Lessons learnt from the implementation of maternal immunization programs in England

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Introduction

Maternal immunization is increasingly being recognized as an important platform for the prevention of severe maternal and infant morbidity and mortality from vaccine preventable diseases. Since the 1980s, the widespread use of tetanus toxoid vaccines for pregnant women in developing countries has had a major impact on the burden of neonatal tetanus, with WHO estimating a 94% global reduction in newborn tetanus deaths.1

More recently, many developed countries have recommended influenza and pertussis vaccines for pregnant women. Despite the wealth of evidence supporting the significant morbidity and mortality associated with influenza infection for pregnant women and for both influenza and pertussis in young infants, these programs have been implemented with varying degrees of success. In this paper, we describe the experience of the implementation of the influenza and pertussis vaccination programs for pregnant women in England and consider some of the key factors that have impacted on the coverage achieved across the country.

Influenza vaccination for pregnant women

In recognition of the increased risks of maternal morbidity and congenital anomalies associated with influenza infection during pregnancy, influenza vaccination has been recommended for pregnant women in countries such as the USA for over 20 y.2 The effectiveness of trivalent inactivated influenza vaccination (TIV) in pregnant women and their infants has been demonstrated in a number of studies.3-6 Studies assessing the effectiveness in pregnant women have primarily been based on reduction in medical attendances for respiratory illnesses with one trial estimating a 36% reduction in the incidence of respiratory illness and fever in the vaccinated group compared to the control group who received pneumococcal polysaccharide vaccine.3 In the same study, 6 of the 159 infants born to TIV-vaccinated mothers and 16 of the 157 in the control arm developed influenza infections, a 63% (95%CI: 5–85%) reduction among infants less than 6 months of age. Data on the safety of influenza vaccination during pregnancy have demonstrated no increased risk of a range of maternal and fetal outcomes including preterm delivery, small for gestational age, miscarriage and major birth defects.7,8 In the UK, maternal immunization against influenza has been recommended by the Joint Committee on Vaccination and Immunisation (JCVI) since 2010. Vaccine should be administered during September to January each year to offer protection to women and their new-borns during the peak disease months.9 This recommendation was supported by cost effectiveness10 largely based upon data collected during the 2009 A/H1N1 pandemic which demonstrated the significantly increased risk of severe influenza among pregnant women in terms of hospitalization, intensive care admission and death when compared with healthy non-pregnant women of child-bearing age.11 Data from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity for 2009-2012 further highlighted the severity of maternal influenza with 1 in 11 maternal deaths reported to be attributable to influenza infection. Some women in this report died during the influenza A/H1N1 pandemic before vaccine became available, but a number of unvaccinated women died after the program was routinely recommended.12

During the 2013/14 season in England, the effectiveness of the seasonal influenza vaccination in pregnancy was estimated at 71% (95%CI: 24–89%) in preventing infant influenza infection and 64% (95%CI: 6–86%) effective in preventing infant influenza hospitalizations.13 These studies have supported the effectiveness of vaccination of pregnant women for preventing infection and severe complications from influenza in their infants.

Pertussis vaccination for pregnant women

Routine pertussis immunization using whole cell vaccine was introduced into the UK childhood immunization schedule in 1957, with the primary objective to prevent severe disease and deaths in young infants, the group at highest risk of complications. While the childhood immunization program has been highly successful in reducing the overall burden of disease in England, in particular infant deaths, cyclical peaks in activity have continued to occur every 3 to 4 years.14 Pertussis resurgences have been reported in a number of countries with longstanding vaccination programs including
the USA and Australia\textsuperscript{17,18} and in response, countries such as the UK, Belgium, USA, Argentina and Australia have introduced vaccination programs for pregnant women.\textsuperscript{19} In the UK, pertussis vaccine was recommended for pregnant women in 2012, ideally between 28–32 weeks in every pregnancy to maximize the transplacental transfer of maternal antibodies and optimise protection for infants from birth. This advice was agreed at an emergency meeting of the UK’s expert advisory committee, the JCVI, in August 2012 following an increasing number of reported young infant cases and deaths and the declaration of a national outbreak in April 2012 by Public Health England (previously Health Protection Agency).\textsuperscript{20} In 2012, there were 14 pertussis deaths in England, all in unimmunized infants under 3 months of age; this compared with 6 pertussis infant deaths in the previous peak year, in 2008. Recently the advice in the UK has been updated to offer vaccine from as early as 16 weeks.\textsuperscript{21}

