

# Predictive clinicopathological features derived from systematic autopsy examination of patients who died with A/H1N1 influenza infection in the UK 2009–10 pandemic

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## *Executive summary*

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## Executive summary

### Background

From April 2009 to January 2010, the pandemic of A/H1N1 influenza affected the UK. There were > 30,000 infections and 457 deaths (all ages). Reports from other countries had indicated that certain comorbidities (young age, asthma, pregnancy, diabetes, obesity) were associated with a higher risk of death from H1N1 infection, and there was a need to identify these factors in the UK population as knowledge of them could lead to improved treatment in the current epidemic and reduced mortality in future epidemics. In addition to clinical observation research in life, examination of autopsy data would provide information on the important comorbidities.

### Objectives

- To gather all the available clinical pathology information from autopsies performed on patients – adults and children – dying with known or suspected influenza A/H1N1 infection, across the UK.
- To evaluate comorbidities present in these deceased patients; correlate them with the H1N1-related pathology and treatment-associated pathology, determine their relative contributions and estimate the significant features associated with death.

### Methods

To obtain the autopsy reports, which would comprise the results of both medico-legal autopsies and hospital/consented autopsies, help was obtained from the Royal College of Pathologists (RCPath), the Coroner Society of England and Wales, the Crown Office and Procurator Fiscal Service and the Centre for Maternal and Child Enquiries.

Standard request letters were sent by e-mail to all histopathologists in the UK on the RCPath list, all the coroners' jurisdictions in England, Wales and Northern Ireland, and to procurators fiscal in Scotland. The letters asked for autopsy reports

with the following case definitions of the autopsied deceased:

- From pathologists:
  - those with H1N1 infection, *proven* before or after death, *and* those in whom swine flu was unproven but most likely to have been present
  - those in whom H1N1 was a minor pathology, as well as those in whom it was the immediate cause of death.
- From coroners and procurators fiscal:
  - mention of '*swine flu*', '*swine influenza*' or '*H1N1 infection*' in any part of the cause of death, i.e. in Part 1 *or* in Part 2 of the cause of death statement
  - any age from infancy to old age.

### Results

Sixty-eight autopsy reports were received: 19 children (0–15 years) and 49 adults (16+ years). All but two autopsies were medico-legal, and only two (3% of the total) were consented. This sample thus represents 15% of the known 457 deaths from H1N1.

The total number of autopsied H1N1-associated deaths was not identified. The information obtainable from autopsy reports was dependent on the amount provided therein, but, overall, the standard and quality of the medico-legal reports was higher than the average for this type of autopsy.

Median age for children at death was 6 years, for adults it was 41 years.

Deaths in children were associated with congenital diseases (47%, 9/19), particularly of the heart and central nervous system. The autopsied children were not obese. Death in adults were associated with pregnancy (three cases in the study, but nationally 12/457 H1N1-associated deaths were noted), obesity (50% of adults had a body mass index  $\geq 30$  kg/m<sup>2</sup>), and chronic respiratory disease (12%, 6/49 adults). Diabetes did not emerge as a risk factor for death, but learning difficulties did.

Nearly all the deaths (94%, 64/68) were a consequence of H1N1 infection in the respiratory tract. In more than one-third (41%, 28/68) of the deaths, bacterial secondary infection was the significant complication; the pneumococcus was the most common agent identified (25%, 7/28).

## Conclusions

Corroborated from the UK data, the major comorbidities associated with death from H1N1 infection were: obesity, chronic respiratory disease and pregnancy. Young age at death was confirmed. Congenital disease in children and learning difficulties in adults were also important, but diabetes was not.

This methodology of gathering data for research has potential for use in other public health questions, but is dependent on the co-operation of the medico-legal services (which have no accountability to the Department of Health or the NHS). The almost complete lack of academic investigative consented autopsies is regrettable, and indicates a lack of interest among clinicians in the clinical autopsy process, and/or an unwillingness to approach relatives for such consent.

## Recommendations for future research

1. Why are disabled children, pregnant women and obese adults particularly at risk of death?
2. Given the importance of secondary pneumococcal lung infection, what better preventive measures can be instituted?
3. How can patients *over*-diagnosed as H1N1 be better systematically identified, so that diagnostic protocols can be refined and thus reduce remediable fatalities?

## Funding

The National Institute for Health Research Health Technology Assessment programme.

## Publication

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The NIHR provides the NHS with the support it needs to conduct first-class research funded by the Government and its partners alongside high-quality patient care, education and training. Its aim is to support outstanding individuals (both leaders and collaborators), working in world-class facilities (both NHS and university), conducting leading-edge research focused on the needs of patients.

This themed issue of the *Health Technology Assessment* journal series contains a collection of research commissioned by the NIHR as part of the Department of Health's (DH) response to the H1N1 swine flu pandemic. The NIHR through the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) commissioned a number of research projects looking into the treatment and management of H1N1 influenza.

NETSCC managed the pandemic flu research over a very short timescale in two ways. Firstly, it responded to urgent national research priority areas identified by the Scientific Advisory Group in Emergencies (SAGE). Secondly, a call for research proposals to inform policy and patient care in the current influenza pandemic was issued in June 2009. All research proposals went through a process of academic peer review by clinicians and methodologists as well as being reviewed by a specially convened NIHR Flu Commissioning Board.

The final reports from these projects have been peer reviewed by a number of independent expert referees before publication in this journal series.

## **Criteria for inclusion in the HTA journal series**

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reports in this themed issue were funded through the Cochrane Collaboration; the Health Services Research programme (HSR); the Health Technology Assessment programme (HTA); the Policy Research Programme (PRP); the Public Health Research programme (PHR); and the Service Delivery and Organisation Programme (SDO).

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The HTA programme produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

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The PHR programme evaluates public health interventions, providing new knowledge on the benefits, costs, acceptability and wider impacts of non-NHS interventions intended to improve the health of the public and reduce inequalities in health. The scope of the programme is multi-disciplinary and broad, covering a range of interventions that improve public health.

The SDO programme commissions research evidence that improves practice in relation to the organisation and delivery of health care. It also builds research capability and capacity amongst those who manage, organise and deliver services – improving their understanding of the research literature and how to use research evidence.

The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' reports and would like to thank the referees for their constructive comments on the five draft documents. However, they do not accept liability for damages or losses arising from material published in this report. The views expressed in this publication are those of the authors and not necessarily those of the NIHR or the Department of Health.

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