

EVALUATING THE IMPORTANCE OF POLICY AMENABLE FACTORS IN EXPLAINING INFLUENZA VACCINATION: A CROSS-SECTIONAL MULTINATIONAL STUDY

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ABSTRACT

Objectives: Despite continuous efforts to improve influenza vaccination coverage, uptake among high-risk groups remains suboptimal. We aimed to identify policy amenable factors associated with vaccination and to measure their importance in order to assist in the monitoring of vaccination sentiment and the design of communication strategies and interventions to improve vaccination rates.

Setting: The US, the UK and France.

Participants: A total of 2,412 participants were surveyed across the three countries.

Outcome measures: Self-reported influenza vaccination.

Methods: Between March and April 2014, a stratified random sampling strategy was employed with the aim of obtaining nationally representative samples in the US, the UK and France through online databases and random-digit dialling. Participants were asked about vaccination practices, perceptions and feelings. Multivariable logistic regression was used to identify factors associated with past influenza vaccination.

Results: The models were able to explain 64-80% of the variance in vaccination behaviour. Overall, socio-psychological variables, which are inherently amenable to policy, were better at explaining past vaccination behaviour than demographic, socio-economic and health variables. Explanatory variables included social influence (physician), influenza and vaccine risk perceptions and traumatic childhood experiences.

Conclusions: Our results indicate that evidence-based socio-psychological items should be considered for inclusion into national immunisation surveys to gauge the public's views, identify emerging concerns, and thus proactively and opportunely address potential barriers and harness vaccination drivers.

ARTICLE SUMMARY

Strengths and limitations of this study

- We generated regression models comprised of a broad set of variables, most of which have been linked to vaccination behaviour.
- We also aimed to use representative samples of the population of interest in three different developed countries (the US, the UK and France).
- The employed survey measures concerned the individual and conditioned perceptions on their vaccination status.
- Our research may have suffered from respondent-related biases. For example, people for whom vaccination issues are particularly salient may have been more prone to participate.

BACKGROUND

Upper respiratory tract infections are a leading cause of mortality and morbidity in high-income countries, mostly among adults¹. Influenza is a major contributor to this burden of disease; estimates show that up to 49,000 people die every year in the US² and 40,000 in the European Union³ from influenza-related illness.

In most developed economies, an annual influenza vaccine is recommended and offered free of charge to those at higher risk of death from influenza complications, including pregnant women, individuals with eligible chronic illnesses and people aged 65 years and older. The vaccine is also available at a cost – usually in pharmacies or private healthcare facilities – to those who do not belong to a risk-group, but wish to protect themselves. In the US, for example, where the vaccine is recommended to all adults, approximately one third of healthy adults under 65 years old vaccinate against influenza every year⁴.

Despite continuous efforts to improve influenza vaccination coverage, uptake among high-risk groups remains low. In 2013/2014, for example, 65% of older adults (≥ 65 s) and 46% of younger adults with eligible health conditions were vaccinated against influenza in the US⁴. In the same season, vaccination rates in the UK, one of the highest in Europe, were 73% in ≥ 65 s and 53% in eligible under 65s, both below the minimum 75% coverage recommended by the World Health Organisation^{5, 6}. Worryingly, a 151% rise in excess winter deaths in England and Wales in 2014/15, partly attributed to the circulation of a mutated A(H3N2) influenza strain which made the vaccine significantly less effective⁷, alongside unseasonable warm weather in 2015/2016, resulted in the lowest vaccination uptake in more than a decade⁸.

Vaccination decisions are shaped by a myriad factors, including demographic, socio-economic and socio-psychological factors⁹⁻¹². The latter are of particular interest, given that they are inherently amenable to policy and interventions to change behaviour. Yet, few countries routinely collect data on people's beliefs and perceptions towards vaccination, and those that do often use one open question (e.g. "Why didn't you get a flu shot last winter?")¹³. Although cheaper and easier to administer, this form of enquiry does not take into account people's tendency to fall back on readily available information (e.g. the first thought that comes to mind) or report post-decisional rationalisations of their behaviours (e.g. "I did not

vaccinate, hence it must not be necessary”) rather than actual drivers^{14, 15}. Moreover, these data do not allow comparative analyses between vaccinated and unvaccinated people.

Multilateral efforts to measure and improve confidence in vaccines are gathering pace^{16, 17}, yet they are built upon a body of evidence which, although extensive and insightful, has a number of gaps. One key limitation is that many studies evaluating the link between socio-psychological factors and influenza vaccination do not use multivariable analysis, thus the importance of a given variable in relation to others often remains unknown. Studies that do employ multivariable analysis seldom perform (or report) robustness checks and usually comprise a limited number of variables, which can result in omitted-variable bias, whereby the model compensates for the missing variables by over or underestimating the effect of the included variables^{9, 18-19}. For example, omitted-variable bias could explain why the model developed by Weinstein et al. – comprised of seven variables – showed that anticipated regret of not vaccinating was more important than other established influenza perceptions or why they did not find an association between vaccine effectiveness and vaccination uptake in this US sample¹⁸. Moreover, these studies frequently include proxies of vaccination uptake, such as historical vaccination (i.e. vaccination in previous seasons not including the most recent) in the case of retrospective studies or intention to vaccinate in the case of prospective studies, as independent variables^{9, 19, 20}, thereby artificially boosting the explanatory ability of the model – because most people who vaccinate against influenza do so periodically – without necessarily explaining vaccination behaviour (e.g. people vaccinate because they feel vulnerable and/or receive a reminder from their GP every winter). As Brewer and colleagues note, other important methodological shortcomings are the prevalent use of weak survey measures (e.g. generic risk perceptions rather than own perceived risk) and small convenience samples, which may affect the validity and generalisability of findings¹¹. A related drawback is that most of the evidence in this area is produced in the US, thus important contextual issues remain unexplored. Furthermore, vaccination coverage and factors underpinning uptake among healthy adults are often unknown.

We sought to address these limitations by generating regression models comprised of a broad set of variables, most of which have been linked to vaccination behaviour, by employing measures that gauge individuals’ own perceived risk (e.g. “The flu could make *me* severely ill”) and condition their perceptions upon having or not having received the vaccine (e.g. “*With no flu vaccine*, I would feel very vulnerable to the flu”) ¹¹, and aiming to use

representative samples of the population of interest in three different developed countries: the US, the UK and France. In order to assist in the monitoring of vaccination sentiment and the prioritisation and design of communication strategies and interventions to increase influenza vaccination across different contexts, this study aimed to answer three research questions: (1) What are the variables that consistently explain recent influenza vaccination uptake? (2) What is the importance of policy amenable factors in relation to demographic, socio-economic and health characteristics in explaining past vaccination behaviour? (3) Are the factors associated with influenza vaccination comparable across countries?

