The Foundation for Science and Technology
Debate Record Note

Is the UK well prepared for a repeat of the 1918 influenza pandemic?

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Chair: The Earl of Selborne GBE FRS
Chair, The Foundation for Science and Technology

Speakers: Professor Chris Whitty CB FMedSci
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PROFESSOR CHRIS WHITTY said that the 1918 to 1920 pandemic had killed 50 to100 million people globally. Seasonal flu by comparison could cause 250,000 to 500,000 deaths.

There were a number of factors that had to be considered in planning for any infectious epidemic. Those most pertinent to a flu pandemic were speed of spread, mortality/virulence and public health countermeasures (both in relation to transmission and mortality.) Pandemic influenza remained the highest risk on the UK National Risk Register for a good reason. A flu pandemic could have an impact on a scale unlike any other infectious pandemic (with the arguable historical exception of HIV). It is an airborne disease. It could be sudden; the speed of spread was rapid; and high proportions of the population would be affected. For example, in 1919 the pandemic swept across the US in a matter of a few weeks. The death rate per 1000 population in October that year spiked dramatically at 50, rising from around 15 in September at the start of the pandemic and falling back to 20 in November and December (in all cases compared to a normal monthly average of 12-15 per 1000 for those months).

The virulence of the last pandemic we had experienced, in 2009, had been relatively low. But it could be much higher next time; and that was why Government planning was done on the basis of the reasonable worst case.

We were not necessarily more vulnerable to flu pandemics than in the past, though global transport links were potentially a factor in transmission and, in the case of the UK, Heathrow was of course, a major, central hub for international flights. Indeed better nutrition, better housing, clean plentiful water, cleaner heating were all mitigating factors compared to 1918. Nevertheless we

remained vulnerable and had to plan accordingly.

In 2009 epidemic there had been 43 to 89 million cases globally, causing between 8,000 and 18,000 deaths between April and July that year. In the UK there were officially 457 deaths. There had been two or three waves, with a main peak in July, all outside the 'flu season'. A vaccine had become available, but only well after the main peak.

It was important to recognise that there was no link between the transmissibility of a new flu strain and its virulence. Between 2013 and 2018 avian flu, which carried a low transmission risk, had been associated with a 30% mortality rate from less than 2000 confirmed cases. Highly transmissible flu strains could be associated with low mortality (0.3% from 10-200 million cases in 2009, to high mortality (around 3%) in 1918.

Societal impact depended on who was affected. Generally influenza mortality concentrated on the extremes of life: pregnant women and the chronically unwell. However the 1918 'pandemic' had a major peak in young adults. No particular occupation is inherently more vulnerable in a flu pandemic, although health care workers are likely to get it early.

Not all epidemics were amenable to a vaccine counter measure. Influenza usually was; and in the case of a pandemic a vaccine might come to the rescue if, as in the case of 1918, the first wave was not the most serious. But it was important not to bank on it. The lead time for producing a vaccine to counter a pandemic was currently a minimum of four months, which could be after the peak wave had occurred (as in 2009); and it had to be remembered that seasonal flu vaccines varied in their efficacy.

A pan flu vaccine remained the Holy Grail, with the focus of basic research being on how to attack the stem of the virus. But this target remained elusive. On the other hand the move from egg based to cell based production did hold out the promise of faster production of virus specific vaccines.

Anti-viral drugs for influenza could reduce the severity and duration of symptoms. However, the size of their effect might be modest (as they needed to be taken early) and the virus could develop early resistance to them. There had been some controversy following the 2009 epidemic over the policy of stockpiling and distributing anti-virals; but there was likely to be criticism whatever way the planners jumped on this issue.

Antibiotics were a valuable counter measure in relation to secondary disease. In 1918 of course they were not available; and a high proportion of deaths in the course of that pandemic probably most were from secondary bacterial pneumonia - another key difference between then and now. On the other hand there would be huge global demand for antibiotics in a virulent flu pandemic and existing supplies would run down very quickly.

