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Woodcock, Thomas; Novov, Vesselin; Skirrow, Helen; Butler, James; Lovett, Derryn; Adeleke, Yewande; Blair, Mitch; Saxena, Sonia; Majeed, Azeem; Aylin, Paul

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Health and socio-demographic characteristics associated with uptake of seasonal influenza vaccination amongst pregnant women: Retrospective cohort study

Thomas Woodcock (Corresponding Author), PhD, Senior Research Fellow, 0000-0002-4735-4856
Department of Primary Care and Public Health, Imperial College London

Vesselin Novov, MSc, Software Developer
Department of Primary Care and Public Health, Imperial College London

Helen Skirrow, MBBS, BSc, MSc, MFPH, Clinical Research Fellow, 0000-0002-4383-0616
Department of Primary Care and Public Health, Imperial College London

James Butler, MSc, Research Assistant
Department of Primary Care and Public Health, Imperial College London

Derryn Lovett, BSc, GIS Analyst
Department of Primary Care and Public Health, Imperial College London

Yewande Adeleke, MSc, Research Assistant
Department of Primary Care and Public Health, Imperial College London

Mitch Blair, MBBS, MSc , FRCPH, FFPH , Professor of Paediatrics & Child Public Health
Department of Primary Care and Public Health, Imperial College London

Sonia Saxena, MD, Professor of Primary Care, 0000-0003-3787-2083
Department of Primary Care and Public Health, Imperial College London

Azeem Majeed, MD, Professor of Primary Care and Public Health, 0000-0002-2357-9858
Department of Primary Care and Public Health, Imperial College London

Paul Aylin, MBChB, FFPH, Professor of epidemiology and public health, 0000-0003-4589-1743
Department of Primary Care and Public Health, Imperial College London, London

Address for correspondence: *Dr Thomas Woodcock, Department of Primary Care and Public Health, Imperial College London, Room 328, Reynolds Building, St Dunstan's Road, London W6 8RP*

Abstract

BACKGROUND:

Pregnant women are at increased risk from influenza, yet maternal influenza vaccination levels remain suboptimal.

AIM:

This study aimed to estimate associations between socio-demographic and health characteristics and seasonal influenza vaccination uptake among pregnant women, and understand trends over time to inform interventions to improve vaccine coverage.

DESIGN AND SETTING:

A retrospective cohort study using linked electronic health records of women in North-West London with a pregnancy overlapping an influenza season between September 2010 and February 2020.

METHODS:

We used a multivariable mixed-effects logistic regression model to identify associations between characteristics of interest and primary outcome of influenza vaccination.

RESULTS

451,954 pregnancies, among 260,744 women, were included. In 85,376 (18.9%) pregnancies women were vaccinated against seasonal influenza. Uptake increased from 8.4% in 2010/11 to 26.3% in 2018/19, dropping again to 21.1% in 2019/20. Uptake was lowest among women: aged 15-19 years (12%; reference category) or over 40 years (15%; OR 1.17, 95% CI 1.10 to 1.24); of Black ethnicity (14.1%; OR 0.55, 95% CI 0.53 to 0.57), or unknown ethnicity (9.9%; OR 0.42, 95% CI 0.39 to 0.46), lived in more deprived areas (OR least vs most deprived (reference category) 1.16, 95% CI 1.11 to 1.21), or with no known risk factors for severe influenza.

CONCLUSION:

Seasonal influenza vaccine uptake in pregnant women increased in the decade before the COVID-19 pandemic, but remained suboptimal. We recommend targeted approaches to reducing inequalities in access to vaccination should focus on women of Black ethnicity, younger and older women, and women living in deprived areas.

HOW THIS FITS IN:

Seasonal influenza vaccination for pregnant women is recommended internationally, yet uptake remains suboptimal. We used electronic health record data, for a population of 2.3 million patients, to understand which groups of women are less likely to get vaccinated for seasonal influenza during pregnancy. Whilst uptake increased over the duration of the study, there was significant variation with women less likely to get vaccinated if they were younger or older than average, of Black or undocumented ethnicity, living in more deprived areas, or did not have a risk factor for severe disease. Future research should inform tailored programmes to improve vaccine uptake in groups with low uptake, as well as improved access to vaccination services.