METHODS

Study sample

Using stratified random sampling, we aimed to survey nationally representative adult samples from the US, the UK and France, about vaccination between March and April of 2014. Interlocking quotas based on gender, age and income were set. In addition, to ensure national representativeness, regional, settlement type (rural / urban) and ethnicity non-interlocking quotas were put in place.

Since some of the included variables had not been previously tested and others were not consistently correlated with vaccination in previous studies, we assumed that the correlation coefficient between dependent and independent variables was 0.1 (a small effect size), the minimum sample was calculated to be 782 subjects per country ($\alpha=0.05$; $1-\beta=80\%$) with PASS version 11.

The American Institutes for Research (US) and the Imperial College Research Ethics Committee (UK) granted research ethics approval. The French *Commission nationale de l'informatique et des libertés* and *Comités de protection des personnes* granted waivers to approval. Participants were informed about the nature of the study and provided consent.

Procedure

A market research company (Double Helix) was responsible for piloting, programming the online survey and conducting the telephone interviews. Ten pilot interviews (seven face-to-

face and three telephone interviews) were conducted with purposively selected participants in the UK to test the survey's face and content validity, and ease of completion. Additionally, 10 pilot interviews were conducted over the phone in the US and 10 in France with the aid of a screen sharing platform. Interviews were conducted by a trained researcher while the rest of the team observed via live broadcast. The pilot showed the survey was easy to complete and understand, and lasted approximately 20 minutes. The refinements to the study materials were related to wording and format. Self-completion online surveys were then sent to a non-probability online panel and random-digit dialling was employed to recruit a proportion of the 65+ age category and those belonging to D/E socio-economic groups, due to their limited access to or lack of familiarity with internet-based applications²¹ (see Box S1 in Supplementary material for more details about non-probability online panels).

As a quality control measure, participants classified as 'speeders' (completed the survey in half of the average length – 16 minutes) and 'flat-liners' (gave homogenous responses and completed the survey in less than half of the optimum survey length – 20 minutes) were removed and replaced²².

Instrument

The measures reported here are a subset of a larger vaccination survey (available from the authors upon request). Our analyses included 32-34 items (Table S1 in Supplementary material). We selected socio-psychological items that had been linked to influenza vaccination based on existing evidence. These comprised adapted constructs from the Health Belief Model²³ and Protection Motivation Theory²⁴ – notably, influenza and vaccine risk perceptions, vaccine effectiveness and self-efficacy^{9-12, 25} –, perceived knowledge of the vaccine¹⁰ and items assessing trust in key vaccination stakeholders²⁶. Additional policy amenable factors which had infrequently been used in the context of vaccination, but were considered potential explanatory variables, were also tested. These were worry of infecting other people (if unvaccinated)²⁷ – a measure aimed at evaluating the extent to which people vaccinate to protect others –, perceived control over influenza^{28, 29}, regret of contracting influenza³⁰, childhood traumatic health experiences³¹ – to evaluate their influence on adult vaccination behaviour – and health decision-making preferences^{32, 33} – to further explore the effect of the doctor-patient relationship on vaccination acceptance. Participants' socio-

economic, demographic and health characteristics previously associated with influenza vaccination were prioritised^{9, 34}.

We used 11-points likert scales (0-10) for the majority of socio-psychological items, as these are recognised for their reliability and ease of completion³⁵, and multiple-choice items and alternate-choice items when appropriate. Except for trust, health decision-making preferences, and childhood traumatic health experiences items, socio-psychological measures were disease or vaccine-specific to avoid misinterpretation. As illustrated in the introduction, our questions also aimed to capture the respondent's perception of their own personal risk rather than their views on risk of illness in the wider population. Thus, we asked how likely it is that they might become ill rather than how likely people generally are to get influenza. We also wished to specifically focus their attention on the risk of influenza in the presence or absence of vaccination, as people may feel more or less protected depending upon their vaccination status. The questions were therefore in the form of 'Without a vaccine, it is likely I will get the flu' rather than simply assessing their views on the likelihood of getting influenza. Finally, when thematic hierarchy (e.g. from general to specific) was not important, items were rotated to minimise response bias.

Data analysis

We used the following formula to calculate response rates: number of surveys completed divided by sent emails or interviews attempted minus ineligible individuals, multiplied by 100. Descriptive statistics, Pearson's Chi-square and t-tests were computed to explore the relationships between the assessed variables and self-reported past vaccination behaviour. Point-biserial correlations were calculated and Chi-square statistics were converted into correlation coefficients to explore whether the relationship between the dependent and independent variables matched or exceeded a coefficient of 0,1 – the assumption employed to calculate the sample size. Cronbach's alpha was used to explore the reliability of the proposed measures across countries. The outcome measure was receiving an influenza vaccine in the last 6 months (2013/2014 influenza season).

Given that the dependent variable was binary, logistic regression analysis was conducted to identify the variables associated with past influenza vaccination. Four continuous variables with "I don't know/not applicable" responses were dichotomised as follows: values

expressing agreement with a given statement (6-10) were coded as 1 = “yes” and the rest (0-5 and “I don’t know/not applicable”) were coded as 0 = “other than yes” (see Tables S2-S4 in Supplementary material).

Although a software-based stepwise approach is widely used in logistic regression, in recent years the purposeful selection of variables has been favoured over deterministic model-building methods. This is because the latter tend to rely on automatic selection of variables based only upon mathematical criteria, which can lead to over-fitting or under-fitting models. Therefore, we used a manual stepwise, hierarchical approach, whereby blocks of variables were entered in a sequence based upon previous evidence and our aim of assessing the importance of policy amenable factors in explaining influenza vaccination (see Box S2 in Supplementary material for a full description of the approach)³⁶.

Two goodness-of-fit tests – chi-square and Nagelkerke R^2 – were used to assess the overall model (M1) and each of the 7 models (blocks) generated using the hierarchical approach. Employing a classification cut-off point of 0.5, a final model with a Nagelkerke R^2 value close to 1, which indicates optimal model fit, was sought.

