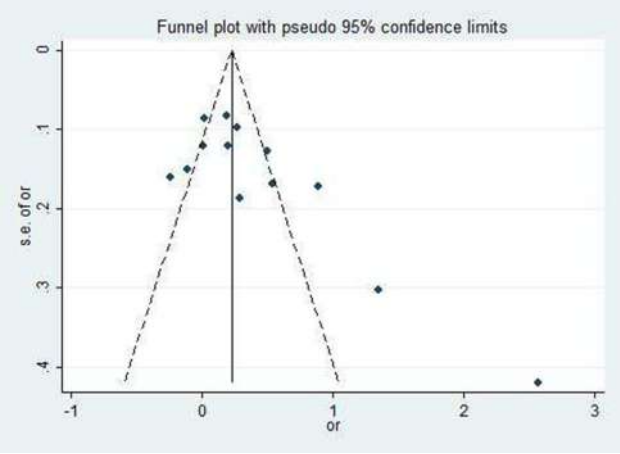

Fig. 4. A funnel plot was performed to investigate the risk of publication bias. Weighted mean differences of OR, funnel plot with 95% confidence limits.

countries to reduce the risk of water contamination. Another study found that children from households using surface water (e.g. rivers) for domestic purposes were 13 times more likely to be stunted than children from households using tap water.[10] Sanitation, therefore, is critical to improving access to safe drinking water and reducing the risk of diarrhea incidence and improving linear growth in children.[14] The synergy between sanitation, environmental impacts, the processes of infection, malnutrition, and child stunting is evident.

Access to sanitation is still a global challenge, where 46% of the world lacks access to safely managed sanitation.[22] This reflects the challenges of promoting structural public policies that help improve sanitation and consequently contribute to the adequacy of children's nutritional status. Currently, these issues are part of the global compact for sustainable development proposed by the United Nations 2030 Agenda.[23] Universal access to sanitation is established in Sustainable Development Goal 6. This goal seeks to establish global targets to stimulate the development of public policies by regional and local governments to overcome this sanitation crisis.

Our study has special relevance in light of the development of public policies and interventions for better child development. In addition to confirming the relationship between lack of access to WASH and child stunting, the main insight from the results was to identify sanitation as a determinant component. This finding suggests that WASH interventions to address child stunting should focus on access to safe sanitation and not just access to safe drinking water and hygiene. Child stunting goes beyond the contexts of poverty and food and nutrition insecurity, which are often addressed in the literature.[24,25] Our results suggest, as in other studies, that the environmental health of where people live is also directly related to child stunting.[26,27]

As for the methodological variability, we observed that the sample size of the studies was diverse, as well as the results generated from the analysis of the height deficit, presented in percentage value, OR, mean Z-score with a CI, and mean in centimeters. This justifies the limitation of the low number of studies included in the MA that met the eligibility criteria chosen for this study. For this reason, the MA considered: the values of height-for-age in OR and 95% CI values. Other limitations found in the study were articles that were not found in full (four articles) and studies that considered, but did not relate, WASH vulnerability and stunting in children and therefore were not included in this review. Also, some relevant articles in the literature may not have been included in this review, as there are other synonyms for WASH and stunting besides those mentioned.

Conclusion

The results of this SR and MA confirmed that stunting in children aged < 5 years is greater in locations with higher vulnerability to WASH. It was also shown that lack of improved sanitation is a component of WASH that is significantly associated with child stunting. Based on our findings, we recommend incorporating WASH strategies, especially sanitation, into the formulation of interventions integrating with health promotion policies for healthy early childhood development. It is recommended that future studies focus on the formulation of methodologies and systems for collecting data on the reality of sanitation and the nutritional status of children that are more inclusive and feasible for developing countries.

Author statements

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Ethical approval was not sought for this study, as it includes an analysis of secondary data.

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Competing interests

The authors have no competing interests to declare.