KEYWORDS

Vaccines, Influenza, Pregnancy, Sociodemographic Factors

Introduction

Seasonal influenza vaccination (SIV) is recommended in pregnant women to reduce the risk of infectious complications and adverse outcomes such as pre-term birth. [1–3] Antenatal SIV is safe and reduces the risk of severe influenza and adverse outcomes for both mother and child.[4–8] However, maternal influenza vaccination levels are suboptimal worldwide.[9–12]

In the UK, since 2010, the Joint Committee on Vaccination and Immunisation has recommended that pregnant women get the SIV to provide protection during the winter flu season.[13] Despite these recommendations, data from Public Health England show that in 2020-21, SIV uptake among pregnant women was only 43.6%.[14] London remains below the national average with only 36.7% of pregnant women vaccinated in the 2020-21 flu season and only 36.0% in North West London (NWL).[15] Accurate local population estimates are needed to identify which women are less likely to get vaccinated, and inform targeted interventions to increase uptake.

Access to vaccines through strong primary care systems is needed for high maternal uptake.[16] Misconceptions about the safety and efficacy of antenatal vaccinations play a role in pregnant women being unvaccinated, while recommendation by health professionals improves uptake.[9,17–20] Several studies have found that younger women (aged under 25),[21,22] women from some minority ethnic groups (for example, Black in UK studies and Black and Hispanic in US studies),[23–28] women living in poorer households,[28,29] and those with fewer educational qualifications,[30] are less likely to have SIV. However, these are either single-centre studies, limited in their generalisability, or survey-based studies susceptible to sampling bias, recall bias, and response bias. Furthermore, there is a lack of evidence concerning trends in uptake

rates since 2015. The Covid-19 pandemic has also highlighted the importance of maternal vaccination as pregnant women are at increased risk of severe Covid-19 disease and designated a priority group for Covid-19 vaccination in the UK.[31]

To address gaps in the current evidence, this retrospective cohort study used individual-level routinely collected data, covering a diverse regional population, to identify characteristics such as demographics, socio-economic status, and at-risk conditions associated with uptake; and secondly, to explore trends in uptake over time independently of these factors.

Methods

Data Source and Study Cohort

The NWL Discover database is a large de-identified healthcare dataset, containing linked primary, acute, mental health and community care records for 2.3 million patients registered with a general practitioner (GP) in NWL, 1.1 million previously registered, and 208,000 previous residents now deceased.[32] In this study, we extracted data from primary care records to identify women with at least one pregnancy between September 2010 and February 2020. For each pregnancy overlapping an influenza vaccination season, we further extracted data on maternal influenza vaccination status, along with covariates concerning demographics and known risk factors for developing serious complications from influenza infections.

We identified pregnancies using a method developed for the Clinical Practice Research Datalink (CPRD) primary care database.[33] Adaptations were necessary due to differences between the Discover and CPRD data, reflecting differences between the underlying GP electronic health record systems. Of 4,200 Read Clinical Terms Version (CTV) 2 codes used by Minassian et al., 589 are not used in the Discover database. We used the remaining 3,611

codes to identify all recorded events relating to pregnancy.[33] This process produced a dataset with one record for each pregnancy, and variables including pregnancy outcome type, and estimated start and end dates.

We defined an influenza season to run from 1st of September to the end of February the following year. Pregnancies *overlapped* with an influenza season if i) their start date was before or equal to the season's end date; and ii) their end date was after or equal to the season's start date. Pregnancies were included in the analysis if the estimated start date fell between 1st September 2010 and 29th February 2020, the woman was aged between 15 and 49 at the estimated pregnancy start, and the pregnancy overlapped with an influenza season. All included pregnancies were deemed eligible for SIV.

Influenza Vaccination

For each woman with at least one identified pregnancy, all influenza vaccination records were extracted from the primary care data using the set of Read CTV2 codes specified by Public Health England.[34] The primary outcome for this study was vaccination status, established for each pregnancy to be either "vaccinated" or "not vaccinated" according to the presence or absence of an influenza vaccination record during the corresponding influenza season, and prior to the end of the pregnancy. The percentage of vaccinated pregnancies in each season is referred to as the vaccine coverage for that season.