Thorough checks to ensure the robustness of the models were conducted, including variance inflation factor (VIF) to assess collinearity, standardised residuals to detect and evaluate outliers and Cook’s distance to identify influential cases. Separate analyses entering the blocks of variables in reverse order were also performed (i.e. from block 7 to block 1) to evaluate whether the order in which variables were entered significantly modified our results. Data were analysed using IBM SPSS Statistics version 22.

RESULTS

Participants

The online survey was completed by 814 participants in the US, 791 in the UK and 787 in France. Online response rates were low (US=1%; UK=1,7%; France=2,4%), albeit consistent with research on non-probability online panels showing that, in recent years, response rates have fallen to a point where in many cases they are 10% or less³⁷. Eighty participants were interviewed via the telephone in the US, 100 in the UK and 100 in France. Telephone

response rates were 6-9%. Telephone interviews targeted older people and those belonging to low socio-economic strata, two populations with particularly low response rates³⁸. Recruitment flow diagrams for the online and telephone samples are presented in Figures S1a-S3a and S1b-S3b, respectively (Supplementary material). Except for education in the US – the sample was more educated than the general population –, there were no significant differences between the characteristics of the final samples (US=801; UK=806; France=805; total sample N=2,412) and those of the general population, when available (Table 1). To facilitate survey completion and improve data accuracy, household income data for this study was collected using a limited number of bands relevant to each country. Therefore, it cannot be directly compared against census data, which collects more granular income information per household. However, we have used as a reference the band that most approximate to the census median household income (Table 1). In the US and the UK, roughly half of the sample was below the reference band and the other half was above; whereas in France, the number of participants who reported a household income below the median was substantially higher than those over the median (Table 1).

Healthcare professionals were excluded from the final samples as their decision-making processes are influenced by those they care for or regulated by healthcare authorities, thus some of their motivations and concerns may differ from those of the general population³⁹. Subgroup analyses confirmed these differences (available upon request).

Differences between vaccinated and non-vaccinated participants

Overall, the responses of vaccinated and unvaccinated participants were significantly different ($p < 0.05$ - 0.001) and comparable across countries (Tables S2-S4 in Supplementary material). Those who had received an influenza vaccine were older, reported having an eligible health condition, had a private or public health insurance, lived with a partner (US/France), were wealthier (US/France) and more educated (US). They were also less constrained by practical barriers and more likely to report that their physician and relatives thought they should vaccinate than those who had not received a vaccine. Vaccinated participants were more concerned about the risks of influenza, less worried about the risks of the vaccine and more trusting of vaccine manufacturers and providers than unvaccinated participants. Vaccinees reported possessing a better understanding of the influenza vaccine

Table 1. Participant characteristics

Characteristic	Categories	US (N=801) ¹		UK (N=806) ²		France (N=805) ³	
		Sample	Population	Sample	Population	Sample	Population
Gender	Female	50%	51%	52%	51%	53%	52%
Age	18-64	80%	80%	77%	77%	76%	76%
	≥65	20%	20%	23%	23%	24%	24%
Ethnicity	White	69%	78%	88%	87%	-	-
	Other	30%	22%	11%	13%	-	-
	Prefer not to say	1%	-	1%	-	-	-
Annual household income ^a	<\$50,000/£20,000/€26,000	43%	-	46%	-	53%	-
	≥\$50,000/£20,000/€26,000	49%	-	46%	-	34%	-
	Prefer not to say	8%	-	9%	-	13%	-
Marital status	Living as a couple	60%	Unavailable ^b	56%	58%	54%	Unavailable ^c
	Not living as a couple	39%	Unavailable ^b	44%	42%	45%	Unavailable ^c
	Prefer not to say	1%	-	1%	-	1%	-
Education	No university degree	49%	71%	60%	73%	64%	76%
	University degree	45%	29%	37%	27%	29%	24%
	Prefer not to say	5%	-	3%	-	7%	-
Settlement type	Urban	76%	81%	77%	81%	78%	78%
	Rural	24%	19%	23%	19%	22%	22%
Vaccination status	<65 vaccinated	43%	37%	27%	Unavailable ^d	16%	Unavailable ^c
	≥65 vaccinated	66%	65%	75%	73%	50%	53%

¹Population estimates for gender, age, ethnicity, income, marital status, education and settlement type are 2012/2013 estimates from the US Census Bureau⁴⁰. Influenza vaccination status is from the 2013/2014 season⁴. ^aThe reference income band was the closest to the US 2012/2013 median household income (\$53,046)⁴⁰. ^bCensus data only includes persons who are married with spouse present, married with spouse absent and separated (42%).

²Population estimates for gender, age, ethnicity, marital status, education and settlement type are 2011 and 2012/2013 estimates from the UK Office for National Statistics^{41,42}. Influenza vaccination status is from the 2013/2014 season⁵. ^dAvailable data for <65s include children. ^aThe reference income band was the closest to the UK 2012/2013 median household income (£22,880)⁴³.

³Population estimates for gender, age, income, marital status, education and settlement type are 2011 and 2012/2013 estimates from France's National Institute of Statistics and Economic Studies⁴⁴. Ethnicity was not collected due to country-specific data protection restrictions. Influenza vaccination status is from the 2013/2014 season⁴⁵. ^eAvailable data for <65s include children. ^aThe reference income band was the closest to France's 2012/2013 median household income (€29,330)⁴⁴. ^cCensus data only includes people who are legally married (49%).

Note: Differences between samples and populations were evaluated using Fisher's Exact test. Except for education in the US (p<0.001), we found no significant differences. Percentages may not total 100 due to rounding.

and were more prone to let physicians make decisions about their health (US/UK) than those who had not vaccinated. Lastly, vaccinated participants were less likely to have had a bad vaccine or injection-related experience (UK) and more likely to have had a scary health-related experience in childhood than unvaccinated participants.

Factors associated with past influenza vaccination in regression analyses

When all variables were assessed concurrently, the models that best fitted the data (M6-M8) explained 73% of the variance in past vaccination behaviour in the US, 80% in the UK and 64% in France (Nagelkerke $R^2 = 0.644-0.795$) (Tables 2-4). The first models (M1) included all the variables, thus were less parsimonious than M6-M8, yet they explained a similar share of the variance (66-80%). When using the hierarchical approach, the first-step models (M2), which included demographic, socio-economic and health variables, fitted the data poorly-to-moderately and accounted for 22% the variance in past vaccination behaviour in the US, 38% in the UK and 19% in France. Practical barriers only explained 3% of the variance in the US (M3) and were not significant in the UK and France. Social influence explained 14% of the variance in the US (M4), 21% in UK and 25% in France (M3). Influenza perceptions accounted for 30% of past vaccination behaviour in the US (M5), 17% in the UK and 18% in France (M4), whereas influenza vaccine perceptions only explained 1% of this behaviour in the US (M6), 2% in the UK and 1% in France (M5). Finally, trust items explained less than 1% of the variance in the US, whilst decision-making preferences and childhood experiences explained 2% of the variance in the UK and 1% in France.