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Original Research

When religion prevails: examining religious and mainstream news coverage of measles-rubella vaccination in Indonesia

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ABSTRACT

Objectives: Indonesia's measles-rubella (MR) vaccination campaign faced public refusal due to religious objections. The government then lobbied the religious organization to issue a decree to permit the consumption of the MR vaccine, which would enhance public approval. Media outlets, including religious and mainstream media, played a crucial role in promoting the decree and the vaccine. Learning from this MR vaccination campaign in 2018, this study examined how the mainstream and alternative or religious media framed the MR vaccination and how it changed before and after the decree.
Study design/methods: A content analysis was performed on 234 news articles from Indonesian religious and mainstream media.
Results: Mainstream media positively framed MR vaccines, which were further amplified after the decree was issued. In contrast, religious media consistently depicted the opposing sides of the vaccine and its campaign. Both media types also predominantly cited the government and religious leaders in their articles.
Conclusion: While the mainstream media agenda aligns with the national agenda to promote the MR vaccine, religious media still emphasizes the risk of the vaccine. The prevalence of religious leaders in alternative media also suggests that the public, including religious leaders, may not necessarily accept the decree. Hence, more effort should be devoted to encouraging the media and religious leaders to accept the vaccine, as they may act as opinion leaders.

Introduction

The threat of measles and rubella (MR) haunts many countries, including Indonesia, where the MR vaccination rate remains low.[1] To solve this issue, the government undertook one of the world's largest MR vaccination campaigns, targeting more than 68 million children with an investment of nearly US$100 million. The first phase of the campaign in 2017 gained massive success, with 35 million vaccine uptakes. However, the second phase in August 2018, targeting 32 million children, encountered resistance and caused almost 10 million children to be uninoculated.[2]

Religious objections become the primary factor of vaccine hesitancy. The narrative that the vaccine is not 'halal' (permissible under Islamic law) as it contains pork materials widely circulates in this largest Muslim-majority country.[3] Indonesia's health ministry then lobbied the Indonesian Ulama Council (MUI), the supreme authority for religious affairs. On August 20, 2018, the MUI issued a decree declaring that the vaccine was 'haram' (religiously forbidden) as it contained materials from pigs, but it was permitted for use due to the emergency and lack of viable *halal* alternatives.[4]

Media outlets are essential in informing the religious decree and educating the public. Mass media can disseminate health messages and report health-related issues.[5] Studies have found compelling evidence concerning how exposure to media content can promote engagement in protective measures, including vaccination uptake.[6,7] However, aside from mainstream media, alternative media, such as religious media, become increasingly popular. This media discuss topics about current affairs as well as religion and provide alternative or counter-narrative.[8] Hence, religious media may portray a health issue differently from mainstream media.[9] Given this unique context, this study examines how mainstream and religious media present the news about the MR vaccine, which may influence public perception and knowledge regarding the vaccine.

Several message factors may affect the effectiveness of media campaigns, including message framing and source. Framing is the

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selection of specific issues of a message to define problems, promote a particular audience interpretation, and recommend solutions.[10] In the context of health, the message can emphasize the benefits of adopting a particular health behavior and the risk associated with the promoted behaviors.[11] This message frame affects how the audience interprets and comprehends an issue, which later alters the attitude and behaviors of individuals,[12] including their vaccination uptake.[13] Aside from framing, sources, defined as figures or characters delivering the message to the audience, are also vital.[11] The source referenced in a health message may affect people's support or acceptance of the promoted issue and influence the visibility of the health campaign.[14] However, little is known about the Indonesian mainstream and alternative media's frames when covering news about the MR vaccination and sources cited in the report. Moreover, it is unclear whether the media highlight different frames before and after the religious decree was announced.

Guided by the framing theory, this study scrutinizes the portrayal of the MR vaccination in Indonesian mainstream and religious media, which may influence public acceptance of immunization. This study examines how these two media types depict the MR vaccination and how the frame changes pre- and post-religious decree. In addition, this investigation identifies the sources covered in the news articles. This study extends the application of framing theory and carries important insights for Indonesia's public health efforts.