Covariates

For each pregnancy, the following demographic covariates were extracted: the woman's age at start of pregnancy, woman's ethnicity, GP practice code (a unique identifier for each GP practice), Local Authority district name, and Index of Multiple Deprivation (IMD) quintile –

a measure of socio-economic deprivation calculated for small local geographic areas. In addition, data were extracted to establish the presence of the following risk factors at the start of the pregnancy: asthma, chronic respiratory disease, chronic heart disease, chronic kidney disease, asplenia, liver disease, chronic neurological disease, diabetes, immunosuppression, and morbid obesity. These conditions, as well as the Read CTV2 codes used to identify them, were those used in the annual Public Health England assessment of SIV uptake in 2019 to 2020.[34,35] In all cases, we considered any previous diagnosis of the condition as an indication of the presence of the risk factor.

Technical details of the methods used are presented in web-only supplementary appendix A.

Analysis

The unit of observation was a pregnancy. For all included pregnancies, distributions of women's' characteristics and risk factors were described, by vaccination status. To determine factors associated with SIV uptake, a two-level (pregnancy, and GP practice) mixed effects multivariable logistic regression model was fitted using vaccination status as the outcome. A random intercept term was used, all other terms were fixed effects. The following variables were used as fixed effect covariates: influenza season, woman's age (start of pregnancy), ethnicity, IMD quintile, and the presence of at-risk conditions (see above). Regression diagnostics were performed, including a check for collinearity, goodness of fit (marginal and conditional R^2),[36] and examination of residuals. Missing data on ethnicity and index of multiple deprivation were treated as a separate level in the main analysis, and analysed through multiple imputation as a sensitivity analysis (see supplementary appendix B for further details). Results were reported as odds ratios with 95% confidence intervals, and p-values with statistical significance for $p < 0.05$. All analyses were conducted using R

Statistical Software (version 3.6.1; R Core Team 2019), using the lme4 package (version 1.1-21) to fit mixed effects models.[37,38]

Results

We identified 451,954 pregnancies meeting the inclusion criteria, among 260,744 women. The age of women at the start of pregnancy was most commonly 30 – 34 years (142,965, 31.6%), with women aged between 25 and 39 accounting for 76.8% of pregnancies. Women were of White ethnicity in 202,823 pregnancies (44.9%), and Asian or Asian British in 135,821 pregnancies (30.1%). The ethnicity of the woman was unknown in 5,836 pregnancies (1.3%). The highest number of pregnancies (142,532 pregnancies, 31.5%) were for women living in areas in the second IMD quintile, with fewer pregnancies among women in the most deprived quintile (65,925 pregnancies, 14.6%) and progressively fewer in each of the less deprived quintiles, with fewest pregnancies in the least deprived quintile (32,261 pregnancies, 7.1%). IMD was unknown in 28,118 pregnancies (6.2%). The most common risk factor was asthma, affecting women in 39,671 pregnancies (8.8%). The least common risk factors were chronic respiratory disease, chronic kidney disease, and liver disease, each affecting fewer than 1,000 pregnancies (0.2%).

For 85,376 (18.9%) pregnancies meeting the inclusion criteria, the woman received SIV during the overlapping influenza season (Table 1). Uptake increased each season from 2010/11 (7.6%) to 2017/18 (26.9%), and then dropped to 20.4% in 2019/20 (Figure 1). Uptake was lowest among women aged 15 – 19 (11.9%), rising with age until reaching a peak in those aged 35 – 39 (20.7%), before falling again in those aged 40 – 44 (15.7%) and 45 – 49 (12.5%). Women of Asian or Asian British ethnicity were most likely to be vaccinated (24.8%) and women of Black or Black British ethnicity (14.1%) and those whose ethnicity was not recorded (9.9%) were least likely to be vaccinated. Overall, the proportion

of pregnancies vaccinated was highest for those living in less deprived areas (25.0% in the least deprived decile of IMD), and lowest for those living in more deprived areas of NWL (15.3% in the most deprived decile).

Women with each of the influenza risk factors were more likely to be vaccinated than those without the risk factor, although by differing amounts. Among pregnancies in women with diabetes, 40.7% (1,604 of 3,945) were vaccinated, the highest proportion for any risk factor; compared with 18.7% of those without diabetes (83,772 of 448,009). Of all the risk factors, vaccination rates were lowest among pregnancies in women with morbid obesity (22.3%, 1,767 of 7,926), liver disease (23.1%, 231 of 999) and chronic kidney disease (23.4%, 132 of 564).

