Study Title: **Maternal and perinatal outcomes of pandemic influenza or novel coronavirus in pregnancy.**

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# Project Protocol

## 1 Project title

**Maternal and perinatal outcomes of pandemic influenza or novel coronavirus in pregnancy.**

Project reference 11/46/12.

## 2 Planned investigation

### 2.1 Research objectives

a) To determine:

i) The incidence of hospitalisation with pandemic-type influenza or novel coronavirus in pregnancy.

ii) The outcomes of pandemic-type influenza or novel coronavirus in pregnancy for mother and infant.

b) To investigate:

i) The influence of demographic or pregnancy characteristics on outcomes for mother and infant.

ii) The influence of prior immunisation with seasonal influenza vaccine or specific influenza vaccine on outcomes for mother and infant, including an assessment of reasons for non-immunisation.

iii) The influence of timing of delivery, particularly in relation to the use of extracorporeal membrane oxygenation on outcomes for mother and infant.

iv) The influence of other variations in management on outcomes for mother and infant.

b) To produce guidance on the management of pandemic-type influenza or novel coronavirus infection in pregnancy by monthly review of emerging data from this study such that outcomes for women and infants are optimised during the pandemic.

### 2.2 Existing research

Evidence from the last influenza pandemic (2009/H1N1) showed that pregnant women were particularly vulnerable to severe infection (1-5), resulting in increases in both maternal and perinatal mortality (5-7). Further investigations, including through the UK Obstetric Surveillance System (UKOSS) (5), highlighted specific groups of women who were at higher risk of morbidity after 2009/H1N1 infection in pregnancy. Factors associated with admission to hospital with 2009/H1N1 in pregnancy included maternal obesity, asthma, multiparity, multiple pregnancy, black or other minority group ethnicity and smoking among women younger than 25 years (1, 3, 5).

Active data collection on pregnant women admitted to hospital with confirmed AH1N1 influenza, conducted using the UKOSS, as well as identifying particular subgroups of pregnant women who were at risk of the severest disease and hence a particular target for preventive interventions, also pinpointed important aspects of management which resulted in improved outcomes for women, including the importance of early antiviral treatment (5). Monthly analysis of emerging data was used to inform ongoing clinical guidance during the pandemic. Admission to an intensive care unit, taken as a proxy for severe morbidity, was also associated with delay in starting treatment with antiviral medication (more than two days after the onset of symptoms) in other population studies (1, 3, 4, 8).

Most studies of 2009/H1N1 in pregnancy reported very incomplete outcomes or outcomes for only a subset of severely affected women (table 1) (1, 3, 4, 8-10). Half of outcome rates were calculated using subsamples of less than fifty per cent of the study cohort. The majority of studies did not follow up women to the end of their pregnancy (3, 4, 8, 10) or in some cases the follow up time was too short to collect outcome information on women infected at all gestations (8, 9). This approach will bias any results towards reporting preterm births which is likely to lead to overly pessimistic results.

The UKOSS study (6) followed up 94% of the original study cohort (n=256) and demonstrated that poor perinatal outcomes, in addition to poor maternal outcomes, were associated with 2009/H1N1 influenza infection in pregnancy. The risks of poor outcomes persisted after adjustment for maternal and pregnancy characteristics known to be associated with poor perinatal outcomes. The study suggested an increased risk of perinatal mortality in women infected with 2009/H1N1 compared with the general population (perinatal mortality rate 39 per 1,000 total births (95%CI 19 to 71) compared to 7 per 1,000 total births (95%CI 3 to 13), aOR: 5.7; 95%CI 2.2 to 15.1), which was explained almost entirely by an increased risk of stillbirth. The study was cited by the European Center for Disease as an important European advance, strengthening the evidence for offering routine immunisation to pregnant women in Europe (11).