When it came to supportive treatment, however, we might not in practice be substantially better off than in 1918. Conventional health services, including intensive care units, would quickly be overwhelmed, although oxygen would be available for some people. Basic nursing care remained the most important need – and did not require professionally trained nurses.

We could put the building blocks in place for a response to pandemic influenza: mathematical models to predict the global and national course of a pandemic from early data; a global virus identification network; plans for which bits of the health system to switch off; optimising vaccine production; antiviral and antibiotic stockpiles; plans for communicating with the public and for minimising societal impact. But no plan ever survived contact with the enemy. Each pandemic was different and would throw up new and unpredictable challenges.

KATHARINE HAMMOND said that the policy responsibilities of the Civil Contingencies Secretariat in the Cabinet Office, of which she was the director, include the National Risk Assessment (identifying and assessing risks to national safety and security arising from terrorism, major industrial accidents and national hazards); leading a cross government programme on resilience capabilities, to improve the public sector response to such emergencies; contingency planning and capability building for the risks of catastrophic emergencies; and policy for secure and resilient national infrastructure and wider resilience (which included working with industry and community groups).

As Professor Whitty had said, pandemic flu was number one on the UK Risk Register. The UK government had developed a reasonable worst case scenario for emergency planning purposes: designed to exclude possible scenarios which had so little probability of occurring that planning for them would lead to a disproportionate use of resources. These were not predictions of what would happen, but of the worst case that might realistically happen.

In the case of pandemic flu this scenario was based on a number of key assumptions. Up to 50% of the population would experience symptoms,

with infection rates up to 80% to 85%; up to 5% of symptomatic patients would require hospital care; illness rates would peak at 10% to 12% in each week in the peak fortnight; up to 2.5% of those with symptoms would die; and staff absence rates of would rise to 17% to 25% in the peak weeks of a pandemic.

The UK had a robust 'defence in depth' preparedness strategy for all potential pandemic threats. These included surveillance and monitoring to detect and assess the impact of potential pandemic threats; measures to reduce spread through good infection precaution and control practices and provision of personal protective equipment for front line health and social care staff; stockpiling clinical counter measures, such as antivirals; advanced purchase agreements for vaccines, to guarantee access to pandemic specific vaccines for use where possible and appropriate; reducing pressure on primary care and hospitals, for example by activating the National Pandemic Flu Service (NPFS) to enable antivirals to be rapidly authorised for patients without the need to see a doctor; and research to support all these areas.

A major exercise had been carried out in 2016 to test preparedness for and response to flu pandemic, at a level close to the reasonable worst case planning scenario. Over 950 representatives of different organisations had been involved, including from eight local resilience forums. The lessons learned from this exercise had resulted in a joint Department of Health and Social Care and Cabinet Office programme of work to further enhance preparedness – involving all Government Departments including the devolved nations.

Overall the exercise showed that medical/health system preparations were good. But a key learning point was the reminder that the response to pandemic flu needed to be broader than just the health and care sector. All sectors – and at all levels – had a responsibility to be prepared to respond. The programme had therefore engaged a number of key stakeholders to enhance preparedness, including local resilience forums, other Government Departments such as the Department for Education and the Prison Service, and business groups.

This work had focussed on four key areas: ensuring that critical sectors have adequate resilience to anticipated levels of employee absence; improving the plans of the health sector to flex systems and resources to expand beyond normal capacity levels; understanding and expanding social care and community healthcare capability and capacity to respond to increased demand; and reviewing and enhancing the capabilities for managing excess deaths. Cross cutting these areas of work were also a number of enablers which were being addressed. These included communications, moral and ethical issues that could arise, and possible legislative easements.

All this amounted to a genuine cross government initiative to enhance preparedness. She would not attempt to answer the question raised by the debate, not least because of the uncertainties which Professor Whitty had illustrated. But she hoped she had been able to give some flavour of the seriousness of the government's commitment to preparedness and to keep refining its plans and assumptions.

DR COBURN said that the Cambridge Centre for Risk Studies approached this issue from the perspective of the threat to the global economy presented by an influenza pandemic. It was an economic as much as a healthcare and humanitarian issue.