When blocks were entered in reverse order, demographic, socio-economic and health variables contributed little to the variance in past vaccination behaviour – 3% (US), 1% (UK) and 0% (France). This is not surprising, since people's characteristics have an effect on their perceptions, thus they explain some of the same variance. This result further proves that poorly specified models – which are not evidence-based – lead to biased estimates (the detailed results of these analyses are available from the corresponding author upon request).

Robustness checks showed that the variables which were significant in M1, remained significant across most 11-21 specifications, with some exceptions. In the US, “vaccine is painful” became non-significant when non-significant influenza perceptions were removed. This suggests that the latter had a suppressor effect on the former, i.e. their inclusion

Table 2 Factors associated with past influenza vaccination in regression analysis – US

Variables	M1		M2		M3		M4		M5		M6		M7		M8	
	OR	SE			OR	SE	OR	SE	OR	SE	OR	SE	OR	SE	OR	SE
Age	1.019	0.458	1.369	0.271	1.210	0.275	1.116	0.292	1.230	0.396	1.006	0.443	1.093	0.441	1.057	0.446
Eligible health condition	2.528**	0.329	3.050***	0.204	3.079***	0.208	2.469***	0.222	2.145**	0.296	2.549**	0.320	2.531**	0.320	2.531**	0.323
Private insurance	3.463***	0.386	2.833***	0.242	2.611***	0.246	2.197**	0.265	2.394**	0.337	3.062**	0.367	3.269***	0.372	3.374***	0.377
Public insurance	4.507***	0.415	3.461***	0.258	3.143***	0.262	2.542***	0.282	3.163***	0.362	4.137***	0.391	4.158***	0.391	4.273***	0.397
Gender	0.916	0.269	0.913	0.166	0.948	0.171	0.859	0.185	0.907	0.240	0.931	0.253	0.867	0.257	0.898	0.259
Marital status	0.672	0.294	1.093	0.185	1.062	0.188	1.032	0.204	0.890	0.266	0.743	0.281	0.759	0.283	0.728	0.286
Income	1.146*	0.074	1.198***	0.046	1.166**	0.049	1.140**	0.052	1.145**	0.067	1.143*	0.070	1.130*	0.070	1.145*	0.070
Education	1.052	0.095	0.740	0.182	1.036	0.062	0.983	0.067	1.025	0.088	1.046	0.093	1.042	0.093	1.035	0.093
Ethnicity	0.664	0.287	1.369*	0.271	0.681**	0.186	0.665**	0.202	0.681	0.254	0.677	0.266	0.695	0.270	0.693	0.271
Vaccine access	1.277	0.384														
Time to vaccinate	2.182**	0.356			2.804***	0.220	2.565***	0.239	2.417**	0.303	2.194**	0.319	2.535**	0.329	2.432**	0.331
Physician's opinion	4.361***	0.345					6.909***	0.211	2.946***	0.276	3.700***	0.309	4.260***	0.322	4.285***	0.321
Relatives' opinion	0.866	0.312														
Vulnerable to influenza	1.335***	0.069							1.359***	0.056	1.291***	0.059	1.284***	0.059	1.290***	0.060
Susceptible to influenza	1.013	0.056														
Likelihood of catching influenza	1.235***	0.060							1.238***	0.049	1.238***	0.055	1.226***	0.056	1.216***	0.056
Severity of influenza (bed days)	1.121	0.126														
Severity of influenza	0.908*	0.061							0.911*	0.051	0.902*	0.055	0.909*	0.055	0.903**	0.055
Fear of influenza	0.973	0.063														
Worry of transmitting influenza	0.932	0.056														
Perceived control over influenza	0.752***	0.056							0.741***	0.047	0.757***	0.052	0.748***	0.052	0.744***	0.052
Regret of catching influenza	1.165**	0.054							1.112**	0.043	1.117**	0.049	1.126**	0.049	1.122**	0.050
Perceived knowledge of vaccine	0.406**	0.390									0.368**	0.361	0.368**	0.366	0.388**	0.367
Effectiveness vaccine	1.249***	0.066									1.188**	0.062	1.222**	0.064	1.225***	0.064
Vaccine transmits influenza	0.848**	0.054									0.827***	0.046	0.835***	0.046	0.836***	0.047
Vaccine contents are dangerous	0.961	0.055														

Vaccine is painful	1.775*	0.329				1.712*	0.304	1.585	0.309	1.558	0.310
Vaccine-related self-efficacy	1.010	0.053									
Trust in physician (scale)	0.836*	0.096						0.796**	0.090	0.809**	0.091
Trust in manufacturers	0.895	0.081									
Trust in health authorities	1.013	0.086									
Shared decision-making doctor	0.953	0.147									
Bad experience vaccines - child	1.449	0.417									
Scary health experience - child	2.126*	0.464								2.153*	0.450
Number of participants	724	724	724	724	724	724	724	724	724	724	724
Nagelkerke R	0.734	0.215	0.252	0.389	0.686	0.719	0.725	0.727			

OR = Odds ratio; p = p-value; SE = standard error; *p < 0.1, **p < 0.05, ***p < 0.001. The change in model fit indicated by chi-square test for each block of variables was always significant (p < 0.1).

