

Institution: The University of Oxford
Unit of Assessment: 2
Title of case study <p style="text-align: center;">UNDERPINNING EVIDENCE-BASED POLICY FOR MANAGEMENT OF INFLUENZA IN PREGNANT WOMEN</p>
Summary of the impact <p>Researchers at the University of Oxford instituted a rapid study of pregnant women hospitalised across the UK with 2009/H1N1 infection, which demonstrated that early antiviral treatment improved maternal outcomes of infection and led to actions by the Department of Health to ensure rapid availability of antivirals specifically for pregnant women. The poor maternal and perinatal outcomes identified by this study also led to an on-going policy change, so that all pregnant women in the UK are now recommended to receive annual immunisation against seasonal influenza.</p>
Underpinning research <p>Following the outbreak of the 2009/H1N1 influenza pandemic, pregnant women were identified as a probable high-risk group. The existence of UK Obstetric Surveillance System (UKOSS) [1] developed and led by Professor Marian Knight and colleagues at the National Perinatal Epidemiology Unit, University of Oxford, enabled the rapid initiation of a study of pregnant women hospitalised across the UK with 2009/H1N1 infection [2]. Data were analysed on a monthly basis to inform the development of on-going policy and guidance issued by the Department of Health. This allowed for real-time changes to policy and guidelines as the data accumulated, enabling a rapid response to the emerging pandemic.</p> <p>The study findings demonstrated that early antiviral treatment for pregnant women led to a 90% reduction in the odds of admission for critical care. This resulted in actions by the Department of Health to ensure rapid availability of antivirals specifically for pregnant women, through the modification of the clinical algorithms in use, enabling availability of antivirals for pregnant women through the National Pandemic Flu Service. Guidance for obstetricians and other clinicians involved in the care of pregnant women was also modified [2].</p> <p>The poor maternal and perinatal outcomes identified by the study, showing a five times increase in the risk of perinatal death and a more than three times increase in the risk of premature birth amongst the infants of infected women, also led to a change in immunisation policy in the UK during the course of the pandemic. The updated policy classified pregnant women as an “at-risk group” eligible for influenza vaccination [3,4].</p> <p>These data have also led to an on-going policy change, so that all pregnant women in the UK are now recommended to receive an annual immunisation against seasonal influenza. The European Centre for Disease Control and Prevention (ECDC) also issued a subsequent recommendation, based on UKOSS data, that universal influenza immunisation for pregnant women should be offered throughout Europe [see reference G in impact section].</p>
References to the research <p>[1]. Knight M, Kurinczuk JJ, Tuffnell D, Brocklehurst P. The UK Obstetric Surveillance System for rare disorders of pregnancy. <i>Br J Obstet Gynaecol</i> 2005; 112: 263-5. PubMed ID: 15713136. <i>Paper describing the establishment of the UK Obstetric Surveillance System.</i></p>

- [2]. Yates L, Pierce M, Stephens S, Mill AC, Spark P, Kurinczuk JJ, Valappil M, Brocklehurst P, Thomas SH, Knight M. Influenza A/H1N1v in pregnancy: an investigation of the characteristics and management of affected women and the relationship to pregnancy outcome for mother and infant. *Health Technol Assess* 2010;14:109-82. PubMed ID: 20630123. <http://www.hta.ac.uk/execsumm/summ1434-02.shtml> [accessed 9/10/13]. **Monograph describing the maternal outcomes of 2009/H1N1 influenza. Oxford researchers led the secondary care study.**
- [3]. Knight M, Pierce M, Seppelt I, Kurinczuk JJ, Spark P, Brocklehurst P, McLintock C, Sullivan E on behalf of the UK's Obstetric Surveillance System, the ANZIC Influenza Investigators, and the Australasian Maternity Outcomes Surveillance System. Critical illness with AH1N1v influenza in pregnancy: a comparison of two population-based cohorts. *Br J Obstet Gynaecol* 2011;118:232-9. doi: 10.1111/j.1471-0528.2010.02736.x. PubMed ID: 21040393. **Paper showing better outcomes of 2009/H1N1 influenza in the UK compared to Australasia, after public health measures were introduced.**
- [4]. Pierce M, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M on behalf of UKOSS. Perinatal outcomes after maternal 2009/H1N1 infection: a national cohort study. *Br Med J* 2011 Jun 14;342:d3214. doi: 10.1136/bmj.d3214. PubMed ID: 21672992. **Paper detailing the perinatal outcomes of 2009/H1N1 influenza, after all on-going pregnancies were completed.**