**Table 1: Studies of pregnancy outcomes among 2009/H1N1 infected women**

| Study | Study period | Study population | Number of pregnant women reported | Number of women with outcome data (%) | Pregnancy outcome | Number affected (%) |
|---|---|---|---|---|---|---|
| Siston 2010 (4) | 14/04/2009 – 21/08/2009 | Pregnant women with 2009/H1N1 influenza, USA | 788[a] | 169 (21) | Preterm delivery | 51 (30) |
| | | | | 200 (25) | Spontaneous Abortion | 8 (4) |
| Louie 2010 (3) | 23/04/2009 – 11/08/2009 | Women with confirmed 2009/H1N1 requiring intensive care, California, USA | 18 | 12 (67) | Preterm delivery | 10 (83) |
| | | Hospitalised (>24 hrs) or dead women with confirmed 2009/H1N1, California, USA | 94 | 37 (39) | Spontaneous Abortion | 2 (5) |
| Creanga 2010 (8) | 01/05/2009 – 30/06/2009[b] | Hospitilised women with H1N1v infection, New York, USA | 62 | 40 (65) | Preterm delivery | 6 (15) |
| | | | | | Neonatal death | 2 (5) |
| Hewagama 2010 (10) | 20/05/2009 – 31/07/2009 | Hospitalised pregnant women with 2009/H1N1 infection, Victoria, Australia | 43 | 15 (35) | Preterm delivery | 6 (40) |
| | | | | 24 (55) | Stillbirth[d]/ Neonatal death | 3 (13) |
| ANZIC 2010 (1) | 01/06/2009 – 31/08/2009 | Pregnant or recently postpartum women admitted to intensive care unit with 2009/H1N1, Australia and New Zealand | 64 | 61 (95) | Miscarriage[c] | 2 (3) |
| | | | | | Stillbirth[d] | 4 (7) |
| | | | | | Preterm delivery | 22 (37) |
| | | | | | Low birth weight | 18 (31) |
| Dubar 2010 (9) | 01/08/2009 - 31/12/2009 [e] | Pregnant women admitted to hospital with confirmed 2009/H1N1, France | 314 | 146 (46) | Stillbirth | 2 (1) |
| | | | | | Loss of pregnancy prior to 24 weeks | 4 (2) |
| | | | | | Low birth weight | 22 (16) |
| | | | | | Preterm birth | 26 (19) |
| Pierce (UKOSS) 2011 (6) | 01/09/2009 - 31/01/2010 | Pregnant women admitted to hospital with confirmed 2009/H1N1, UK | 272 | 256 (94) | Loss of pregnancy prior to 24 weeks | 5 (2) |
| | | | | | Stillbirth | 7 (3) |
| | | | | | Neonatal death | 3 (1) |
| | | | | | Preterm birth | 59 (24) |

[a] Including 509 hospitalised women.
[b] Followed up until 18/09/2009
[c] Defined as in utero death <20 weeks gestation
[d] Defined as in utero death ≥20 weeks gestation
[e] Followed up until 31/04/2010

In addition to the mortality risk, infants were at greater risk of preterm birth (aOR 4.0, 95%CI 2.7 to 5.9). The data suggest that women with 2009/H1N1 infection who gave birth preterm were more likely to have been infected in their third trimester. Secondary infection with pneumonia played an important role in preterm delivery in this 2009-10 cohort; secondary pneumonia was also associated with preterm birth in women with pandemic influenza in 1919 (12). In the UK data, the risk of preterm birth associated with 2009/H1N1 infection persisted even after accounting for the role of secondary pneumonia which suggests that the excess risk cannot be explained by this factor alone.

Almost half of the infants delivered preterm were delivered early because of maternal compromise. Women are typically delivered during the third trimester in order to aid mechanical ventilation. However, emerging evidence suggests that when women are referred for management with extracorporeal membrane oxygenation (ECMO), in the absence of fetal compromise there may not be an indication to deliver the fetus early (13). This is noted particularly at gestations below 30 to 32 weeks, when the size of the uterus is unlikely to affect mechanical ventilation. Increased availability and use of ECMO may therefore have the potential to impact positively on infant outcomes even in the presence of maternal critical illness.

Overall, these studies show a clear increase in risk of poor maternal and pregnancy outcomes in women infected with AH1N1v influenza. Importantly, immunisation against AH1N1v influenza for pregnant women is thus likely to have a significant impact on health outcomes for both mother and baby. Almost half of the preterm deliveries were due to early delivery for maternal compromise, indicating that the health of pregnant women, which is improved with rapid treatment with antiviral agents, is an important public health priority in future waves of this and other influenza pandemics.