Table 3 Factors associated with past influenza vaccination in regression analysis – UK

Variables	M1		M2		M3		M4		M5		M6	
	OR	SE	OR	SE	OR	SE	OR	SE	OR	SE	OR	SE
Age	2.044	0.437	6.204***	0.238	3.560***	0.277	2.231**	0.389	1.786	0.399	1.919	0.421
Eligible health condition	4.088***	0.413	8.627***	0.226	4.002***	0.260	4.107***	0.343	4.215***	0.368	4.351***	0.393
Private insurance	3.115**	0.472	1.864**	0.280	1.855*	0.332	2.858**	0.412	3.227**	0.429	2.871**	0.451
Gender	0.629	0.321	0.611**	0.188	0.677*	0.222	0.508**	0.286	0.475**	0.298	0.580*	0.312
Marital status	2.018**	0.337	1.993***	0.207	1.795**	0.244	1.897**	0.303	1.908**	0.314	1.897**	0.323
Income	0.918	0.105	0.946	0.062	0.967	0.072	0.943	0.089	0.905	0.096	0.906	0.100
Education	0.962	0.103	0.979	0.061	0.966	0.072	0.981	0.089	0.947	0.094	0.976	0.098
Ethnicity	1.768	0.478	0.877	0.305	1.549	0.361	1.953	0.423	1.695	0.452	1.757	0.464
Vaccine access	1.380	0.457										
Time to vaccinate	1.295	0.427										
Physician's opinion	3.447***	0.371			7.751***	0.247	4.296***	0.331	2.962**	0.347	3.097**	0.359
Relatives' opinion	2.205**	0.355			3.061***	0.245	2.193**	0.316	2.195**	0.333	2.103**	0.344
Vulnerable to influenza	1.183**	0.081					1.268***	0.071	1.264**	0.075	1.233**	0.076
Susceptible to influenza	0.889*	0.066					0.863**	0.058	0.904*	0.061	0.882**	0.063
Likelihood of catching influenza	1.355***	0.078					1.214**	0.063	1.298***	0.070	1.311***	0.073
Severity of influenza (bed days)	1.317**	0.130					1.295**	0.116	1.277**	0.119	1.314**	0.121
Severity of influenza	1.062	0.073										
Fear of influenza	0.970	0.068										
Worry of transmitting influenza	0.872**	0.066					0.881**	0.059	0.865**	0.060	0.870**	0.062
Perceived control over influenza	0.832**	0.064					0.787***	0.056	0.812***	0.058	0.811***	0.060
Regret of catching influenza	1.324***	0.064					1.348***	0.057	1.301***	0.057	1.326***	0.060
Perceived knowledge of vaccine	2.098*	0.410							2.123*	0.383	2.100*	0.392
Effectiveness of vaccine	1.112	0.077										
Vaccine transmits influenza	0.901	0.066							0.873**	0.051	0.865**	0.055
Vaccine contents are dangerous	0.896	0.080										
Vaccine is painful	1.732	0.412										
Vaccine-related self-efficacy	1.164*	0.082							1.203**	0.072	1.208**	0.076

Trust in physician (scale)	0.899	0.107					
Trust in manufacturers	0.868	0.088					
Trust in health authorities	0.986	0.098					
Shared decision-making doctor	0.642**	0.165				0.675**	0.158
Bad experience vaccines - child	0.252**	0.557				0.267**	0.526
Scary health experience - child	3.434**	0.496				3.254**	0.460
Number of participants	728	728	728	728	728	728	728
Nagelkerke R	0.798	0.378	0.589	0.759	0.777	0.795	

OR = Odds ratio; p = p-value; SE = standard error; *p < 0.1, **p < 0.05, ***p < 0.001. The change in model fit indicated by chi-square test for each block of variables was always significant (p < 0.1).

Table 4 Factors associated with past influenza vaccination in regression analysis – France

Variables	M1		M2		M3		M4		M5		M6		M7	
	OR	SE	OR	SE	OR	SE	OR	SE	OR	SE	OR	SE	OR	SE
Age	2.772**	0.342	4.544***	0.208	4.405***	0.209	2.861***	0.246	3.312***	0.293	3.193***	0.299	2.938***	0.302
Eligible health condition	1.196	0.332	2.142***	0.212	2.154***	0.213	1.565*	0.248	1.173	0.295	1.215	0.300	1.087	0.309
Private insurance	2.423*	0.493	1.525	0.353	1.484	0.355	1.499	0.397	2.221*	0.488	2.234	0.497	2.373*	0.495
Gender	1.281	0.292	0.766	0.196	0.764	0.197	0.944	0.228	1.089	0.265	1.169	0.270	1.207	0.275
Marital status	1.935**	0.316	1.236	0.216	1.245	0.216	1.251	0.246	1.872**	0.292	1.924**	0.297	1.970**	0.301
Income	1.106	0.121	1.148	0.085	1.140	0.085	1.159	0.097	1.056	0.111	1.056	0.112	1.066	0.114
Education	1.151	0.092	1.093	0.062	1.090	0.062	1.103	0.072	1.224*	0.086	1.201**	0.087	1.179*	0.088
Vaccine access	0.501*	0.387			1.535*	0.252	1.211	0.283	0.849	0.333	0.726	0.338	0.650	0.343
Time to vaccinate	0.862	0.401												
Physician's opinion	7.464***	0.352					13.69***	0.237	7.327***	0.275	6.904***	0.280	7.161***	0.288
Relatives' opinion	0.806	0.347												
Vulnerable to influenza	1.100	0.065												
Susceptible to influenza	0.922	0.064												
Likelihood of catching influenza	1.231**	0.069							1.229***	0.053	1.252***	0.055	1.243***	0.056
Severity of influenza (bed days)	1.077	0.137												
Severity of influenza	0.999	0.067												
Fear of influenza	0.986	0.058												
Worry of transmitting influenza	1.077	0.064												
Perceived control over influenza	0.846**	0.054							0.812***	0.049	0.844***	0.050	0.836***	0.051
Regret of catching influenza	1.319***	0.063							1.388***	0.051	1.364***	0.052	1.376***	0.053
Perceived knowledge of vaccine	1.319	0.356												
Effectiveness of vaccine	1.067	0.076												
Vaccine transmits influenza	0.958	0.063												
Vaccine contents are dangerous	0.871**	0.058									0.868**	0.046	0.852***	0.047
Vaccine is painful	0.869	0.465												
Vaccine-related self-efficacy	1.006	0.065												

Trust in physician (scale)	1.005	0.105						
Trust in manufacturers	0.955	0.086						
Trust in health authorities	0.900	0.089						
Shared decision-making doctor	0.997	0.164						
Bad experience vaccines - child	0.854	0.448						
Scary health experience - child	4.139***	0.447					3.804**	0.429
Number of participants	699	699	699	699	699	699	699	699
Nagelkerke R	0.734	0.189	0.195	0.445	0.619	0.631	0.644	

OR = Odds ratio; p = p-value; SE = standard error; *p < 0.1, **p < 0.05, ***p < 0.001. The change in model fit indicated by chi-square test for each block of variables was always significant (p < 0.1).