They had modelled a hypothetical scenario of a high infectious – moderate virulence outbreak, in which 45% of the population became infected, with a case fatality rate of 0.7% (similar to seasonal flu). The scenario assumed an outbreak with its origin in poultry farms in Brazil, involving a genetic shift producing a new strain of influenza that would evade the human immune system, no vaccine suitable at the time of the outbreak and an assumption that it would take around five months to develop and produce a vaccine.

The model demonstrated that over a nine month period the pandemic would spread through areas of population right across the globe: meaning nine months of continuous disruption to highly complex, inter-connected global businesses. Demand for healthcare would swamp capacity. For example, in the peak week meeting the demands of the pandemic would take the equivalent over 80% of normal physician consultations in the UK. The demand for extra hospital beds (and to an even greater extent intensive care beds) would far exceed supply.

Some countries would have strategies for both pharmaceutical and non-pharmaceutical counter-measures. Many would still be relying entirely on the latter. What was a global problem would still, in effect be approached nationally.

On this model the GDP loss to the global economy would be between 7 and 23 trillion dollars. Stock market indices would be down 17 to 30 points. Inflation would increase by up to 2.7%. Most investment portfolios would be devalued, threatening savings and

pension schemes. House prices and asset values would be heavily depreciated.

The global death toll would be 19 to 25 million. Life insurance payments would be between 99 and 121 billion dollars; and healthcare insurance payouts between 93 and 144 billion dollars.

The likelihood and potential severity of future pandemics was being increased by a number of trends. One was the increasing prevalence of Anti-Microbial Resistance (AMR) in bacterial strains. For the UK, for instance, the centre estimated that the death toll from a pandemic with AMR would rise from the median estimate of 425,000 on their scenario to 616,000. Other factors increasing the risk included: gain of function scientific research; growing populations of livestock (200 plus zoonotic reservoirs) in emerging economies; reduced surgery capacity in healthcare for reasons of efficiency; reduced investment by pharmaceutical companies in vaccine research; and increasing levels of international travel.

On the other hand some trends were decreasing pandemic risk. In the case of influenza these included the future potential for cell-culture vaccine manufacturing techniques and for a universal influenza vaccine, as well as increasing healthcare expenditure and capacity in emerging economies.

In the case of emerging infectious diseases, positive signs were vaccine development for the worst haemorrhagic fever viruses, improved disease surveillance in emerging countries and international rapid response initiatives.

It had to be remembered that 1918 was the worst pandemic in the past 400 years (although the 1761 pandemic may have been almost as bad). However, many of the estimated 20-50 million deaths then were from secondary bacterial infections that would be treatable with antibiotics today. The key point was that each pandemic had its own characteristics. The permutations of infectiousness and virulence were what mattered.

Each year there was a one in three chance of a significant public health pandemic; and around two thirds of future pandemics would be influenza. Threats currently on the PPP watch list included Middle East respiratory syndrome, avian flu (HSNI), new variant avian flu (H7N9), gain of function research and haemorrhagic viruses (like Ebola).

Could the UK be better prepared for future pandemics? It was certainly not the UK's problem alone. Pandemics were a global threat, requiring much better international infrastructure and funding to tackle them holistically. More investment was needed in hospital and healthcare surge capacity. Stockpiles of drugs were important but had to be specific for a known threat. Vaccine development was too important to be left to the business model of pharmaceutical companies to provide. Radically different incentivisation structures were needed.

He did not think it was sufficient to prepare for a single 'reasonable worst case' scenario. Potential pandemics spanned a wide range of severity and characteristics with different likelihoods. We needed to be prepared for them all.

Finally, he wanted to underline the importance of developing new classes of antibiotic to respond to AMR. This had to be seen as a significant concern in the context of pandemics as well as a primary public health issue.