In a future pandemic, either of influenza or another respiratory virus such as corona virus, however, these observed patterns may differ. A rapid study of this susceptible group (pregnant women) will be important to inform both ongoing preventive and management policies. In particular, a number of clinical questions remain unresolved, which would be informed by the proposed study. In particular, it is important to establish whether pregnancy can be successfully continued in women with severe respiratory viral illness managed with extracorporeal membrane oxygenation (ECMO). Anecdotal evidence currently exists that pregnancy can be continued during and after ECMO treatment, but further data are needed to fully inform management guidance and also service planning. Additionally it will be important to investigate whether the current seasonal influenza immunisation at the time of the pandemic protects women against pandemic influenza. Immunisation policy changed subsequent to the most recent pandemic, such that pregnant women are now offered seasonal influenza immunisation as part of a routine programme. However, uptake remains relatively low. In a new pandemic situation, establishing whether pregnant

women have any protection from existing vaccines, as well as establishing reasons for non-immunisation, will inform immediate public health actions.

These questions are equally relevant in any pandemic of respiratory illness; the emerging novel coronavirus (2019-nCoV) may also differentially impact negatively on pregnant women. Single case reports of 2019-nCoV infection in pregnant women, with vertical transmission of infection to infants, are emerging, and given known adverse pregnancy outcomes of both SARS-CoV and MERS-CoV (14), a rapid study in pregnancy to inform prevention and treatment will be important.

## 2.3 Research methods

### 2.3.1 Research Design

This will be a national prospective observational cohort study using the UK Obstetric Surveillance System (UKOSS). UKOSS is a well-established national system to collect information about severe maternal morbidity through more than 500 collaborating clinicians in all 194 hospitals with consultant-led maternity units throughout the UK (see www.npeu.ox.ac.uk/ukoss for further information). All hospitals in the UK with a consultant-led maternity unit collaborate in UKOSS, and thus it is an ideal mechanism to collect comprehensive information about women hospitalised with pandemic influenza or novel coronavirus in pregnancy, their management and outcomes. In view of the ethical and other difficulties of conducting clinical trials in pregnant women, the collection of national observational data in this way provides the best rapidly available quality evidence to inform ongoing clinical and public health policy and management guidance. This system has been demonstrated to be able to be used to rapidly collect information to inform policy and guidance in a previous pandemic (5, 6).

### 2.3.2 Cohort Identification

Cases will be identified through the UKOSS network of nominated reporting clinicians in each consultant-led maternity unit in the UK. Nominated reporting clinicians will be asked to report all pregnant women with confirmed pandemic influenza or novel coronavirus admitted to their unit. In view of the need for rapid and ongoing data analysis and production of guidance, we will use a specific web-based rapid reporting and data collection system for this study to enable UKOSS nominated clinicians to report cases as they occur. In addition, nominated clinicians will be sent a standard UKOSS reporting card each month to further enhance case ascertainment.

Information about comparison women will be obtained from previously collected UKOSS data. The UKOSS database currently contains detailed demographic, pregnancy and delivery information about a cohort of over 1500 women giving birth in the UK identified from the same hospitals as cohort women and data collection is ongoing. Data from comparison women giving birth in the UK in the two

years prior to any future pandemic, and not reported to have been infected with influenza or novel coronavirus, will be used to minimise any potential bias introduced by service changes, which might be possible if an older historical comparison cohort were used.

### 2.3.3 Data Gathering

On receiving a case report, the central team will ask the clinician to complete an electronic data collection form (see appendix for draft), asking for further detailed information about women's characteristics, diagnosis, management and outcomes. All data collected will be anonymous; no names, addresses, postcodes, hospital or NHS numbers will be collected. Patients will be identified using a unique UKOSS number supplied by the central team. If a completed data collection form is not received back by the central team after three weeks, a further reminder will be sent out. If there is still no response after a further three weeks, the clinician will be contacted by telephone.

### 2.3.4 Monitoring Data Collection

Information concerning pandemic influenza in pregnancy will be compared with information from the Health Protection Agency and from the Intensive Care National Audit and Research Centre (ICNARC) database. In addition, adult ECMO centres functioning at the time of the pandemic will be contacted directly to identify cases. The organisation responsible for monitoring perinatal and maternal deaths (currently under review) will also be contacted and asked to provide information on fatal cases of pandemic influenza in pregnancy, or consequent stillbirths or neonatal deaths. If any cases are identified through these sources which have not been identified through UKOSS, the nominated UKOSS clinician in the relevant hospital will be contacted and asked to provide further information on management and outcomes.