strengthened the effect of the variable in question⁴⁵. In the UK, gender became significant when non-significant vaccine perceptions were removed, and “vaccine transmits influenza” became significant when “vaccine contents are dangerous” was removed. In both cases, this indicates that the removed variables were confounders of those that became significant⁴⁶. In France, “trust in manufacturers” was a confounder of education – the latter became significant in the absence of the former – and “trust in physician” was a suppressor of “vaccine access” – the latter became non-significant when the former was excluded^{46, 47}. Consequently, all the variables that were significant in M1, one non-significant variable that became significant while performing robustness checks (“vaccine transmits influenza” in the UK) and all the controls were included in the hierarchical models. The magnitude and significance of the relationship between independent and dependent variables varied little between the first models (M1) – where all the variables were entered at the same time – and the last models (M6-M8) – where a reduced number of variables were entered in blocks –, which is a further indication of the robustness of our findings. Detailed robustness checks are not presented here for brevity, but are available from the corresponding author upon request.

All the correlation coefficients between the dependent and the independent variables were higher than 0.1, except for two variables which were tested for the first time in this study: “Bad experience vaccines – child” ($r = -0,082$, $p < 0.05$ in the UK; $r = 0.040$, $p > 0.05$ in the US; and $r = -0.064$, $p > 0.05$ in France) and “Scary health experience – child” ($r = 0.090$, $p < 0.05$ in the US (detailed results are available from the corresponding author upon request).

Cronbach’s alpha coefficients ranged from acceptable ($\alpha = 0.65$) to excellent ($\alpha = 0.87$) and they were comparable across countries for each evaluated scale, except for “trust in vaccination stakeholders”, which was considerably less reliable in France (Table S5 in Supplementary material). Overall, these results indicate that the scales worked in a similar manner across the three countries. Further psychometric analyses and scale refinement will be performed and reported in a separate article.

Collinearity diagnostics showed that all variables had VIF values below 5, indicating there is no cause for concern⁴⁸. Standardised residuals were also examined to identify outliers. Less than 5% of the cases had standardised residuals above 2 and no more than 1% had absolute values higher than 3, thus there was no need to eliminate or transform cases⁴⁹. Cook’s

distance statistics were evaluated to identify cases exerting excessive influence on the model. No values were higher than 1, which shows that no case had to be excluded on that basis⁵⁰.

DISCUSSION

This study aimed to identify policy amenable factors associated with recent influenza vaccination uptake among adults in three high-income countries and to quantify their impact. Our results support previous findings and add new insights.

The final models robustly explained 64-80% of the variance in past vaccination behaviour and although some predictors were country-specific, we found important commonalities (Table 5). To the best of our knowledge, ours is the first study to demonstrate that socio-psychological variables consistently explain most of the variance in past influenza vaccination behaviour, over and above demographic, socio-economic and health variables (49% vs. 22% in the US, 42% vs. 38% in the UK and 45% vs. 19% in France). Our findings also show that the most important policy amenable factors were social influence, particularly physicians' (US = 14%, UK = 21% and France = 25% of the variance) and perceptions about influenza (US = 30%, UK = 17% and France = 18% of the variance), communication efforts should, therefore, focus on these factors. Surprisingly, perceptions about the influenza vaccine explained a very small proportion of vaccination behaviour across the three countries. Additionally, our results show that a sizeable proportion of adults under the age of 65 years, both with and without eligible chronic conditions, is vaccinating against influenza in the US (over a third) and the UK (under a third), whilst only 16% do so in France.

Specifically, and in line with previous evidence, we found that age, health status, health insurance, income, gender, marital status and education were associated with past vaccination^{9, 34}. Differences between countries are likely influenced by their healthcare systems and immunisation policies.

For example, having an eligible health condition was more important than age on its own in the US and the UK, whereas the opposite occurred in France. One plausible reason is that a controversy about the effectiveness and safety of the A(H1N1)pdm09 vaccine in 2009/2010, which has had a lasting negative impact on seasonal influenza vaccination rates in France, may have dissuaded some populations – such as younger people with and without eligible

Table 5. Survey items associated with past influenza vaccination

Item	US	UK	France
What is your date of birth?			✓
Have you ever been diagnosed with any of the following (eligible) conditions?	✓	✓	
Do you have a private health insurance?	✓	✓	✓
Do you have public health insurance (e.g. Medicare)?	✓		
What is your gender?		✓	
Which of the following options best describes your current situation (marital status)?		✓	✓
What is your combined annual household income?	✓		
What is the highest level of education you have completed?			✓
Which of the following statements apply to you?			
I can make time to get the flu vaccine	✓		
My physician thinks I should get a flu vaccine	✓	✓	✓
My relatives or close friends think I should get a flu vaccine		✓	
With no flu vaccine, I would feel very vulnerable to the flu	✓	✓	
If I got the flu, I would feel sicker than other people my age		✓	
Without a flu vaccine, I am sure I would get the flu this winter	✓	✓	✓
I believe that if I got the flu I would have to stay in bed for...		✓	
The flu could make me severely ill	✓		
If I don't get the flu vaccine and I get the flu, passing the flu to other people would worry me because it would be my fault		✓	
I am confident I can avoid getting the flu, even without the flu vaccine	✓	✓	✓
If I don't get a flu vaccine and end up getting the flu this winter, I would regret not getting the vaccine	✓	✓	✓
I feel I know enough about the flu vaccine to make an informed decision about whether to get vaccinated or not	✓	✓	
If I get a flu vaccine, I will be protected against the flu	✓		
The flu vaccine could give me the flu	✓	✓	
I am worried that some of the contents of the flu vaccine may be dangerous for me			✓
I am confident I can get a flu vaccine if I want one		✓	
Which of the following statements best represents how much you trust your physician?	✓		
How actively do you participate with your physician in making decisions about health, generally?		✓	
Which of these statements best represents your past experiences as a child?			
I had a bad experience with vaccines or injections		✓	
I had a scary health-related experience	✓	✓	✓

See the full list of included items and response categories in Table S1 in Supplementary material. Highlighted items were significant in two (light grey) or three (dark grey) countries.

