

House of Commons Select Committee Inquiry: Scientific advice and evidence in emergencies**Response by the Wellcome Trust**

August 2010

Introduction

1. The Wellcome Trust is a global charity dedicated to achieving extraordinary improvements in human and animal health. We support the brightest minds in biomedical research and the medical humanities. Our breadth of support includes public engagement, education and the application of research to improve health. We are independent of both political and commercial interests.
2. It is vital that policy makers and practitioners can access robust scientific evidence to ensure appropriate preparation and effective responses to public health emergencies. The Trust therefore welcomes the Select Committee's inquiry on 'Scientific advice and evidence in emergencies'.
3. Given the Trust's remit, our response is focused on the 2009 H1N1 flu pandemic case study, and the importance of research and scientific evidence in informing and strengthening the public health response in an infectious disease outbreak. Key issues that we discuss include:
 - the importance of strategic co-ordination between Government departments, public bodies, private bodies and the research community to ensure a timely and rapid response to the H1N1 pandemic;
 - the need to address regulatory issues to facilitate research that can inform policy during a pandemic and infectious disease outbreak;
 - the importance of international co-ordination to enable effective preparedness and response to global diseases such as the H1N1 pandemic and;
 - the need to enhance pandemic preparedness, by maintaining key skills and research programmes during the inter-pandemic period.
4. Emerging and re-emerging infectious diseases, such as influenza, carry an immense and growing global health burden. It is important therefore to learn from the H1N1 pandemic and continue to support research that will strengthen evidence-based policies and healthcare practices.

Strategic co-ordination between Government departments, public bodies, private bodies and research community

5. The Department of Health played a central role in co-ordinating the UK's response to the 2009 H1N1 pandemic, by providing timely advice, co-ordinating with UK and international partners and directly supporting research in the area.

6. The Health Protection Agency (HPA) also played a pivotal role in the rapid co-ordination of the public health management of the 2009 H1N1 flu pandemic. It conducted a number of important virology and epidemiologic surveillance studies and supported work for the vaccine studies (including facilitating private-public partnership). Indeed, the regional H1N1 flu response centres set up by the HPA in collaboration with the NHS during the containment phase of the H1N1 pandemic, were recently recognised by a Cabinet Office Innovation in Resilience Award at the Emergency Planning Society Awards.
7. It is crucial that these important functions of the HPA, which enabled it to mount a rapid and effective public health response to the H1N1 pandemic, are not lost under the Government's proposed plans to disband HPA and transfer its functions to the Secretary of State as part of the new Public Health Service.
8. It was also important that the research community was able to respond quickly to the pandemic, working together with Government to conduct new research to inform policy-making and to provide valuable evidence about the effectiveness of potential interventions. This was achieved in response to the 2009 H1N1 pandemic. The Wellcome Trust and other UK partners, including the Medical Research Council (MRC) and Department of Health, rapidly convened meetings of the clinical research community (in May 2009) and the veterinary research community (in June 2009) to identify and develop new or enhanced research responses to the pandemic. In a short time-frame, the funders fast-tracked applications using existing robust processes (which the Trust had previously used in response to the Avian flu outbreak in 2005), to enable a rapid initiation of key research projects. In addition, to circumvent potential delays caused by recruitment issues, the funders also agreed to be flexible in deploying skilled clinical and research staff from other grants to the newly funded H1N1 pandemic research projects.
9. Three UK studies were funded through this fast-track process in 2009 following recommendations from the two meetings:
 - **The Mechanism of Severe Acute Influenza Consortium (MOSAIC)** – Led by Peter Openshaw, a wide-ranging multi-centre study of influenza pathogenesis in patients hospitalised with severe H1N1 disease during the pandemic, funded by the MRC and Wellcome Trust. This study built on the existing work of the Centre for Respiratory Infection at Imperial College London to study pathogenesis of respiratory viral diseases and to enhance pandemic preparedness and response.
 - **FluWatch surveillance programme** – Led by Andrew Hayward, a large collaborative, community-based cohort study of national households, examining epidemiology, severity, treatment and vaccination strategies of influenza. Jointly funded by the Wellcome Trust and MRC, it is the largest study of its type. This programme builds on an existing study funded initially by the MRC in 2006.
 - **The Combating Swine Influenza Initiative (COSI)** – Two inter-linked studies led by Ian Brown and James Wood, to monitor and compare the evolution, transmission, infection dynamics and immunopathology of H1N1 in pigs and humans jointly funded by the BBSRC, DEFRA and Wellcome Trust.
10. These studies are still being conducted in the post-pandemic period. The initial results are currently being analysed and can be reported to the Select Committee in due course, if it would be helpful. Community-based surveillance programmes such as FluWatch are not only valuable for providing crucial data on transmission patterns but can also serve as a platform for large-scale public-health intervention studies (e.g. hygiene measures and face masks). For example, preliminary analyses in the FluWatch study indicate that frequent hand washing reduced the risk of acquiring influenza infection, a finding that should inform the advice given regarding risk reduction. The hospital-based cohort is anticipated to provide invaluable data regarding the viral and host factors associated with progression to severe influenza and eventually lead to studies of new interventions that might reduce the risks of complications and fatal outcomes. Furthermore, a better understanding of the animal-human interface of zoonotic