In the multivariable logistic regression analysis (table 2), odds ratios for age, ethnicity and IMD quintile showed the same patterns as in the univariate analysis. The effect sizes seen for IMD in this multivariable model are lower than the corresponding univariate effects; for example, the unadjusted odds ratio for vaccination in IMD quintile five versus one is 1.89, compared with a direct effect of 1.16 after adjusting in the mixed-effects model. Since IMD is likely associated with risk factors included in the model, this suggests that some of the variation in vaccine coverage by IMD may be explained by other covariates. The broad pattern of vaccination by influenza risk factors was also similar, with increased odds of vaccination for those with each risk factor compared with those without. The highest such odds ratio was that for diabetes (2.86, 95% CI 2.67 to 3.06). The only risk factor for which this effect was not statistically significant was chronic kidney disease.

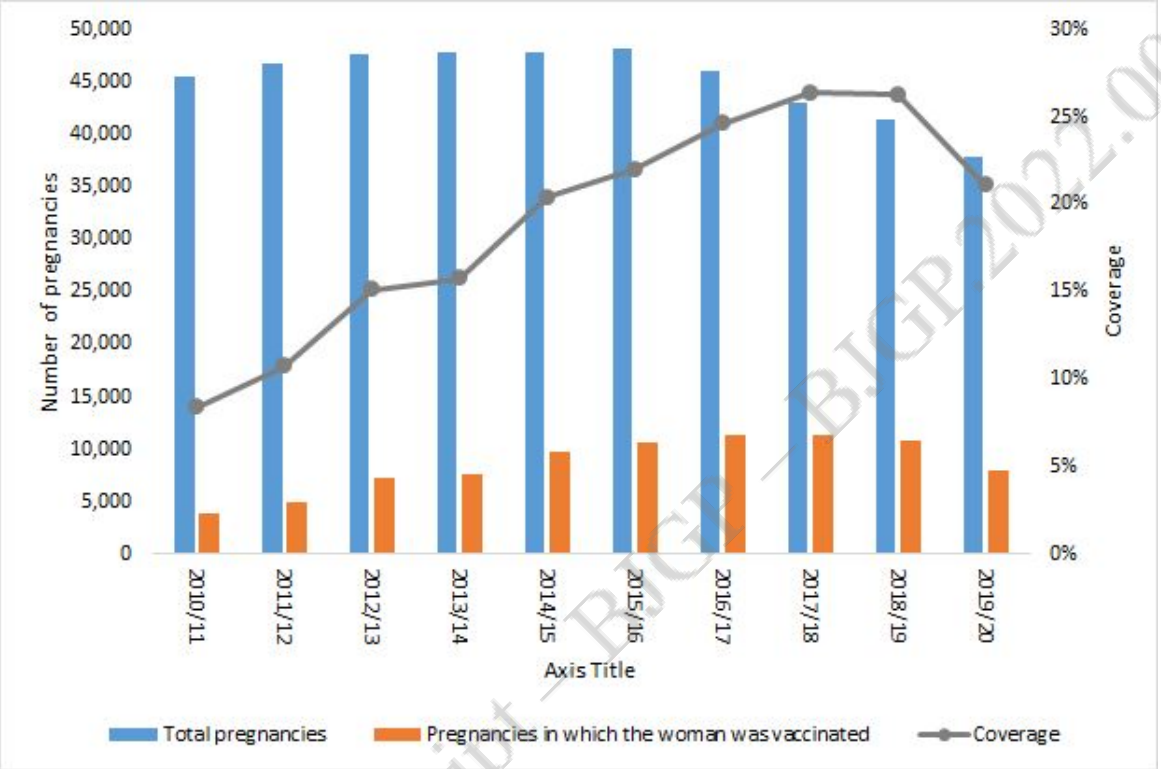
The results of the multiple imputation analysis were consistent with the main analysis and can be found in supplementary table S1.