health conditions who may feel less vulnerable – more than others^{34, 51}. This controversy may also be underpinning the differences in model variance and reliability of the trust scale found between France and the other two countries, both of which had not experienced important influenza vaccination scares in recent years, and hence, had maintained fairly constant vaccination rates for more than a decade at the time of data collection^{4, 5, 12}. Private and public health insurance, and income were associated with past vaccination in the US, a country with a largely privatised healthcare system. Although the UK and France have healthcare systems which are free at the point of delivery or affordable for most, the influenza vaccine is only free of charge for high-risk groups, which may explain the association between health insurance and past vaccination in both countries – albeit weak in France. Marital status was also correlated with past vaccination in the UK and France. Higher vaccination rates among participants living with a partner may be explained by people’s tendency to protect their significant other or encouragement from partners to get vaccinated, yet more evidence is needed to substantiate this assertion. Finally, being male and more educated were positively associated with past vaccination in the UK and France, respectively. Yet, both characteristics were not robustly correlated with past vaccination across all specifications, and the association between gender and vaccination in the UK is weak, thus these findings should be interpreted with caution. Future research testing our findings across adequately powered samples of high-risk people will certainly improve our understanding of the relative importance of demographic, socio-economic and health factors in vaccination decisions among eligible individuals. We hypothesise that socio-psychological factors are likely to be more pivotal and discriminant within high-risk groups, as characteristics such as age may be less predictive of vaccination in samples of over 65s and health status may be less important in samples of younger people with eligible health conditions.

Our results also show that practical barriers were not important, except for time in the US. This finding suggests that a culture of long working hours and short holidays may indeed have a negative effect on vaccination uptake.

Consistent with previous research, we found that physicians’ opinion (and relatives’ opinion in the UK), perceived vulnerability to and likelihood of influenza (and severity of influenza measured in number of bed-days in the UK), perceived vaccine effectiveness (only in the US), the perception that the vaccine transmits influenza (in the US and UK) or that its

contents are dangerous (France), and perceived vaccine-related self-efficacy (UK) were associated with vaccine uptake^{9-12, 25}. As previously reported in the literature¹¹, we also found a small negative association between the perceived severity of influenza and past vaccination in the US, and no association in the UK and France. A possible explanation is that people who believe that influenza could make them severely ill, may also be concerned about the vaccine flu-like symptoms, thus omission bias may induce them to refrain from vaccinating^{31, 52}. Alternatively, the knowledge that influenza could be serious may not necessarily translate into a feeling of personal threat, particularly among younger individuals. A similar result was the lack of or negative of association between perceived susceptibility to influenza and past vaccination in the US and France, and the UK, respectively. These findings indicate that measuring perceived influenza severity as degree of seriousness (“the flu could make me severely ill”) and perceived susceptibility to influenza as individuals’ constitutional vulnerability in relation to that of others (“If I got the flu, I would feel sicker than other people my age”), does not improve our understanding of vaccination behaviour, as previously suggested¹¹.

Interestingly, perceived vaccine knowledge (to make informed decisions) was negatively correlated with past vaccination in the US and positively correlated in the UK. Researchers have long advocated for strategies to increase knowledge about vaccines¹⁰, yet these results suggest that a cognitive approach may not always be effective, particularly when the target population (e.g. US unvaccinated people) perceive themselves as being knowledgeable, and hence are less likely to seek or be receptive to further information.

Factors which are less explored in the literature were also robustly correlated with past vaccination. Perceived control over influenza and regret of catching it (if unvaccinated) were significantly associated with past vaccination behaviour across the three countries. Worry of infecting other people (if unvaccinated) was only linked to past vaccination in the UK, but the direction of the association was unexpected: unvaccinated participants worried more than vaccinated participants of infecting other people if they were to remain unvaccinated. Although this question was hypothetical, it is plausible that unvaccinated participants felt worried about infecting others because of their actual vaccination status, whereas vaccinated participants did not, either because they felt protected by the vaccine or they do not generally worry about infecting others. In any case, this result does not support the notion that altruism motivates people to vaccinate²⁷.

Our results also show that trust in key vaccination stakeholders does not play a significant role in influenza vaccination decisions in these countries. In fact, we found that US vaccinees were less trusting of their physician than those who did not vaccinate. This finding conflicts with the premise that all vaccination decisions are a combination of individuals' perceptions of the information they receive and their trust in those who manufacture, legislate and deliver vaccines²⁶.

A striking finding from a qualitative study³¹ held true when tested quantitatively. UK participants who had a bad experience with needles in childhood were less likely to vaccinate later in life, consistent with evidence showing that traumatic experiences can linger through to adulthood and significantly influence health decisions⁵³. This was further supported by the increased likelihood of vaccinating exhibited by those who reported a scary health-related experience in childhood across the three countries, although less so in the US, possibly due to a lasting perception of vulnerability that resulted in enhanced preventive behaviours in adulthood. To our knowledge, this is the first quantitative study linking adult vaccination behaviour with childhood experiences. Therefore, further testing these results across different samples would be desirable to ensure that the link (or lack thereof) between these variables and influenza vaccination is a true one. Additionally, future research could unpack this synergistic effect using qualitative approaches.

Finally, we found that UK vaccinees were more likely to let their doctors make decisions about their health. This finding resonates with findings from Opel and colleagues which showed that parents were more likely to resist advice if the doctor used a participatory (e.g. "What do you want to do about shots?") rather than a presumptive initiation approach (e.g. "Well, we have to do some shots")⁵⁴. Researchers could test the replicability of Opel's study on adult vaccination and further explore the role of health decision-making preferences on doctor-patient communication about vaccines.

Policy implications

This study offers evidence that can inform policy and practice. Socio-psychological factors associated with influenza vaccination can be used to track vaccination sentiment and forecast uptake. These factors are currently not consistently monitored and rarely used as a basis for

effective service delivery and communication strategies. If we are to improve or at least sustain current immunisation rates, we must start actively listening to the public by including these aspects into national immunisation surveys. An important challenge for policymakers is prioritising what to monitor and to what extent. As a first step, influenza vaccination surveillance systems should include the explanatory variables reported here, particularly those accounting for a significant proportion of the variance in vaccination behaviour (i.e. social influence and influenza perceptions), and make additions or adjustments over time.