Opening the discussion period, **PROFESSOR MCKENDRY** said the speakers had painted a striking picture of the impact of an influenza pandemic on the population, the healthcare system and the economy. This inevitably raised questions about true levels of preparedness in practice. For example the NHS was already at the tipping point in terms of dealing with seasonal flu; and the primary care system was known to be operating under huge pressure. Surveillance methodologies and vaccine development were also issues for debate.

However, she also wanted to surface a number of questions relating to digital preparedness. For example, the risks – and opportunities – of new communications channels needed consideration. We were now acutely aware of the risk of deliberate misinformation on social media – whether from people with axes to grind, from trolls or from organised attempts to destabilise countries and populations. The insistent use of discredited research evidence to undermine the use of vaccines or other treatments was one obvious example. Should we not be using social media proactively to build public trust in preparedness and the counter measures which had been described?

Should it not also be possible to use new technologies, based on data sets now available from smart phones for example, to improve surveillance systems and accelerate early indications of a pandemic. Even extra early warnings of up to a week of the beginning of a pandemic would be a significant gain. Similarly a combination of remote monitoring systems

and smartphone technology should enable more people to be monitored and treated at home in the course of a pandemic. This might be something that could be developed and piloted in the context of seasonal flu.

In short, the tool kit for preparing for and responding to a pandemic should surely evolve to take more account of new technologies, many of which had developed exponentially even since 2009.

The issue of communications was a theme developed by a number of participants in the subsequent discussion. Individuals should be expected to take more responsibility to prepare themselves for this kind of threat. In fact published alongside the Government's Risk Assessment were ten simple, practical measures that would make a huge difference if every household acted on them. The advice was there. The problem was to ensure people acted on it. It had, at one time, been available in pamphlet form. But questions had been raised about the effectiveness of this approach and its value for money. The evidence suggested that the advice was more likely to be effective when read alongside the risk assessment – hence the current approach. The message also seemed to be more effective when delivered locally.

A number of participants argued for a more pro-active and sophisticated approach to the use of social media, to support positive communications to the public about the threat, to build confidence in the counter-measures that were planned and to promote precautions the public could take themselves. Gamification was, for example, an approach that was being followed with good effect by businesses for training staff in understanding risk and promoting positive behaviours. It could be used in this context.

These tools could also be used to counter misinformation on the web, which it was agreed posed an increasingly significant threat. Spurious evidence and arguments against vaccines were, for example, being deployed with great sophistication. Scientists had a responsibility to engage in equally sophisticated counter arguments and in finding new ways to communication positive, evidence based public health information and advice. People would seek out credible, trusted sources of information. The NHS Choices website was used by 50 million people across the world. Could not an NHS 'app' giving advice on pandemic risk, preparedness and counter-measures be developed? However, a cautionary note was also struck. Pandemics varied in impact. In a mild pandemic it would be important, for example, not to induce behaviour changes which might have an unnecessary adverse impact on the economy through a 'one size fits all' approach.

Discussion of this issue also touched on the question of whether service providers should be asked or required to take down misinformation on social media which could be damaging in any response to a pandemic. It was suggested it was important to enter into a dialogue with service providers on this issue. We were in the foothills generally in learning how to manage content circulating on the internet and where necessary intervene.

It was also strongly argued, however, that being seen to suppress or censor such material only played into the hands of the perpetrators. Fake news needed calling out for what it was – and to be countered systematically with evidence and the truth.

On the issue of counter measures, there was a call for renewed investment in vaccine development – and in particular the search for a universal flu vaccine. Basic science was still needed alongside developmental research. The fact that a universal vaccine had proved elusive so far should not be taken as a counsel of despair. Past investment in research in this area should not be discounted. It was necessarily a long term game. The sea changes in treatment for Hepatitis C and HIV emphasised the need to keep at the issue – and to take an optimistic view.

Nevertheless new, more visionary approaches might be required. This was not an area where genetic engineering appeared to offer a way forward. Focussing on the pathogen itself showed greater promise. It could be enhanced by more investment and by a more concerted international approach – for example in releasing and sharing related data sets. It had also had to be remembered that viruses as well as counter measures would continue to adapt and evolve resistance.