Table 1: Seasonal Influenza Vaccination Rates in Pregnant Women registered with a GP in North West London from September 2010 to February 2020

Characteristics	Pregnancies (N = 451,954)		Seasonal influenza vaccinations (N = 85,376)		Coverage
Age (years)	n	(%)	n	(%)	%
15 - 19	16,169	(3.6%)	1,922	(2.3%)	11.9%
20 - 24	62,656	(13.9%)	10,091	(11.8%)	16.1%
25 - 29	123,352	(27.3%)	24,096	(28.2%)	18.3%
30 - 34	142,965	(31.6%)	29,658	(34.7%)	19.5%
35 - 39	80,956	(17.9%)	15,659	(18.3%)	20.7%
40 - 44	22,149	(4.9%)	3,487	(4.1%)	15.7%
45 - 49	3,707	(0.8%)	463	(0.5%)	12.5%
Ethnicity					
Asian or Asian British	135,821	(30.1%)	33,737	(39.5%)	24.8%
Black or Black British	47,160	(10.4%)	6,662	(7.8%)	14.1%
Mixed	14,837	(3.3%)	2,350	(2.8%)	15.8%
Other Ethnic Groups	45,477	(10.1%)	8,005	(9.4%)	17.6%
White	202,823	(44.9%)	34,047	(39.9%)	16.8%
Unknown	5,836	(1.3%)	575	(0.7%)	9.9%
IMD Quintile					
1 (most deprived)	65,925	(14.6%)	10,107	(11.8%)	15.3%
2	142,532	(31.5%)	26,510	(31.1%)	18.6%
3	116,715	(25.8%)	22,795	(26.7%)	19.5%
4	66,403	(14.7%)	13,534	(15.9%)	20.3%
5 (least deprived)	32,261	(7.1%)	8,063	(9.4%)	25.0%
Unknown	28,118	(6.2%)	4,367	(5.1%)	15.5%
Asthma					
No	412,283	(91.2%)	75,734	(88.7%)	18.4%
Yes	39,671	(8.8%)	9,642	(11.3%)	24.3%
Respiratory					
No	451,414	(99.9%)	85,239	(99.8%)	18.8%
Yes	540	(0.1%)	137	(0.2%)	25.4%
Heart					
No	449,455	(99.5%)	84,747	(99.3%)	18.9%
Yes	2,499	(0.6%)	629	(0.7%)	25.2%
Kidney					
No	451,390	(99.9%)	85,244	(99.9%)	18.9%
Yes	564	(0.1%)	132	(0.2%)	23.4%
Liver					
No	450,955	(99.8%)	85,145	(99.7%)	18.9%
Yes	999	(0.2%)	231	(0.3%)	23.1%
Asplenia					
No	449,944	(99.6%)	84,822	(99.4%)	18.9%
Yes	2,010	(0.4%)	554	(0.7%)	27.6%
Neurological					
No	450,545	(99.7%)	85,037	(99.6%)	18.9%
Yes	1,409	(0.3%)	339	(0.4%)	24.0%
Diabetes					
No	448,009	(99.1%)	83,772	(98.1%)	18.7%
Yes	3,945	(0.9%)	1,604	(1.9%)	40.7%
Immunosupression					
No	450,659	(99.7%)	85,015	(99.6%)	18.9%

Yes	1,295	(0.3%)	361	(0.4%)	27.9%
Morbid Obesity					
No	444,028	(98.3%)	83,609	(97.9%)	18.8%
Yes	7,926	(1.8%)	1,767	(2.1%)	22.3%

Figure 1: *Seasonal influenza vaccination coverage by influenza season, for women registered with a GP in North West London.*



The left-hand axis shows counts of the number of pregnancies recorded overlapping with each season, and the number of these in which the woman was vaccinated for seasonal influenza. The right-hand axis shows coverage as a percentage (% pregnancies for which the woman was vaccinated during the overlapping influenza season).

Table 2: *Adjusted odds ratios comparing odds of seasonal influenza vaccination among pregnant women registered with a GP in North West London from September 2010 to February 2020.*