Method

Sample

This study analyzed the news articles using qualitative and quantitative content analysis. The qualitative approach enables researchers to obtain interpretations of the media message and identify emerging codes for the coding scheme development, whereas the quantitative analysis identifies trends and patterns of the news stories.[15] Hence, a combination of both approaches allows researchers to acquire a holistic understanding of the content analyzed in this study, particularly news articles published in four religious media and four mainstream media listed in Comscore Media Metrix.[16] Several keywords were used to identify the articles, including *measles-rubella*, *vaksin MR* (MR vaccine), *vaksinasi MR* (MR vaccination), *imunisasi MR* (MR immunization), *vaksin* (vaccine), *vaksinasi* (vaccination), and *imunisasi* (immunization). The duration of the articles was from August 6 to September 4, 2018, two weeks before and after the decree was issued on August 20, 2018. In total, 247 articles were collected (n mainstream media = 196; n religious media = 51). One of the authors conducted a manual data cleaning to remove duplications and irrelevant articles, leaving 234 articles for the final analysis (see Table 1).

Coding procedure

This study used a hybrid approach to develop the coding scheme, which integrated deductive and deductive approaches to balance codes from existing theoretical frameworks and codes derived from the analysis.[16] The final coding scheme consisted of four primary codes: frames, sources, types of media, and time.

The codes for message frames consisted of benefit frames and risk frames.[11] The benefit frames entailed the advantages or positive sides of the vaccination, whereas the risk frames pertained to potential problems or negative consequences of the MR vaccination. The inductive analysis generated the subcodes for the benefit (i.e. safe procedure, reliable manufacturer and vaccine, avoiding impacts of being unvaccinated, religiously permitted, and advantages of taking the vaccine, affordable cost, successful campaign) and risk frames (i.e. *haram* substance, uncertainty about *halal* certification, negative impacts of being vaccinated, and failure of the campaign). An article could have more than one source when they quoted different people. The articles were also labeled into religious and mainstream media based on their publishers. Regarding the time, the news stories were coded into 'before' and 'after the decree.'

Data analysis

One of the authors and a research assistant analyzed the news articles manually. Before coding the whole data set, both native Indonesian-speaking coders analyzed a subsample ($n = 30$) independently to test the intercoder reliability. The Cronbach's alpha coefficients from each item were calculated, and the lowest score was 0.92, indicating acceptable intercoder reliability.

Results

Message frames

The results revealed that more than half of the articles from the mainstream media used benefit frames ($n = 132$, 69.1%; see Table 2). In particular, 50 articles (26.2%) informed that the MR vaccine was religiously permitted. Although the vaccine contained *haram* substance, the MUI had declared a decree stating that people were allowed to take the jab in an emergency. Moreover, 22 news articles (11.5%) promoted the advantages of being vaccinated, especially preventing illnesses and protecting children. Around 16 articles (8.4%) also claimed that the vaccine came from reputable companies and had been approved by the World Health Organization. In addition, 16 articles (8.4%) highlighted the harmful impact of refusing the vaccine and MR, including pneumonia, brain inflammation, and death. Therefore, taking the jabs was crucial to avoid adverse consequences. Furthermore, 15 articles (7.9%) emphasized that vaccination was a safe procedure and would not cause severe side-effects. Some reports also talked about the campaign's success, given the high vaccination rate in several cities ($n = 12$, 6.3%) and how the public could take the jab at an affordable price or even for free ($n = 1$, 0.5%).

On the other hand, 59 articles (30.9%) from the mainstream media used risk frames. Moreover, 38 stories (19.9%) reported the uncertainty of the *halal* certification, which induced public hesitancy to get vaccinated and caused some areas to suspend the vaccination program. Some ($n = 13$, 6.8%) also shared the negative impacts of taking the jabs, including physical disability and death.

Table 1
Final data set.

Mainstream media	Number of articles	Alternative media	Number of articles
Tribunnews.com	32	Eramuslim.com	10
Detik.com	69	Islampos.com	16
Kompas.com	44	VOA-Islam.com	16
Liputan6.com	46	Muslimmedianews.com	1
Total	**191**	**Total**	**43**

Table 2
Message frames before and after the decree.