influenza will help reduce the risks of zoonotic infections that might lead to new influenza outbreaks, reduce transmission of influenza between household members, and improve care of those infected and help inform surveillance and reporting procedures.

11. Unfortunately, the MOSAIC and FluWatch studies could not be completed in time to inform the response strategies for the H1N1 pandemic due to regulatory hurdles (see below, paragraphs 12-15). However, the findings from all three studies will be invaluable in informing the strategies and policies for the next influenza pandemic and strengthen the UK's preparedness and capacity to respond effectively to the next influenza pandemic and to seasonal epidemics.

Obstacles to conducting research to inform policy during the pandemic

12. While the research community and funders were able to respond rapidly during the first wave of the pandemic, both the MOSAIC and FluWatch studies were unable to roll-out their studies in a timely manner during the autumn wave of the pandemic due to unnecessary delays in gaining regulatory approval.
13. The MOSAIC group were delayed primarily by the multiple and disparate NHS Research and Development (R&D) approval processes at the various hospitals involved in the study. In one instance it took eight months to secure R&D approval from a participating hospital. Similarly, the FluWatch study was delayed in rolling-out its large scale community study by the R&D approval process for recruiting subjects through multiple primary care sites, with applications taking over a month to be approved. Consequently, the researchers (especially MOSAIC) missed the peak in cases, which hampered recruitment of a sufficient number of subjects.
14. In order to effectively respond to outbreaks of infectious disease and pandemics such as the H1N1 pandemic, it is crucial that there are appropriate mechanisms in place that are capable of 'fast-tracking' approvals to facilitate research in the context of public health emergencies. We note that, for the flu vaccine trials, it was possible to fast-track approvals to allow these trials to progress in a timely manner.
15. There are increasing concerns that regulatory burdens and unnecessary red tape are significantly delaying biomedical research in the UK, and the Government has commissioned the Academy of Medical Sciences (AMS) to undertake an independent review of these issues to inform future policy. In our response¹ to the AMS call for evidence we highlight concerns from researchers that NHS R&D offices as the single biggest barrier to medical research. There is an urgent need for R&D offices to be made more efficient and harmonised, and for rationalisation of multiple layers of approvals and bureaucracy. The proposals to introduce a single research regulator provide a real opportunity to simplify and streamline the approvals process. We strongly urge the Government to ensure that any new governance framework facilitates research, and includes appropriate mechanisms to enable a fast response in a public health emergency situation.
16. At a Satellite workshop meeting at the Pacific Health Summit 2010 hosted by the Wellcome Trust Influenza Research team, researchers also suggested a system whereby there was ethics pre-approval of projects and pre-positioning of generic protocols at qualified sites as a way to reduce delays in the event of a pandemic or novel outbreak. This would be worth exploring in more detail. Establishing a network to study severe acute respiratory infection was also suggested as a way forward to help overcome regulatory hurdles. Such a network could also provide an established research platform that could address relevant research

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http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/WTX060175.PDF

questions in the inter-pandemic period and be rapidly scaled up during a future influenza pandemic (also see paragraphs 22-24 on preparedness).