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Details of the impact

The key to being able to rapidly mount a study of pregnant women, hospitalised with 2009/H1N1 pandemic influenza, was the prior establishment in 2005 of the novel UKOSS system, which allows for rapid institution of research into pregnancy complications in the event of a public health emergency such as this. For the influenza study, data were analysed cumulatively on a monthly basis, enabling Professor Knight to feedback results in real-time via weekly teleconferences and monthly meetings at the Department of Health. In this way the UKOSS findings were central to immediate policy development, for guidance on the management of pregnant women infected the with 2009/H1N1 virus, as the course of the pandemic evolved [A, B, C]. The UKOSS results indicated that pregnant women treated earlier with antiviral therapy had better maternal and perinatal outcomes than those treated later in their clinical course or not at all. National advice and the clinical algorithm was changed as a result leading to the earlier initiation of antiviral therapy particularly for pregnant women and action by the Department of Health to ensure the availability of antiviral therapy to pregnant women through the National Pandemic Flu Service and Antiviral Collection Points [C].

The extent of maternal morbidity, and maternal and perinatal deaths quantified by the UKOSS study, contributed to the change in immunisation policy in the UK during the course of the pandemic to actively offer pregnant women immunisation. This policy change has now been adopted as an on-going recommendation that annually all pregnant women should be immunised against seasonal influenza [D, E]. The number of pregnant women immunised against influenza in England has subsequently increased, from 118,000 in 2009/10, to 124,000 in 2010/11 and 196,000 in 2011/12 [F].

The impact of the research was achieved by the direct input of real-time research results by Professor Marian Knight into the decision making systems at the Department of Health for

England. Results were also shared with the Influenza planning group at the Royal College of Obstetricians and Gynaecologists during the course of the evolving pandemic. Later impact is demonstrated by the subsequent recommendation, which incorporated the study data, issued by the European Centre for Disease Control and Prevention (ECDC). The recommendation states that universal influenza immunisation for pregnant women should be offered throughout Europe [G].

Once the pandemic had abated it became clear from data collected by UKOSS and the National Confidential Enquiry into Maternal Deaths that 13 pregnant women in the UK had died as a direct result of 2009/H1N1 influenza virus infection. These deaths could have been prevented by prior immunisation. In addition, the study results suggested that early treatment with antiviral medication led to a 90% reduction in the odds of admission for critical care. The resulting substantial changes in practice, which were instituted as a result of the UKOSS study findings, were, and continue to be, instrumental in preventing the deaths and serious morbidity for pregnant women and their babies in the UK and elsewhere. The study is referenced in guidance for critical care clinicians [H]. It is also referenced in current media campaigns to highlight the importance of on-going immunisation to women [I], and in policy documents recommending immunisation against influenza in pregnancy in countries other than the UK [J].

Sources to corroborate the impact

- [A]. Minutes and action logs available from the Influenza Clinical Information Network (FLU-CIN) meetings/teleconferences. ***These documents demonstrate the use of the study data to inform policy development during the H1N1 influenza pandemic.***
- [B]. Factual statement provided by the Department of Health Clinical Advisor. ***Written statement describing the use made of the study data to develop policy and clinical guidelines.***
- [C]. H1N1 (2009) winter flu: Updated guidance for providers of maternity services. London: Department of Health 2011.
http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1294740886540 [accessed 4/11/13].
This is the key Department of Health policy document describing immunisation and antiviral prescription recommendations.
- [D]. <http://www.nhs.uk/news/2011/10October/Pages/swine-flu-H1N1-risk-pregnancy-still-birth.aspx> [accessed 9/10/13]. ***This immunisation campaign article references the BMJ paper and advises women to get the vaccine.***
- [E]. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733756886 [accessed 9/10/13]. ***The Health Protection Agency link to vaccine uptake information for 2009-2012.***
- [F]. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/147958/Green-Book-Chapter-19-v4_71.pdf [accessed 4/11/13]. ***Department of Health guidance on immunisation for influenza in pregnancy (updated for 2012/13 winter influenza season). See page 202.***
- [G]. <http://www.ecdc.europa.eu/en/publications/publications/seasonal%20influenza%20vaccination%20of%20children%20and%20pregnant%20women.pdf> [accessed 4/10/13]. ***This is the ECDC European advice that all women should be immunised against influenza in pregnancy. See pages 2, 3, 12, 14.***
- [H]. http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1287148502205 [accessed 4/11/13]. ***Guidance from the Health Protection Agency on critical care management of adults with influenza with particular reference to H1N1.***

- [I]. <http://www.guardian.co.uk/politics/2010/sep/30/pregnant-women-flu-jab-list> [accessed 9/10/13]. **Guardian article citing the government campaign to encourage women to have immunisation against seasonal influenza.**
- [J]. <http://www.hpsc.ie/hpsc/A-Z/Respiratory/Influenza/SeasonalInfluenza/Guidance/PregnancyGuidance/File,13162,en.pdf> [accessed 4/11/13]. **Guidance from the Republic of Ireland citing the study and recommending immunisation against seasonal influenza for pregnant women.**