It was also crucial to watch for developments in the animal sector. Zoonotic strains were vital indicators; and both researchers and surveillance teams were always monitoring strains circulating in the animal world and in the fowl and bird population in particular.

On other counter measures there was agreement that ensuring a supply of antibiotics that worked for secondary infections would be a key success factor in preparing for and responding to a flu pandemic. Flu antivirals also had a part to play. In both cases early treatment was essential, raising questions about distribution. One option, for example, might be to deliver antivirals to the population through the post with advice on when to use them. But that might also mean a lot of unnecessary medication was taken. The point that had been made about current pressures on

the NHS was also endorsed. The NHS would need to be supported in preparing for the longer term impact of an epidemic, with a particular emphasis on engaging primary care.

There was a strong argument for investing more now in new technologies to support the response to seasonal flu – in respect of health promotion, awareness and treatment - which might then support the response to a pandemic. The case for doing this in its own right was comparable to the proposed investment in new technologies for chronic disease prevention and management. It was suggested that seasonal flu preparations could also be used to run pilots and train staff in relation to pandemic preparedness; though a counter view was that a pandemic was categorically different from seasonal flu, not least because the correct emphasis on infection prevention in the latter was impractical in the face of a pandemic.

School closures was one of the best evidenced means of reducing the transmission risk, though it created other difficulties – for example, in terms of the number of healthcare workers who would have additional child care responsibilities in such circumstances.

The assumptions about 17% to 25% absence rate in the scenario that had been given by the speeches had been subject to sensitivity testing. But it was acknowledged that behaviours and public attitudes in a pandemic were not always easy to predict. Staff absences were likely to vary by sector and then might not be uniform. Employers, as well as employees themselves would take a view on essential staff – and on their own liability in relation to their duty of care. These were interesting issues for the social sciences. As were the issues that had been raised in relation to the management of death. These were not just logistical and ethical issues. The death toll pandemic would have a huge cultural impact. Things were different now compared to 1918. There was now, for example, a very strong association between death and what was, by historical stands, extreme old age. It was rare for young people to die. People were no longer injured even to mass casualties of young service men and women in war. The deaths of a large number of young people in a pandemic could have a devastating impact – although there was interesting evidence from the Ebola outbreak that the population had adjusted surprisingly quickly.

On a related issue one of the problems that had been identified after the 2009 epidemic was the late registration of deaths, particularly in cases referred to coroners. This remained a problem and should be addressed as a priority, not least in the context of pandemic preparedness.

The emphasis on the fact that this was a global issue, calling for a stronger, and broader and more concerted international response was welcomed. There were good examples of international collaboration in this field; and the international networks on health were well developed, particularly in comparison to some other sectors. However, while progress had been made on a revised pandemic strategy, more needed to be done, particularly at the global level. All countries had to pull together to make progress. Some current developments in global and national politics undoubtedly made this a difficult climate in which to pursue a multilateral agenda. But better international institutions and structures to tackle the issue of pandemics at a supra national level was, for some, the single development that could do most to enhance global resilience.

A related point of discussion was the role of the World Health Organisation (WHO) in 'calling' the pandemic. This was a vital step, not least in triggering action on vaccine development (away from seasonal flu vaccine development and production). So it had to be timely, based on precise science and unequivocal. WHO had now adopted a less rigid definition for making this decision (which had arguably been delayed too long in 2009); and it was noteworthy that they had released funds at an earlier stage in the case of the Ebola outbreak.

UK systems surveillance systems were well developed; and, though it was an unlikely, an outbreak could of course have its origins here. We would act on our own judgement on the outbreak of a pandemic in terms of the response and counter-measures, not wait for the WHO decision. But the timing of the latter certainly had implications for vaccine development.

Finally, a strong point was made in relation to the way politics and science could interact in responding to a pandemic. Some decisions where the science pointed in one direction – for example keeping international flights going – might be over ridden, justifiably perhaps, on political grounds relation to public perception and tolerance of the risk. In some countries there were strong economic disincentives to calling a pandemic. This inter-action between politics and sciences was a necessary complexity that had to be factored into preparations for a pandemic and the process of managing the response.