17. In addition, FluWatch faced significant delays recruiting appropriately qualified research staff, with international expertise often crucial. We are concerned that the current visa restrictions brought in early 2010 by the Labour Government and the proposed restrictions on Tier 1 and 2 visa criteria would prevent or significantly delay the timely recruitment of talented and highly skilled researchers from non-EU countries that would be needed to carry out urgent research during a future pandemic or infectious disease outbreak.

International co-ordination and research

18. Infectious diseases such as influenza are global threats that the international community must work together to address. An effective response requires a co-ordinated global approach. With the H1N1 pandemic, this was effectively led by the World Health Organisation (WHO), with local support from member countries.
19. Effective communication and rapid sharing of information, as achieved in the UK, are an integral part of international co-ordination and key for an effective global response. These key factors are particularly important in the complex and challenging pandemic setting in which there is usually a limited time-frame to mount an effective response.
20. On the research front, the Trust was an active partner with WHO on the development of the WHO Public Health Research Agenda for Influenza², on a range of influenza vaccine-related activities³ and on meetings related to clinical aspects and management of pandemic H1N1 patients⁴. A summary of the Trust's full range of activities can be found at www.wellcome.ac.uk/influenza.
21. The South East Asia Infectious Disease Clinical Research Network (SEAICRN) is an international and collaborative partnership of hospitals and research institutions in Thailand, Vietnam, Indonesia and Singapore, with technical and administrative support provided by the Centre for Tropical Medicine, University of Oxford. Formed in September 2005 and funded by the US National Institutes of Health's National Institute of Allergy and Infectious Diseases and the Wellcome Trust, SEAICRN focuses on clinical research on human and avian influenza and other infectious diseases of public health importance in the South East Asia region. The network is key for preparedness, providing a clinical monitoring system in a region where new infectious diseases can emerge and serving as a clinical research platform to respond to new threats. Further examples of some of the international influenza-related projects funded by the Trust are provided in Box 1.

BOX 1 Influenza-related research in the Trust's Major Overseas Programmes in Africa and Asia

- Studies of severe pneumonia and respiratory viruses at hospital and community level in Kenya (led by James Nokes).
- Hospital-based surveillance for influenza in an African population with a high burden of HIV, malaria and malnutrition in Malawi (led by Rob Heyderman).
- A range of clinical research on serious human, including H1N1, and avian influenza and other infectious diseases of public health importance in the South East Asian region (through the SEAICRN).

² http://www.who.int/csr/disease/influenza/2010_04_29_global_influenza_research_agenda_version_01_en.pdf

³ <http://www.who.int/csr/disease/influenza/inforesources/en/index.html>

⁴ http://www.who.int/csr/resources/publications/swineflu/clinical_managemnt_h1n1.pdf