Frames	Mainstream media		Alternative media	
	Before, *n* (%)	After, *n* (%)	Before, *n* (%)	After, *n* (%)
Benefit frames	**30 (46.2)**	**102 (81)**	**2 (22.2)**	**13 (38.2)**
Safe procedure	7 (10.8)	8 (6.3)	–	–
Reliable manufacturer and vaccine	2 (3.1)	14 (11.1)	–	–
Avoiding the impacts of being unvaccinated	1 (1.5)	15 (11.9)	–	–
Religiously permitted	5 (7.7)	45 (35.7)	2 (22.2)	10 (29.4)
Advantages of taking the vaccine	11 (16.9)	11 (8.7)	–	3 (8.8)
Affordable	1 (1.5)	0 (0)	–	–
Successful campaign	3 (4.6)	9 (7.1)	–	–
Risk frames	**35 (53.8)**	**24 (19)**	**7 (77.8)**	**21 (61.8)**
Haram substance	2 (3.1)	4 (3.2)	–	3 (8.8)
Uncertainty about *halal* certification	28 (43.1)	10 (7.9)	7 (77.8)	15 (44.1)
Negative impacts of being vaccinated	5 (7.7)	8 (6.3)	–	3 (8.8)
Failure of the campaign	0 (0)	2 (1.6)	–	–

Around 3.1% ($n = 6$) of the total articles from mainstream media also highlighted that the MR vaccine contained *haram* substance. Finally, two articles (1%) discussed how the campaign failed to reach the target, indicating public resistance toward the MR vaccination.

In contrast, more than half of the articles from alternative media emphasized the risk frames ($n = 28$, 65.1%). Many ($n = 22$, 51.2%) discussed the uncertainty of the *halal* certificate and how taking a vaccination violated Islamic law. Some also questioned the decree, which allowed vaccination in an emergency, although the current state did not appear urgent. In addition, three articles (7%) elucidated the negative impacts of vaccination, including disability and death. Three others (7%) mentioned *haram* substances in the vaccine; thus, they should not be consumed.

Furthermore, 15 articles (34.9%) published by the religious media used benefit frames. Around 27.9% of the total articles ($n = 12$) informed how the religious decree allowed the vaccine to be consumed in emergencies. However, it was worth noting that most of these articles first mentioned that despite the decree, the vaccine was still *haram*. There was also content promoting the benefits of MR vaccination, such as protecting the children ($n = 3$, 7%).

Message frame before and after the decree

The Chi-squared tests for the mainstream media revealed a statistically significant difference in the message frames used before and after the decree. In particular, the use of benefit frames was significantly higher after the decree than before the decree ($\chi^2 = 24.32$, df = 1, $P < .001$, Cramér's V = 0.36). In contrast, the overall frames before and after the decree in religious media showed no significant difference, indicating the consistent promotion of risk frames ($\chi^2 = 1.1$, df = 1, $P > .05$).

Message source

The analyses discovered that articles from mainstream media predominantly cited government officials ($n = 92$, 42.5%) or religious leaders ($n = 61$, 28.4%). On the other hand, articles from alternative media mainly quoted religious leaders ($n = 26$, 56.5%; see Table 3).

Table 3
Message sources in mainstream and alternative media.

Message sources	Mainstream media		Alternative media	
	n	%	*n*	%
No source	6	2.8	3	6.5
Health expert	25	11.6	3	6.5
Government	92	42.8	6	13
Religious leaders or organizations	61	28.4	26	56.5
Advocacy groups	9	4.2	2	4.3
Citizens	19	8.8	6	13
Total	**215**	**100**	**46**	**100**

Discussion

Learning from the MR vaccination campaign in Indonesia, this study examines how Indonesian mainstream and alternative media, particularly the religious press, depicted the MR vaccine and its campaign in the country, which encountered religious objection due to the *haram* substance in the vaccine. In particular, this study analyzes how both types of media frame the MR vaccine before and after a religious decree was declared, as well as the source cited in the article. The findings enrich the literature on framing by examining news frames of different media types. In addition, this study offers recommendations for public health programs that aim to boost the vaccination rate.