### 2.3.5 Study activation

UKOSS is an ongoing research system with a rolling programme of studies. Preparation of the relevant paperwork (study protocol and data collection form) and programming, together with obtaining UKOSS Steering Committee, ethics committee and NHS management approval in advance (as appropriate) would allow the study to be activated very rapidly (within two weeks) in the event of a future pandemic.

## 2.4 Planned inclusion/exclusion criteria

The cohort will be all pregnant women in the UK admitted to hospital with confirmed pandemic influenza or novel coronavirus. Women not meeting the inclusion criteria will be excluded.

In order to facilitate a rapid study without placing an additional data collection burden on clinicians in the context of an influenza or novel coronavirus pandemic, information about comparison women will be obtained from previously collected UKOSS data. This approach was successfully used in the most recent 2009-10 influenza pandemic (5, 6). The UKOSS database currently contains detailed demographic, pregnancy and delivery information about a cohort of over 1500 women giving birth in the UK identified from the same hospitals as cohort women and data collection is ongoing. Data from comparison women giving birth in the UK in the two years prior to any future pandemic, and not reported to have been infected with influenza or novel coronavirus, will be used to minimise any potential bias introduced by service changes, which might be possible if an older historical comparison cohort were used.

The denominator population will be all women giving birth in the UK.

### 2.5 Ethical arrangements

This study seeks to collect anonymous information only about women who have pandemic influenza during pregnancy. This information is key to identifying evidence to inform ongoing policy and guidance in the context of a pandemic. The collection of information about individuals in this way raises these main ethical issues:

1. Consent. It will not be practicable to obtain consent for data collection from individual women, as this would prevent the achievement of the primary objective of the study, namely to document the numbers of women who are affected in the UK. Accurate measurement of incidence requires documentation about ALL cases occurring in the UK. The National Information Governance Board (NIGB) Ethics and Confidentiality Committee considers that organisations seeking to use NHS information for research purposes without consent should seek anonymised or pseudonymised data only and not any personally identifiable information (15). Accordingly, this study will not collect names, addresses, postcodes, dates of birth, NHS or hospital numbers. Collection of anonymised data in this way in the absence of consent is unlikely to cause significant harm. This UKOSS methodology has received the approval of the North London REC1 (study reference 10/H0717/20).
2. Confidentiality and data security. In order to maintain patient confidentiality, no names, addresses, postcodes, dates of birth, hospital or NHS numbers will be collected as outlined above. The security of all data will be maintained by storage on a secure University network, accessible only by the key researchers and responsible members of the University of Oxford who may require access to data to ensure compliance with regulations. Access by any other individuals for the purposes of any other study will only be allowed after review by the UK Obstetric Surveillance System Steering Committee and further reference to a Research Ethics Committee. Prof Jenny Kurinczuk, Director of the National Perinatal Epidemiology Unit, University of Oxford will act as custodian of the data.

### 2.6 Proposed sample size

As the study we propose is a national observational study, the study sample size will be governed by the disease incidence. As an estimate, based on our experience in the 2009-10 pandemic, we anticipate identifying 300-500 infected pregnant women admitted to hospital. Information on up to 700 comparison women is available from existing UKOSS data. We have estimated the study size based on estimated incidence and not any specific outcomes. However, as a guide, the table below indicates the odds ratios detectable by a study of this size, assuming 80% power and a 5% level of significance with a 1.4:1 ratio of unexposed to exposed:

| Frequency of outcome in comparison cohort | Odds ratio detectable by the study |
|---|---|
| **1%** | 3.38 |
| **5%** | 1.90 |
| **10%** | 1.64 |
| **20%** | 1.47 |

### 2.7 Statistical analysis

The following analyses will be conducted:

a) Estimation of the incidence of hospitalisation with pandemic influenza or novel coronavirus amongst pregnant women with 95% confidence intervals, using the denominator of total maternities in the UK over the relevant time period.

b) Comparison of the rates of individual adverse outcomes (maternal death, level 3 critical care unit admission, other major complication, preterm birth, congenital anomaly, stillbirth, early neonatal death, perinatal death) between women infected with pandemic influenza or novel coronavirus admitted to hospital and the comparison cohort. Adjustment for potential confounders will be undertaken using Poisson regression (for rare events) or logistic regression (if the outcomes are more frequent). Confounders included in the model will be those known to be associated with the relevant outcomes (age, parity, marital status, ethnicity, smoking status, socioeconomic status, previous preterm delivery, previous perinatal death).