The UK was the first country to demonstrate the impact and effectiveness of the maternal pertussis immunization program on infant disease. Evaluation of the first year of the program in England, demonstrated protection of more than 90% for infants whose mothers’ received vaccine at least one week prior to delivery.\textsuperscript{22,23} In addition to the high effectiveness of the program, a large observational study of more than 20,000 pregnant women demonstrated no increased risk for either the mother, fetus or newborn in those who received pertussis vaccine during pregnancy.\textsuperscript{24} The high levels of protection conferred by this program in the face of heightened pertussis circulation in the population and the reassuring data on the safety of the program informed the decision by JCVI to advise the continuation of the program in 2014 for a further 5 years as part of the ongoing outbreak response.\textsuperscript{25}

**Program planning**

In England, following a JCVI recommendation, the Department of Health is responsible for policy and funding of the national program. Public Health England (PHE), in collaboration with NHS England, implements the program. The latter involves undertaking the contractual negotiations for the delivery of the programs, the procurement of national vaccine stock (with the exception of the inactivated seasonal influenza vaccines), the development of public and professional communication materials, the provision of appropriate training resources and ensuring surveillance systems are established to evaluate the coverage, impact, effectiveness and safety of new vaccine programs (the latter is undertaken by the Medicines and Healthcare Products Regulatory Agency, MHRA).

NHS England is responsible for commissioning the local provision of immunization services and the delivery of new programs. In England, General Medical Practices deliver the majority of the infant immunization program but increasingly other providers have been commissioned to deliver immunization services to other age groups where relevant, including pharmacists.

The seasonal influenza vaccination program for pregnant women which became routine, following the 2009 A/H1N1 pandemic, resulted in the inclusion of an additional eligible group in the existing national program which was being delivered in General Practice. The key planning required for such an addition to an existing program largely involved updating and agreeing provider contracts and national service specifications, updating healthcare professional resources such as the annual influenza plan and letter,\textsuperscript{26} the influenza chapter of the ‘Immunisation against infectious disease’ book (principal immunization resource for healthcare professionals),\textsuperscript{27} training materials, public communications, and ensuring systems were in place to monitor coverage in this target group.

In contrast, the pertussis immunization program for pregnant women was introduced as an outbreak response measure and therefore, the time for implementation was extremely limited. There was less than 8 weeks from the advice being agreed by JCVI and the announcement of the program by the Chief Medical Officer, requiring rapid production of public and professional communication materials. Given the emergency nature of the response, there were considerable challenges for local commissioners and providers of immunization services to prepare for the program and undertake additional training for immunizers. The recommended vaccine at the time of the introduction of the program was DT\textsubscript{aP}/IPV, the same vaccine which was being offered as a pre-school booster dose in the routine childhood program. The choice of vaccine ensured that the emergency program could be initiated rapidly, in view of the continued increase in disease.

**Coverage of maternal immunization programs in England**

Despite good evidence supporting the effectiveness and safety of influenza vaccination for pregnant women, coverage in many countries has been sub-optimal. Although annual coverage for pregnant women in the USA has increased from 8.8% to 50.9% in 2002-2012, this remains below the Healthy People 2020 national target of 80%.\textsuperscript{2} Coverage of the program in England has shown some improvement since its routine introduction increasing from 27.4% in 2011/12 to 44.1% in 2014/15 and 42.3% for the 2015/16 season.\textsuperscript{28-30} However, this continues to remain considerably lower than the coverage for other eligible groups with coverage reported at 71% for adults aged 65 years and over for the most recent season.\textsuperscript{30}

In the early months following introduction of the pertussis program, coverage rapidly reached 54.5% in December 2012.\textsuperscript{31} In the subsequent years of the program this level of uptake has been sustained with average pertussis vaccine coverage in 2014/15 around 56% although it varied by month of delivery and was highest in the winter months, coinciding with the delivery of the seasonal influenza vaccination program.\textsuperscript{32} The most recent published data for January to March 2016 estimated coverage at just over 60% by March 2016.\textsuperscript{32} National coverage for maternal pertussis vaccination programs in other countries is limited to local surveys of vaccine coverage, for example 25% uptake in women delivering in October 2013 in Californian hospitals\textsuperscript{33} and 51% of women delivering during March 2014 in Wisconsin\textsuperscript{34} while uptake of 51-67% was reported in Argentina between 2012, when the program was introduced, and in 2014.\textsuperscript{35}

Although coverage for the maternal pertussis program has consistently reported higher than the seasonal influenza
program in England, the difference in the uptake probably reflects the subtle differences in target population and the time period over which immunization is to be achieved. For the seasonal influenza program, as vaccine is offered to all pregnant women (at any stage of pregnancy) during the season, the denominator is defined as all women already pregnant and those who become pregnant during the influenza season (1st September to 31st January). The coverage assessment reflects cumulative coverage during the influenza season and may underestimate coverage as women who deliver during the season but before receiving vaccination will remain in the denominator and those who become pregnant near the end of the season are added to the denominator but have less time to be vaccinated. In contrast, coverage of the maternal pertussis program is assessed on a monthly basis with the denominator based on the number of pregnant women who delivered in that month, and the number of women receiving a pertussis vaccine after 28 weeks, as the numerator.