Overall, the findings reveal that both mainstream and religious media outlets in Indonesia played a significant role and used different strategies in framing the MR vaccination campaign. In particular, more than half of the articles from mainstream media promoted the benefits of MR vaccination, such as the reliable manufacturer, protection of the children, and many others. Greater attention to the positive sides of vaccination is crucial for vaccine promotion. It may lead to favorable perceptions toward the jab and encourage the public to get vaccinated.[17] This framing effect has also been articulated in prospect theory, which proposes that exposure to gain-frame is especially effective for people who are risk-averse or would like to avoid uncertainty and can motivate them to take safe health behaviors, including actions to prevent diseases.[18–20] However, despite the dominance of benefit frames, mainstream media also used risk frames, with many reports highlighting the uncertainty of the *halal* certification and the negative consequences of taking the jabs.

On the other hand, religious media framed the MR vaccine differently as they predominantly used risk frames, focusing on the issues surrounding the *halal* certification and the adverse sides of the vaccine. The prominence of risk frames in religious media may negatively impact the success of the vaccination campaign. According to framing theory, the way media frame an issue affects the audience's attitude and evaluation of the subjects.[21] In a similar vein, agenda-setting theory postulates that news agenda shapes

public opinion and discourses.[22] Hence, the prevalence of negative coverage related to vaccination in religious media may intensify vaccine hesitancy, as it generates undesirable evaluations of vaccination.

The shift of frames in mainstream media after the issuance of the decree is also a noteworthy finding. The result discovers that the benefit frames significantly increased after the MUI declared the religious decree. This finding demonstrates the ability of the decree to change media attention. Apart from that, it also indicates alignment between media and national agendas. Consistent narratives or frames between the government and media are crucial to direct public opinion and induce a positive perception of the vaccine, which subsequently increases vaccine uptake.[23,24]

Although the number of benefit frames increased after the decree was announced, the alternative media still emphasized the risks of MR vaccination, especially the uncertainty of the *halal* certification, which remains the most significant concern contributing to vaccine hesitancy. Interestingly, the prevalence of discussion regarding *halal* certification still exists even after the decree was issued. This finding suggests that the decree may not be enough to convince the public and gain the public trust. Furthermore, it indicates religious media may provide an alternative opinion that may contradict the mainstream perspectives regarding an issue and intensify individuals' pre-existing attitudes toward vaccination.[25]

The findings also discover the prominent role of religious leaders, especially in alternative media. Interestingly, many articles published in religious media still used risk frames, implying that not all religious figures in the country agree with the religious decree declared by the central MUI. For instance, the religious leaders in Aceh, the only province enforcing Islamic law in Indonesia, still rejected the vaccine despite the issuance of the religious decree.[26] Hence, more effort should be devoted to convincing local religious figures, who may act as opinion leaders in their community, to accept the vaccination.

This study is not without limitations. First, this study analyzes articles from mainstream and religious media. However, the number of reports from the mainstream media is significantly more than the alternative media, which makes the comparison somewhat unbalanced. Moreover, this study focuses on the articles published 2 weeks before and after the decree. However, it may take time to inform the public regarding the decree and convince the people. Hence, future studies may extend the period of the sample articles.

Despite the aforementioned limitations, this study enriches health communication and promotion literature, as this investigation identifies similarities and differences in how the mainstream and alternative media frame health issues and public health campaigns. This study also contributes to current and future efforts to increase public understanding and acceptance of vaccination, which remains an important issue for the Indonesian government.[27] The results suggest that there should be better collaborations between the government and related actors, including media organizations and local religious leaders, in public health programs. The government should communicate more intensely with media outlets to direct their agenda, as some media organizations still promote narratives opposing the advocated issue. Apart from that, the findings underscore the need for effective communication strategies that take into account the concerns of different segments of the population, including religious communities. The results show that uncertainty about the *halal* status persists despite the religious decree. Moreover, some groups, including religious leaders, still do not accept the MR vaccine, which may also occur due to various cultural factors, such as the system of belief, values, and communication patterns.[28] Therefore, policymakers and health authorities should work with key opinion leaders, including religious figures, in the local communities to overcome public resistance and increase vaccine uptake.

Author statements

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No potential competing interest was reported by the authors.

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