c) The management of pregnant women hospitalised with confirmed pandemic influenza or novel coronavirus will be described. Differences in outcomes will be explored in different subgroups according to management. The initial subgroups examined will be as follows (although note that these may be revised as more becomes known about the patterns of disease during the pandemic):

   Antiviral treatment received within 48hr of symptom onset (Yes/No)

   Type of antiviral received

   Dose of antiviral received

   Use of ECMO during pregnancy

   Delivery prior to institution of respiratory support (Yes/No)

Mode of delivery

Guidance on the management of pregnant women with pandemic influenza or novel coronavirus in pregnancy, informed by ongoing data analysis, will be produced and reviewed monthly with the relevant organisations, for example, the Department of Health, Royal College of Obstetricians and Gynaecologists, Royal College of Midwives and Royal College of General Practitioners, in order to improve outcomes for women and infants based on the available evidence.

### 2.8 Proposed outcome measures

The following outcomes will be compared between women with influenza or novel coronavirus and comparison women, and explored in different subgroups according to management variations:

Maternal death
Maternal level 3 critical care unit admission
Other major maternal complication
Preterm birth
Congenital anomaly
Perinatal death

### 2.9 Research governance

Research Ethics Committee and NHS management approval will be obtained as appropriate prior to the start of the study. The University of Oxford will act as sponsor of the study.

The overall conduct of the study will be monitored by a Management Group consisting of the Co-Applicants, Information Scientist, Researcher, Project Programmer, Statistician and other external members as considered necessary for the project.

## 3 Project timetable and milestones

### 3.1 Timetable

**Pre-activation phase (provisional start date 1 June 2012)**

| | |
|---|---|
| June 2012 | Apply for necessary approvals, develop web-based reporting systems, finalise and format data collection form and clinician information. |

**Activation phase**

| | |
|---|---|
| Week 1 | Study information mailed/emailed to clinicians |
| Week 3 | Data collection commenced |
| Months 2-25 | Ongoing reporting of new cases, data analysis, production of management guidance and dissemination. |

| | |
|---|---|
| Months 26-31 | Collection of remaining pregnancy outcome data |
| Month 37 | Final pregnancy outcome analysis, production of guidance and dissemination |

### 3.2 Milestones

**Pre-activation phase**

| | |
|---|---|
| July 2012 | Web-based reporting system in place, data collection form finalised and formatted |
| August 2012 | Approvals completed (assuming no expedited process) |

**Activation phase**

| | |
|---|---|
| Month 2 | First data analysis, first guidance issued |
| Months 3-17 | Ongoing monthly data analysis, revised guidance issued |
| Month 18 | Final report on immediate maternal and pregnancy outcomes, revised guidance |
| Month 21 | Final report on complete pregnancy outcomes, including data on pregnancy outcomes of women undelivered at the time of interim reports |

## 4 Expertise

The research team has the necessary expertise to carry out this comprehensive national study, including public health (MK, JK), congenital malformations (JK), perinatal epidemiology and statistics (MQ, MK, JK, PB), obstetric surveillance (MK), guideline development (JK, PB), and obstetrics (PO'B, PB).

The National Perinatal Epidemiology Unit (NPEU) has a national and international reputation for conducting studies which change policy, influence practice and improve the care of women and their babies. MK developed and launched UKOSS and led the initiative from its inception; since its establishment in 2005, UKOSS has generated evidence to improve prevention and management of a range of severe pregnancy complications in the UK involving a network of over500 collaborating clinicians at all 194 hospitals with consultant maternity units throughout the UK. The infrastructure is thus in place to allow rapid identification of women hospitalized with pandemic influenza or novel coronavirus infection in pregnancy through an established active surveillance system.