Characteristics	**OR** (95% CI)	**p-value**
Age (15 – 19 rc)		
20 - 24	1.32 (1.25 to 1.40)	p < 0.001
25 - 29	1.58 (1.50 to 1.67)	p < 0.001
30 - 34	1.68 (1.59 to 1.76)	p < 0.001
35 - 39	1.56 (1.48 to 1.64)	p < 0.001
40+	1.17 (1.10 to 1.24)	p < 0.001
Ethnicity (Asian or Asian British rc)		
Black or Black British	0.55 (0.53 to 0.57)	p < 0.001
Mixed	0.63 (0.60 to 0.66)	p < 0.001
White	0.66 (0.65 to 0.68)	p < 0.001
Other Ethnic Groups	0.72 (0.70 to 0.74)	p < 0.001
Unknown	0.42 (0.39 to 0.46)	p < 0.001
IMD Quintile (Q1 rc) (most deprived)		
Q2	1.03 (1.00 to 1.06)	p = 0.06
Q3	1.06 (1.03 to 1.09)	p < 0.001
Q4	1.07 (1.04 to 1.11)	p < 0.001
Q5 (least deprived)	1.16 (1.11 to 1.21)	p < 0.001
Unknown	1.00 (0.96 to 1.04)	p = 0.94
At-risk Group		
Asthma	1.50 (1.46 to 1.54)	p < 0.001
Respiratory	1.46 (1.19 to 1.80)	p < 0.001
Heart	1.43 (1.30 to 1.57)	p < 0.001
Kidney	1.18 (0.96 to 1.45)	p = 0.13
Liver	1.29 (1.11 to 1.51)	p < 0.001
Asplenia	1.59 (1.43 to 1.76)	p < 0.001
Neurological	1.27 (1.12 to 1.45)	p < 0.001
Diabetes	2.86 (2.67 to 3.06)	p < 0.001
Immunosuppression	1.84 (1.62 to 2.10)	p < 0.001
Morbid Obesity	1.13 (1.07 to 1.19)	p < 0.001
Influenza Season (years)	1.14 (1.14 to 1.15)	p < 0.001

Odds ratios calculated using logistic regression. Reference category denoted by rc for each categorical variable. Note that since prevalence of at-risk conditions may be influenced by demographics, odds ratios for demographic variables represent direct effects rather than total effects.

Discussion

Summary

Our study of over 450,000 pregnancies from 2010 to 2020 found that in only 1 in 5 pregnancies were women vaccinated against seasonal influenza, though this rose to 1 in 4 towards the end of the study period. While encouraging that South Asian women and those most at risk from severe influenza were more likely to be vaccinated, wide variation still exists, with only 1 in 10 pregnant teenagers receiving the seasonal influenza vaccine. Those living in the most deprived areas were half as likely to be vaccinated as those in the least deprived, although some of this effect may be explained by other covariates. Having a chronic condition such as asthma or diabetes, or any of the included risk factors for severe disease, was associated with higher uptake rates. Whilst this effect was not significant for chronic kidney disease, this may be due to the small number of pregnancies recorded for women with this risk factor.

Strength and Limitations

Our population-level approach minimised risk of selection bias compared with a sampling approach. The population of NWL is large and demographically diverse, strengthening the external validity of the study. The adapted algorithm for identification of pregnancies provides a rigorous approach, drawing on GP records from all stages of pregnancy, rather than simply counting instances of pregnancy related codes. The algorithm is widely applicable, using data that is available in all GP practices in England. The multivariable regression analysis provides an understanding of the association of each factor with compliance, independently of other covariates; this allows for targeted approaches to improvement.

This study also had some limitations. The data were routinely collected through delivery of primary care, and as such are dependent on coding practices of primary care teams. The data available did not include some fields used in previous similar studies to identify the outcome of pregnancies, over and above the Read coded data available in the NWL Discover database. This may have resulted in the outcome of some pregnancies being mis-attributed; however, pregnancy outcome was not used in this study. Whilst we included all available Read-coded vaccination data, we did not have data to indicate which vaccinations were undertaken within GP practices, and which in antenatal clinics. Some vaccinations delivered outside general practices, in community pharmacies for example, may not be recorded. This may mean that vaccination uptake identified through this study is an under-estimate; however, the additional data fields were not available across all pregnancies, and this issue is therefore unlikely to bias the findings in relation to the relationships between demographic variables and vaccination uptake. Completeness of data and appropriate coding of pregnancies will always be a challenge in London with its mobile population which will impact on the accuracy of uptake estimates. Whilst we included a range of demographics and risk factors in our analysis, we did not have access to other variables that might influence uptake of influenza vaccines, for example political views and influence of social networks. Our results therefore cannot account for the potential impact of these factors.