Enhancing Pandemic Preparedness and Seasonal Response

22. While the H1N1 pandemic is now over, the virus is still circulating and the long-term threat of a future influenza pandemic remains high. In addition, the annual toll of seasonal influenza outbreaks continues. The UK is already considered to be one of the best prepared countries in the world for a new pandemic, as recognised by WHO. The UK must maintain this status as well as enhance its responses to seasonal influenza and other respiratory illnesses.
23. Effective preparedness and response is dependent on a number of essential factors, in particular:
- Having a **surveillance system** in place to monitor changes in influenza virus activity and patterns in people and animals nationally and globally on a year-round basis. Continued support of national surveillance, which provides essential data on virus strains and their sensitivity to antiviral drugs, and of WHO's Global Influenza Surveillance Network is key.
 - **Ongoing support for the research platforms and skill base** of the type put in place during the H1N1 pandemic. Having skilled staff, for example research nurses already on the ground with the experience and knowledge, will enable ongoing studies in the inter-pandemic period and a much more rapid research response to new infectious disease events. This skills base will facilitate the rapid scale-up and launch of clinical research and acquisition of valuable data during the initial wave of a new threat. Indeed, at the third scientific advisory group meeting the European Centre for Disease Prevention and Control reported that those European countries that did not have skilled and dedicated staff already in place before the H1N1 pandemic were not able to carry out any studies in response to the pandemic.
 - **Ongoing support for research projects.** Continued basic and applied research on zoonotic influenza viruses and maintaining momentum of the research initiated during the H1N1 pandemic is crucial to advance our understanding of the H1N1 virus (and other influenza viruses) and the disease. For example, the H1N1 studies MOSAIC and FluWatch benefited from the influenza virus sequencing 'pipeline' at the Wellcome Trust Sanger Institute set up in 2006 to sequence large numbers of influenza viral genomes, to track the evolution of viruses, which is important for not only monitoring virus with pandemic potential but also in the development of vaccines in general. The state-of-the art sequencing technology was used to rapidly analyse samples from both studies.
24. Further research is needed to understand the emergence, transmission, pathogenesis and control of influenza caused by zoonotic viruses such as H1N1 at the global level. Many of the research gaps identified during the H1N1 pandemic (some examples are provided in Box 2 below) and on the WHO public health research agenda for influenza remain to be addressed, and most can be tackled during the inter-pandemic period. The UK is in a prime position to capitalise on its strong research and skill bases to address these research questions during the inter-pandemic period. The lessons learned should serve the UK and global community in formulating robust evidence-based policies and strategies for better preparedness and response to future pandemics and other infectious disease outbreaks.

Examples of key research gaps for influenza

- **Communication and behavioural research:** further research is needed in order to develop more effective and evidence-based health communication strategies and behavioural interventions in response to future pandemic. For example, investigating how to improve compliance with recommended public health measures and examining why attitudes among professionals are crucial for successful vaccine programmes.
- **Clinical research:** epidemiologic, pathogenesis and intervention studies in the inter-pandemic period, both in the community and in those hospitalised with more severe illness. Such initiatives would serve to not only build this clinical research capacity as a platform for response to new threats but also to understand the impact of annual

outbreaks of influenza and other respiratory pathogens and test measures to mitigate their impact through studies on patient management, particularly those with severe illness.

- **Modelling:** mathematical modelling, a current strength in the UK, can be used to help improve understanding of the epidemiological factors and population processes shaping infectious disease spread in human and animal populations (e.g., modelling influenza transmission and the impact of intervention strategies such as closing schools and wearing masks).
- **Surveillance and operational research** in households and at the human/animal interface to understand viral evolution, risk factors for emergence of threat pathogens and transmission to humans, and interventions to reduce transmission.

Looking to the future – effective public health response in disasters and emergencies

25. Emerging infectious diseases, such as influenza, carry an immense and growing global health burden. It is important therefore to learn from the H1N1 pandemic and continue to support research that will strengthen evidence-based policies and healthcare practices.
26. In the broader context, it is important to note the growing number of emergencies which are triggered by extreme weather events e.g. floods, storms and droughts, both in the UK and particularly in low- and middle-income countries (LMIC). The need for robust scientific evidence to inform the response to such disasters is widely acknowledged by practitioners and policy makers alike. Nevertheless research to strengthen the public health response in such complex settings is challenging.
27. The Trust, as part of scoping work to identify gaps and potential opportunities to strengthen the public health response in disasters and humanitarian emergencies, held a 'Frontiers Meeting' in June 2010 bringing together NGOs, academics, and representatives of multilateral agencies.
28. A number of common challenges and barriers to undertaking research in the field immediately post-emergency were identified. These included for example, the need for a robust pre-agreed ethical framework to guide research in such situations; improving the understanding and cooperation between practitioners and between human and animal health experts; the need for improved and timely evaluation of research studies and their findings; and more rapid dissemination of research findings. Importantly, all agreed on the need for a robust evidence base to inform policies and the public health response in disaster settings.
29. We would happy to provide further details about any of the issues raised in this response.