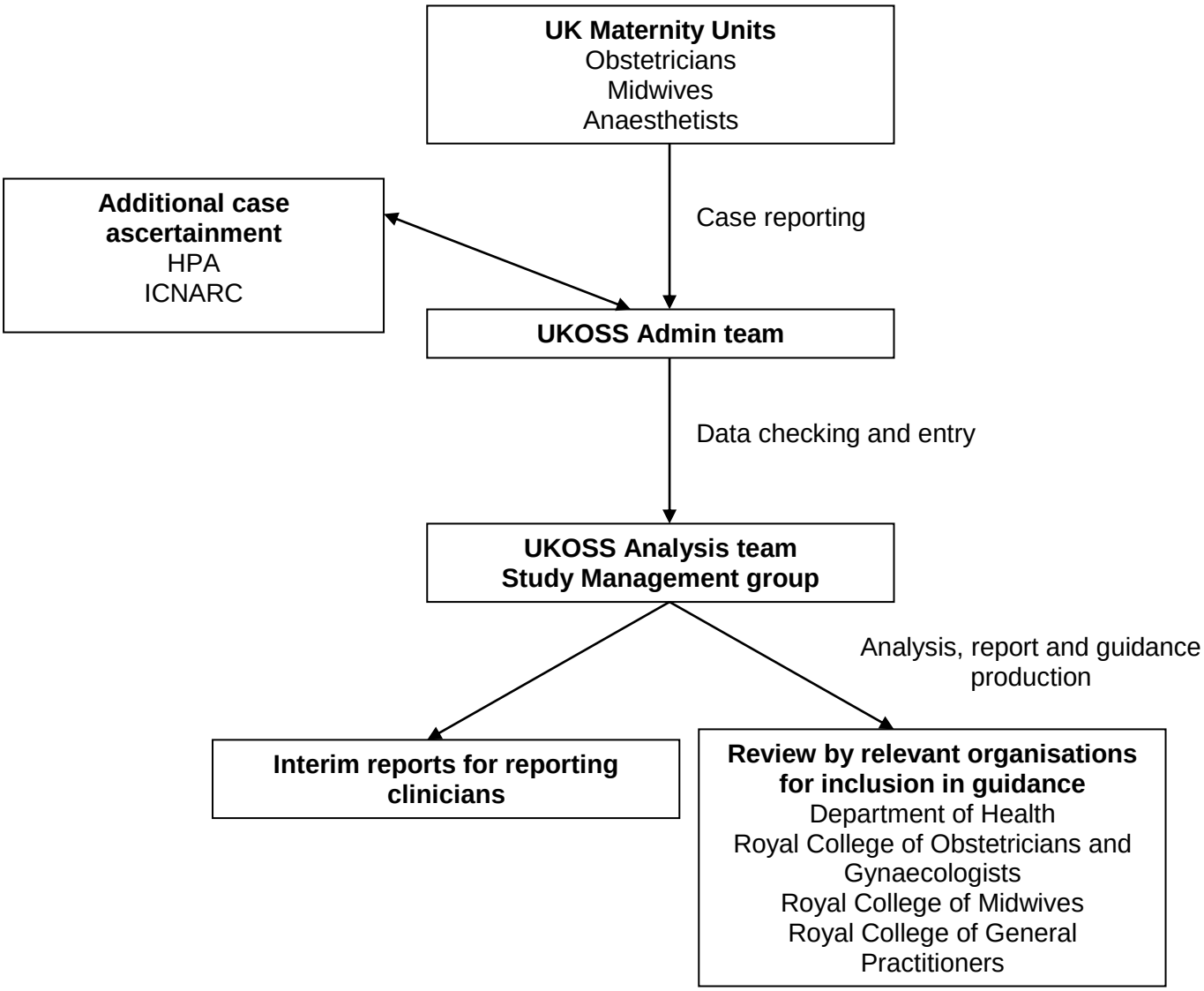
PO'B is the Royal College of Obstetricians and Gynaecologists lead for pandemic influenza planning and will provide a direct link to produce ongoing updated guidance through the RCOG pandemic influenza planning group.

## 5 Service Users

Lay representatives from the UKOSS Steering Committee and Sands, the stillbirth and neonatal death charity, have been consulted about the development and acceptability of the study protocol, data

collection form, information and other materials. As all data collected will be anonymous, we cannot feedback results directly to women whose data are included in the study. The research team will therefore work directly with Sands, the stillbirth and neonatal death charity, and the NCT (formerly National Childbirth Trust), as well as available net fora such as Mumsnet, to ensure that results and advice are disseminated widely to pregnant women and their partners. The NPEU has an active user and voluntary organisations advisory group through whom dissemination will also be undertaken.