Comparison with existing literature

The level of SIV coverage found in this study was lower than that identified for NWL in a national analysis by Public Health England (PHE), although the methods used were different. For example, for the 2019/20 influenza season our study identified SIV uptake of 20.4%, compared with 34% in the national analysis.[39] Whilst we found similar numbers of vaccinations given, we identified larger numbers of pregnancies than the PHE analysis,

perhaps due to our broader inclusion criteria, which helped minimise bias.[33] Our findings of lower vaccine uptake in more deprived areas and in women of black or black British ethnicity are consistent with previous studies of influenza and other maternal vaccines, including a national study examining social determinants of pertussis and seasonal influenza vaccine uptake. [28,29,40] Walker et al. reported that women living in the most deprived areas of England had 29% lower odds of being vaccinated against seasonal influenza. However, their study period was only up until 2015-16 season. Walker et al. also reported lower uptake among women of Black and Black British ethnicity and, consistent with this study, that women in clinical risk groups were more likely to be vaccinated. Local studies examining maternal vaccine uptake in a hospital population of pregnant women have reported lower vaccine uptake among Black-British and Black ethnicities groups.[41,42]

Implications for research and practice

Research is needed to inform tailored programmes for pregnant women living in poorer neighbourhoods and address variation in vaccine uptake among different ethnicities. Strategies to improve vaccine uptake among pregnant women should not focus exclusively on acceptance of vaccination by pregnant women,[43] but also improve access to vaccine appointments as recommendations by trusted healthcare providers remain a key driver of maternal vaccine uptake. [44,45]

The increase in coverage over time in NWL is encouraging, although sustaining this will require more effort as shown by the drop in coverage before the start of the COVID-19 pandemic. Reasons for the increase may include awareness of vaccination in pregnancy over the study period. For example, a study in NWL in 2013-14 found only 63% of women surveyed knew about pertussis vaccine being recommended in pregnancy;[42] however, in a 2020 national UK survey last year over 95% of women knew pertussis vaccine was

recommended for pregnant women.[46] From the data we had available, it is difficult to ascertain how and whether the offer of immunisation was made to all eligible women and the proportion of them that took up the offer. Currently, public health messaging around influenza immunisation for pregnant women is relatively homogenous. A more nuanced programme, seeking to build relationships between providers and communities over time, and targeted social media messaging is worth considering for younger and older women, and those of Black and Black-British ethnicity.[47–49] Women with pre-existing medical conditions are an important group to target because of the additional morbidity and mortality risks associated, and GP information systems are likely to capture this accurately as part of their disease registers, especially if financially incentivised.[50] There may well be questions to address on who is best placed for discussing immunisation with women, especially since they will often be seen by both primary care and antenatal care teams.

The COVID-19 pandemic impacted maternal vaccine programmes in England,[51] and in winter 2020-21 seasonal influenza vaccine uptake increased for all groups apart from pregnant women.[15] Uptake of COVID-19 vaccination among pregnant women is also sub-optimal,[52,53] and as with seasonal influenza uptake, ethnic minority women and women living in more deprived areas are less likely to have been vaccinated against COVID-19.[54] How the addition of COVID-19 vaccines to the vaccine schedule for pregnant women in the UK influences wider maternal vaccine acceptance and uptake needs monitoring.[55]

Our findings provide a robust and detailed understanding of seasonal influenza vaccination uptake among pregnant women. Uptake of seasonal influenza vaccination in pregnancy was lower among women living in more deprived areas, women who were younger or older than average, and women of Black or Black British or undocumented ethnicity. There was an increase in uptake over the ten influenza seasons covered by this study, although there is considerable potential for further increases in uptake, especially with a view to reducing

health inequalities. Our findings support targeted interventions to improve uptake of the seasonal influenza vaccine and other vaccines, including COVID-19, offered to pregnant women, along with more accurate recording of vaccination data in medical records.

Author contributions

TW, YA, AM and PA conceptualised the study and selected the methods. VN and TW wrote the code, and conducted and verified the analysis and visualisation along with DL. VN curated the dataset. TW, VN, HS and JB drafted the original manuscript and all authors contributed further text, and reviewed and edited the manuscript. TW and PA supervised the research and administered the project.

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Ethical approval

This study was approved by the Northwest London Data Access Committee: no reference numbers are given by this committee.

Competing Interests

MB is a member of the Children and Young Persons Clinical and Professional Leadership Group for North West London ICO

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Data Availability

The Discover data used in this study are available from Imperial College Partners, but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Researchers wishing to access Discover data can apply as described in Bottle et al.[32]

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