More importantly, our findings suggest that socio-psychological factors could provide a valuable opportunity to develop and evaluate targeted interventions to improve vaccination coverage. For instance, the influence of physicians' opinions on vaccination, over and above people's trust in immunisation stakeholders (including physicians themselves), indicates that improving communications at the practice level should be prioritised. One possible intervention is to reach under-vaccinated groups (e.g. younger eligible individuals) via consultations and vaccination reminders, a strategy that has been successful in older populations⁵⁵. A complementary initiative is to link influenza vaccination rates to pay-for-performance systems, such as the UK Quality and Outcomes Framework (QoF) which rewards general practitioners for vaccinating some at-risk groups. Yet, further incentivising primary care practices to employ more effective approaches to reach out to eligible unvaccinated patients, may require a stratified strategy that offers larger rewards for vaccinating sub-groups with low vaccination rates and additional incentives for exceeding vaccination targets⁵⁶. However, we acknowledge that the implementation of more complex incentive systems would require additional resources. In the US, programmes to introduce the influenza vaccine in the work place may encourage those with limited time to protect themselves.

Efforts could also focus on addressing the gap between perceived and real risks of influenza. This could be achieved by moving away from generic messages about the threat of influenza (e.g. "influenza is serious") toward tailored messages which take into consideration the needs and characteristics of different at-risk populations. For instance, influenza-related complications in young diabetics may differ from those experienced by elderly people. Specific messages may, therefore, allow individuals and their families to better identify risks relevant to their condition and, in turn, compel them to vaccinate.

Similarly, effective communications as part of the consultation aimed at assuaging concerns around vaccines could take into account decision-making preferences and individual past experiences, particularly in the UK. For instance, communication efforts are likely to be better spent on those who prefer to make decisions about their health independently than those who are more prone to delegate health decisions to their physician. Given the lasting effect of some traumatic childhood experiences, interventions and new products aimed at making all childhood encounters with injections as easy as possible may be a good investment in the success of vaccination programs in the future.

However, in a context of constrained resources, physicians and nursing staff have limited time and resources to improve vaccination services and communications. Hence, increased investment in the provision of training, adequate communication materials and decision aids to enhance patient-doctor communication is urgently needed and much deserved.

Messages delivered in primary care settings could also be complemented with evidence-based mass-communications. For example, a national campaign could combine messages about the risks of influenza (e.g. likelihood of catching it and feelings of vulnerability and regret for not vaccinating) with messages about the limited protectiveness of avoidance strategies (e.g. taking vitamins or evading crowds), and provide – rather than avoid – easy-to-understand and accurate information about vaccine safety (e.g. communicating more effectively the difference between vaccine-induced symptoms and actual influenza symptoms) and effectiveness, particularly in the US. When possible, mass communications should also be tailored to specific at-risk populations.

Finally, given that the influenza vaccine is more effective in healthy working adults⁵⁷ – reducing the number of influenza-like episodes among this population, but also providing indirect protection to at-risk groups –, knowing what motivates them to vaccinate can be valuable to policy-makers seeking to reduce the societal cost of influenza.

Limitations

This study has several limitations, some of which may affect the generalisability of our findings. Although the use of non-probability online panels has become increasingly common^{58, 59}, response rates are generally low^{37, 60}. This is largely because online panel

members become desensitised to survey e-mail invitations from the online panel provider⁶⁰,⁶¹. However, an emerging body of evidence shows that higher response rates may not be associated with more accuracy, in fact, some studies have found that high response rates can yield less accurate results⁶². This suggests that the low response rates we achieved may not be as important a source of bias as using a sample drawn from a non-probability online panel. This is because the relationship between the sample and the non-probability online panel population is often unknown, so it is not possible to estimate how representative the sample is of the population as a whole. Therefore, our research may have suffered from respondent-related biases; for example, people for whom vaccination issues are particularly salient may have been more prone to participate⁶¹. Consequently, responses may have been more polarised, both in favour and against of vaccination. Future studies testing our findings using different sampling strategies, such as the use of probability online panels or random digit dialing, is warranted. A related limitation is that our US sample was more educated than the population, which may have affected the generalisability of our findings, although there is no consensus regarding the link between education and influenza vaccination in the US^{9-10, 12}. Similarly, in France, participants were less likely to disclose their household income and over half reported it to be equal or below the band that was closest to the median income of the population, which could also have biased our results. Further, since we sought to attain samples that were representative of the adult population, they may not have been adequately powered to detect sub-group differences (e.g. whites vs. non-whites).

Another possible drawback is that lengthy instruments may fatigue participants and affect the quality of the data. Although pilot results indicated that participants did not feel the survey was long or difficult to complete, there is a chance that those who did not finish the survey may have found it too lengthy. A related limitation is the dichotomisation of four continuous variables, which could have resulted in loss of information. However, on balance, this was deemed necessary to aid the analysis of survey-items with numerous “I don’t know/not applicable” responses, which are not the same as missing responses. Strategies used to deal with missing responses, such as imputation or case exclusion, would have been inappropriate or would have significantly reduced the size of our samples and affected their composition.

An additional limitation is the use of a subjective outcome measure. Although data from medical records may be preferable, previous research comparing the accuracy of the latter to self-reported influenza vaccination has shown these can coincide in up to 90% of the cases⁶³.

Further, since some people vaccinate at work or alternative facilities such as pharmacies, it remains unclear whether medical records are more accurate than self-reports.

Lastly, although we employed a battery of measures designed to capture people's actual perceptions about influenza and the influenza vaccine, using a prospective design and a representative sample of vaccine-naïve participants would have been preferable to avoid post-decisional rationalisations. However, this research design requires substantial financial resources and time which were not available to us, and hence, a retrospective design was chosen instead. Consequently, and consistent with other retrospective cross-sectional studies, causation cannot be inferred, thus some of the assessed perceptions may have been generated or reinforced by prior vaccination. Moreover, this study's design precludes any attempt to predict future behaviours. Further research testing whether the identified explanatory variables prospectively predict actual vaccination uptake among first-time vaccinees is merited.

CONCLUSIONS

This study identifies policy amenable factors associated with past influenza vaccination and presents a set of robust explanatory variables that aims to attain a comprehensive and more accurate understanding of the constellation of factors underpinning vaccination behaviour. Our findings can prove useful for countries looking to improve vaccination rates by developing more opportune and effective communication strategies and implementing evidence-based interventions. Our results highlight the importance of routinely monitoring vaccination sentiment and using these data to inform immunisation policy.

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AUTHOR CONTRIBUTIONS

AW, MM, AT, CV and NS contributed to the design of the study, the interpretation of the results and write-up of the manuscript. AW led the analysis and drafting of the manuscript. MM provided statistical advice.

DATA SHARING STATEMENT

No additional data are available.

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