## 6 Flow diagram

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**Appendix**

**Draft UKOSS Data Collection Form – Influenza or nCoV CASES**

| **Section 1: Woman's details** | | |
|---|---|---|
| Year of birth | | |
| Ethnic group[1*] | | |
| Marital status | | Single/married/cohabiting |
| Was the woman in paid employment at booking? | | Yes/No |
| IF YES what is her occupation | | |
| IF NO, what is her partners occupation | | |
| Height at booking (cm) | | |
| Weight at booking (kg) | | |
| Smoking status | | Never/Current/Gave up prior to pregnancy/ Gave up during pregnancy |
| | | |
| **Section 2: Previous Obstetric History** | | |
| Gravidity | | Number of completed pregnancies beyond 24 weeks |
| | | Number of pregnancies less than 24 weeks |
| If no previous pregnancies go to section 3. | | |
| Did the woman have any previous pregnancy problems?[2*] | Yes/No | If yes, please specify |
| | | |
| **Section 3: Previous Medical History** | | |
| Please indicate whether any of the following were present: | | |
| Previous or pre-existing medical problems[3*] | Yes/No | If yes, please specify |
| Has the woman been immunised against influenza? | Yes/No | If Yes, please give dates immunised<br>Was this seasonal influenza vaccine or pandemic-type vaccine? |
| | | If No, please state reasons for non-immunisation (tick all that apply)<br>Not offered/Not available/contraindicated/Safety concerns/woman's preference/Not known |
| | | |
| **Section 4: This Pregnancy** | | |
| Final Estimated Date of Delivery (EDD)[4*] | | |
| Was this pregnancy a multiple pregnancy? | Yes/No | If yes, specify number of fetuses |
| Were there problems in this pregnancy[2*] | Yes/No | If yes, please specify |
| | | |
| **Diagnosis of Influenza or nCoV** | | |
| Please indicate presenting symptoms and date of onset in the table below | | |
| *Symptom* | *Yes tick boxes* | *If yes give date of onset* |
| Fever | | |
| Cough | | |
| Sore throat | | |
| Headache | | |

| | | |
|---|---|---|
| Tiredness/lethargy | | |
| Limb or joint pain | | |
| Diarrhoea | | |
| Breathlessness | | |
| Vomiting | | |
| Rhinorrhoea | | |
| | | |
| Has virological testing for influenza or nCoV been carried out? | | Yes/No |
| If Yes, did this confirm the diagnosis? | Yes/No | If yes, specify type identified and sample source |
| | | Date of first positive test |
| | | Date(s) of subsequent positive tests |
| | | |
| Was this a clinical diagnosis only? | Yes/No | |

| **Therapy** | | |
|---|---|---|
| Were anti-viral drugs used? | Yes/No | If yes, specify agent used, date treatment started, date treatment stopped, dose and schedule |
| Were other drugs used during pregnancy? | Yes/No | If yes, please specify |
| Were steroids given to enhance fetal lung maturation? | Yes/No | If yes, please specify agent, date given and dose |
| Was this woman managed with extracorporeal membrane oxygenation (ECMO)? | Yes/No | If yes, please indicate:<br>Date ECMO commenced<br>Name of ECMO centre<br>Was this woman delivered during her ECMO treatment? Yes/No<br>If yes, please give reason for delivery |

| **Section 5: Delivery** | | | |
|---|---|---|---|
| Did this woman have a miscarriage? | Yes/No | If yes, please specify date | |
| Did this woman have a termination of pregnancy? | Yes/No | If yes, please specify date<br>Was the pregnancy terminated due to a congenital malformation? If yes, please specify | |
| Is this woman still undelivered | Yes/No | | |
| IF YES, will she be receiving the rest of her antenatal care from the current hospital | Yes/No | If no, please indicate name of hospital providing future care, then go to section 7 | |
| IF NO, please continue | | | |
| Was delivery induced | Yes/No | If yes, please state indication | |
| | | Was vaginal prostaglandin used? | Yes/No |
| Did the woman labour? | | Yes/No | |
| | | If yes, date and time of onset of labour | |
| Was delivery by caesarean section | Yes/No | If yes: | |
| | | Please state grade of urgency[5*] and give indication for caesarean section<br>Method of anaesthesia: regional/general anaesthetic | |
| | | | |