Factors influencing coverage of maternal immunization programs

Several factors have been identified that may affect uptake of vaccines offered to pregnant women in England and in response to these a number of measures have been put in place for both programs to minimize their impact.

Commissioning and delivery of maternal immunization services in England

The delivery of the maternal immunization programs in England is commissioned through General Practice where the majority of routine vaccines are delivered. However, routine antenatal care in England is increasingly being delivered through separate midwife led maternity services rather than General Practice and therefore the successful delivery of the vaccination program relies on regular communication from Maternity services to ensure that general practice is aware of the pregnancy status of their registered patients. Maternity care in England is commissioned by Clinical Commissioning Groups (groups of General Medical Practices) and while payment for the delivery of neonatal BCG and hepatitis B vaccination is included for maternity services, the maternity payment does not presently include the delivery of vaccination for pregnant women. Although some areas have sought to commission specific maternity services locally, the lack of access to vaccination as part of routine antenatal care within maternity services has been identified as one potential barrier to the successful delivery of these programs. More recently, in an attempt to increase access to immunization, the annual influenza plan has recommended that, where possible, women should be offered immunization as part of maternity services. Some areas have recently started commissioning maternity services to provide immunizations to pregnant women during their routine maternity care, and the impact of this is currently under evaluation. Issues around introducing immunization into maternity services, including staff availability and training, vaccine storage and maintenance of cold chain have been highlighted.

Unlike other routine vaccination programs in England, including the maternal pertussis program, where vaccines are centrally procured and distributed by PHE it is the responsibility of individual General Practices to purchase inactivated seasonal influenza vaccines for pregnant women. General practices are reimbursed for purchasing and administering inactivated influenza vaccines through a nationally agreed contract. Additional financial incentives for achieving set coverage targets is available for vaccination as part of chronic disease management but is not available for pregnant women. More recently, in an attempt to increase access, seasonal influenza vaccination is also being delivered in other settings including community pharmacists.

One of the significant challenges with the delivery of the seasonal influenza program is the short timeframe for identifying and offering all pregnant women the vaccine during the influenza season. This is compounded by the fact that once a woman has been referred to Maternity services for her antenatal care, the General Practice may not receive pregnancy notifications in a timely way to ensure all eligible women are offered vaccination. Although part of the national service specification, not all practices operate active call/recall systems meaning that women may be unaware of the vaccination offer, especially where midwives providing antenatal care have not discussed the importance of vaccination or provided the available written patient information leaflets.

Understanding attitudes to immunization in pregnancy and the diseases they are aiming to protect

Since 1991 the national vaccination program in England has been informed by a series of surveys to establish and track parental views on the diseases, vaccines, information needs and their immunization experience. These were originally commissioned by the Department of Health and since 2014, by PHE. These parental attitudinal surveys have identified that parents in England do not consider influenza to be as serious as many other vaccine preventable diseases. In 2010, when the maternal program started, only 8% of parents thought that influenza could be very serious; this figure increased to 22% in 2015 [PHE unpublished data].

Despite this, in 2013 the majority of women responding to an online survey in England stated that they would be prepared to accept a nationally approved vaccine offered by their midwife or GP surgery during pregnancy to protect either themselves (65% definitely and 29% probably) or their baby when it was born (75% definitely and 21% probably); this is considerably higher than the measured coverage achieved in both the seasonal influenza and pertussis immunization programs for pregnant women. As shown in many other studies vaccine safety and effectiveness were the most important issues for women when making decisions on whether to accept vaccination in pregnancy. In addition more than half of the participants indicated that vaccine recommendation by their GP and by their midwife would influence their decision and that for 90% of women their midwife was the ideal source of information if being offered a vaccine in pregnancy. Understanding attitudes to these programs has been essential in tailoring effective communication strategies for pregnant women.

Effective public communication

The provision of clear information on the risks of influenza and the benefits and safety of vaccination has been important in
raising awareness among pregnant women of the importance of vaccination to protect themselves and their infants. In the early years of the influenza program, most of the public communications materials focused on the protection for the mother until the evidence was generated demonstrating the benefits for the infant; in contrast the emphasis for the pertussis program from the outset was very clear and focused on protecting the infant especially given the context of a high number of infant deaths preceding the introduction of the emergency program. These different messages may have also influenced the relatively high coverage achieved early in the maternal pertussis program. The 2013 attitudinal study of pregnant women and mothers of young children found a 10 percentage point difference between women who would definitely take up the offer of vaccination to protect themselves (65%) or to protect their baby (75%) against a potentially life-threatening disease.36

For both maternal programs a range of national public communication material has been developed in England including written leaflets for women when they attend their first antenatal appointment and materials designed to be used by midwives when they discuss maternal immunizations with their clients.37 For the influenza program specifically, a national influenza plan is published which incorporates a communications strategy including leaflets, posters, social media, digital communications for the public as well as training materials for immunizers, professional letters to health charities, case studies and template invitation letters. The availability of online resources for the public has been an important development in ensuring the dissemination of information on both these programs.