Summing up the debate, the Chairman again thanked the speakers for their contribution and the

sponsors for supporting the event. Events had certainly moved on since 1918. Medical countermeasures, vaccines, antibiotics and flu antivirals would all make a contribution that was not available then. Other wider mitigating factors associated with economic growth and technology would also make a difference. But the debate had illuminated the scale and impact of a modern day pandemic. It had also provided a clear demonstration of the need to enlist a wide range of sciences to face into the scale of the problem – not least the social sciences in relation to issues such as influencing human behaviour and the role of social media.

Sir Hugh Taylor KCB

Useful reading:

UK Influenza Pandemic Preparedness Strategy 2011
Department of Health
www.assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/213717/dh_131040.pdf

Sâo Paulo Virus Pandemic Scenario
Cambridge Centre for Risk Studies, Cambridge Risk Framework
University of Cambridge, Judge Business School
www.jbs.cam.ac.uk/fileadmin/user_upload/research/centres/risk/downloads/crs-sao-paolo-virus-pandemic.pdf

The National Risk Register of Civil Emergencies 2017
www.assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/644968/UK_National_Risk_Register_2017.pdf

Annual Report of the Chief Medical Officer 2017
Health Impacts of All Pollution – what do we know?
www.assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/690846/CMO_Annual_Report_2017_Health_Impacts_of_All_Pollution_what_do_we_know.pdf

Influenza Pandemic Brief, April 2016
www.england.nhs.uk/wp-content/uploads/2016/04/pandemic-influenza-brief-apr16.pdf

NHS Board paper on Influenza Pandemic preparedness
www.england.nhs.uk/wp-content/uploads/2017/03/board-paper-300317-item-10.pdf

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www.esrc.ukri.org

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www.epsrc.ukri.org

Innovate UK, UKRI
www.gov.uk/government/organisations/innovate-uk

Medical Research Council, UKRI
www.mrc.ukri.org

Natural Environment Research Council, UKRI
www.nerc.ukri.org

Research England, UKRI
www.re.ukri.org

Science and Technology Facilities Council, UKRI
www.stfc.ukri.org

Association of Innovation, Research and Technology Organisations (AIRTO)
www.airto.co.uk

Association of the British Pharmaceutical Industry
www.abpi.org.uk

AstraZeneca
www.astrazeneca.co.uk

British Academy
www.britac.ac.uk

Catapult Programme
www.catapult.org.uk

Centre for Risk Studies, University of Cambridge Judge Business School
www.jbs.cam.ac.uk/faculty-research/centres/risk

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www.gov.uk/government/emergency-preparation-reponse-and-recovery

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www.gov.uk/government/organisations/department-for-business-energy-and-industrial-strategy

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www.gov.uk/government/organisations/department-for-education

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www.gov.uk/government/organisations/department-of-health-and-social-care

Francis Crick Institute
www.crick.ac.uk

Government Office for Science
www.gov.uk/government/organisations/government-office-for-science

GSK
www.gsk.com

Home Office
www.gov.uk/government/organisations/home-office

i-sense
The EPSRC IRC in Early Warning Sensing Systems for Infectious Diseases
www.i-sense.org.uk

Jisc
www.jisc.ac.uk

Knowledge Transfer Network
www.ktn-uk.co.uk

Learned Society of Wales
www.learnedsociety.wales

Lloyd's of London
www.lloyds.com

Lloyd's Register Foundation
www.lrfoundation.org.uk

London Centre for Nanotechnology
www.london-nano.com

National Health Service
www.nhs.uk

NESTA
www.nesta.org.uk

Novartis
www.novartis.co.uk

Office for National Statistics
www.ons.gov.uk

Pfizer
www.pfizer.com

Roche
www.roche.com

Royal Academy of Engineering
www.raeng.org.uk

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www.rsc.org

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www.rse.org.uk

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www.turing.ac.uk

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www.statisticsauthority.gov.uk

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