| | | |
|---|---|---|
| **Section 6: Outcomes** | | |
| **Section 6a: Woman** | | |
| Was the woman admitted to Level 3 critical care? | Yes/No | If Yes, please specify duration of stay (days)<br>**Or** Tick if woman is still in ITU<br>**Or** Tick if woman was transferred to another hospital |
| Did any other major maternal morbidity occur[6*] | Yes/No | If yes, please specify |
| Did the woman die? | Yes/No | If yes, please specify date and time of death |
| | If the woman died what was the primary cause of death as stated on the death certificate? | |
| | | |
| **Section 6b: Infant 1** | | |
| Date and time of delivery | | |
| Mode of delivery | | Spontaneous vaginal/ventouse/lift-out forceps/rotational forceps/pre-labour caesarean section/caesarean section after onset of labour |
| Birthweight (g) | | |
| Was the infant stillborn? | Yes/No | If yes, go to section 7 |
| 5 min Apgar | | |
| Was the infant admitted to the neonatal unit? | Yes/No | If yes<br>Duration of stay (days)<br>**Or** Tick if infant is still in neonatal unit<br>**Or** Tick if infant was transferred to another hospital |
| Did any other major infant complications occur?[7*] | Yes/No | If yes, please specify |
| Did the infant have a congenital anomaly? | Yes/No | If yes, please specify |
| Did this infant die | Yes/No | If died specify date of death |
| | | |
| **Section 7** | | |
| Please use this space to enter any other information you feel may be important | | |
| | | |
| **Section 8** | | |
| Name of person completing the form | | |
| Designation | | |
| Today's date | | |
| | | |

If more than one infant, please photocopy and attach additional sheet(s) or download additional forms from the website (www.npeu.ox.ac.uk/ukoss)

*For definitions please see following list

**[1]Coding for ethnic group**

| |
|---|
| WHITE |
| British |
| Irish |
| Any other white background (please specify) |
| MIXED |
| White and black Caribbean |
| White and black African |
| White and Asian |
| Any other mixed background (please specify) |
| ASIAN OR ASIAN BRITISH |
| Indian |
| Pakistani |
| Bangladeshi |
| Any other Asian background (please specify) |
| BLACK OR BLACK BRITISH |
| Caribbean |
| African |
| Any other black background (please specify) |
| CHINESE OR OTHER ETHNIC GROUP |
| Chinese |
| Any other ethnic group (please specify) |

***[2]*Previous or current pregnancy problems, including:**
Thrombotic event
Amniotic fluid embolism
Eclampsia
3 or more miscarriages
Preterm birth or mid trimester loss
Neonatal death
Stillbirth
Baby with a major congenital abnormality
Small for gestational age (SGA) infant
Large for gestational age (LGA) infant
Infant requiring intensive care
Puerperal psychosis
Placenta praevia
Gestational diabetes
Significant placental abruption
Post-partum haemorrhage requiring transfusion
Surgical procedure in pregnancy
Hyperemesis requiring admission
Dehydration requiring admission
Ovarian hyperstimulation syndrome
Severe infection e.g. pyelonephritis

**[3]Previous or pre-existing maternal medical problems, including:**
Cardiac disease (congenital or acquired)
Renal disease
Endocrine disorders e.g. hypo or hyperthyroidism
Psychiatric disorders
Haematological disorders e.g. sickle cell disease, diagnosed thrombophilia

Inflammatory disorders e.g. inflammatory bowel disease
Autoimmune diseases
Cancer
HIV

**[4]Estimated date of delivery (EDD): Use the best estimate (ultrasound scan or date of last menstrual period) based on a 40 week gestation**

***[5]*RCA/RCOG/CEMACH/CNST Classification for urgency of caesarean section:**

| | |
|---|---|
| 1 | Immediate threat to life of woman or fetus |
| 2 | Maternal or fetal compromise which is not immediately life-threatening |
| 3 | Needing early delivery but no maternal or fetal compromise |
| 4 | At a time to suit the woman and maternity team |

**[6]Major maternal medical complications, including:**
Persistent vegetative state
Cardiac arrest
Cerebrovascular accident
Adult respiratory distress syndrome
Disseminated intravascular coagulopathy
HELLP
Pulmonary oedema
Mendleson's syndrome
Renal failure
Thrombotic event
Septicaemia
Required ventilation

[7]**Fetal/infant complications, including:**
Respiratory distress syndrome
Intraventricular haemorrhage
Necrotising enterocolitis
Neonatal encephalopathy
Chronic lung disease
Severe jaundice requiring phototherapy
Major congenital anomaly
Severe infection e.g. septicaemia, meningitis
Exchange transfusion