One of the factors that may have contributed to the success of the pertussis program for pregnant women in England was the generally positive and high profile reporting of the program. During the early months of the outbreak, the increasing number of reported infant pertussis deaths received a considerable amount of media attention in the UK reflecting a growing concern among health professionals and the public. The announcement by the Chief Medical Officer in England of the emergency program targeting pregnant women was therefore seen as a very welcome intervention. Forty-seven percent of women who were aware of the maternal program in the attitudinal survey in England reported hearing about the program through the television, 17% through newspapers or magazines and 13% through the radio.36 In contrast, there has been little media interest in the influenza program for pregnant women since the 2009 pandemic.

Communication, information resources and training for health professionals

Findings from the attitudinal surveys have demonstrated that parents have consistently stated that health professionals are the most trusted source of immunization information,36,38 and therefore ensuring all professionals involved in the discussion and delivery of the maternal program are fully informed, is critical for ensuring its success.

For example, the national influenza vaccination program in England is supported by a range of professional communications including a formal letter to all health professionals involved in the commissioning and delivery of the program setting out the priorities for each influenza season and recommending the General Practices actively make checks for new pregnancies throughout the influenza season. To support the training of health care professionals involved in vaccination against pertussis in pregnancy, PHE developed a detailed information booklet and training slide set which were freely available online.39 These resources were designed to inform health care professionals involved in the program and to help them provide pregnant women with evidence based information about vaccination against pertussis. A range of other materials were also produced to support this program and the discussions with pregnant women.40

As the routine offer of immunization in pregnancy is relatively new and immunization is not considered a core midwifery skill, not all midwives in England may feel confident in talking to pregnant women about the risks of influenza infection in pregnancy and the benefits of the vaccine. This was evident from some of the early training sessions conducted with midwives across the country. These sessions identified that the published information on the impact, effectiveness and safety of immunizing pregnant women against pertussis and influenza to protect themselves and their babies from birth, generated by evaluation of the program in England and research in other countries, was not reaching them.

As a consequence, efforts in England have focused on staff training and closer working with relevant professional groups such as the Royal College of Midwives. This has led to a number of training and conference sessions focused on immunization in pregnancy programs to help ensure midwives have the information necessary to recommend and discuss vaccination with women and to vaccinate or signpost them to their General Practice for vaccination where appropriate. In addition, information on the safety and effectiveness of both programs has been actively disseminated through publications targeting primary care and midwives.36,41,42

Conclusions

The benefits of the maternal immunization programs for influenza and pertussis have been clearly demonstrated with a number of countries introducing programs to protect pregnant women and their new-born infants from these potentially life threatening infections. Despite a growing body of evidence supporting the safety and effectiveness of these programs in England, a significant proportion of women remain unvaccinated. Coverage of the seasonal influenza program for pregnant women is consistently lower than that of the maternal pertussis program in England and this probably reflects a range of factors including perceived lack of disease severity among women and health professionals, challenges in identifying and inviting pregnant women during a relative short influenza season as well as differences in the methods of collecting vaccine coverage data.

Although coverage of the maternal pertussis program has been encouraging and has remained at close to 60%, efforts in England are currently focusing on targeting the 40% women who remain unvaccinated, especially in light of the continued heightened levels of disease in the population and risk of infant deaths. Understanding the attitudes of women and health professionals involved in delivering antenatal care has been pivotal
in tailoring effective communication strategies and training resources. There remains a continued need to educate all those in regular contact with pregnant women so that women can be fully informed of the importance of vaccination during pregnancy and the benefits for them and their babies. In England, the challenge remains on ensuring timely and effective communication between those health professionals involved in providing routine antenatal care and those currently responsible for delivering these lifesaving immunization programs.

**Disclosure of potential conflicts of interest**

The Immunisation, Hepatitis and Blood Safety Department has provided vaccine manufactures with post-marketing surveillance reports which the Marketing Authorisation Holders are required to submit to the UK Licensing authority in compliance with their Risk Management Strategy. A cost recovery charge is made for these reports which have not to date included pertussis. LL, HC, DG, JY and MR have no other reported conflicts. Accommodation costs have been covered by Medscape Education for GA to present on the maternal pertussis immunisation programme.

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