



Department
of Health



Public Health
England

The New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG)

1st Annual Report December 2014-December 2015

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The New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG)

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1. Chair's Foreword

Since the influenza A(H5N1) 'bird flu' virus re-emerged as a human pandemic threat in 2003 and up until the start of the 2009 A(H1N1) 'swine flu' pandemic, a great deal of time was rightly spent by the UK Government, the Health Protection Agency and the NHS in preparing for a future pandemic. At the time when this work was being done, the focus was on H5N1 and Asia; no-one could have predicted that the next human pandemic would have been due to an H1N1 virus, and central America was not 'on the radar' as a likely place from which a pandemic virus might emerge. Nevertheless, the planning and preparation undertaken in the UK and worldwide helped us to deal with, what was in the end, a rather mild 2009 pandemic threat.

In the post-pandemic period we have seen further emerging respiratory virus threats with potential consequences for humans; Influenza A(H7N9), A(H5N8) and A(H5N6), and the Middle East Respiratory Syndrome coronavirus (MERS Co-V). We are reminded that we cannot predict the future, beyond saying that another pandemic is inevitable at some point, but it seems quite clear that the range of major respiratory virus threats to public health may well extend beyond influenza. Likewise, a great many scientific lessons have been learned from the 2009 pandemic and UK preparedness plans updated in line with new scientific evidence.

The above events have set the stage for the establishment of a new independent advisory committee: NERVTAG (New and Emerging Respiratory Virus Threat Advisory Group), which replaces the former UK Scientific Pandemic Influenza Advisory Committee (SPI) and extends the role, rationally, to cover not only pandemic influenza, but any new, emerging (or re-emerging) respiratory virus threat to the UK.

NERVTAG operates under the umbrella of the Department of Health (DH). It provides scientific risk assessments and advice over a wide range of subjects relevant to the threats posed by new and emerging respiratory viruses. Its membership currently comprises a wide range of scientific disciplines including: clinical medicine (predominantly respiratory medicine, infectious diseases and paediatrics), epidemiology and public health, virology, vaccinology, health emergency preparedness and response, and bio-statistical modelling. In future behavioural sciences and animal health experts will also be co-opted to support the committee in its work. The underpinning ethos of NERVTAG will always be that it exists to service the Government's need for timely, independent, scientific and clinical advice; and that it should be task-oriented, responding to requests from DH, Public Health England (PHE) and the NHS, by creating outputs and deliverables to meet these needs. In the first year of its being, NERVTAG has been especially busy. Firstly, bedding down and learning to play its role in a substantially reformed DH structure for pandemic preparedness and response. Secondly, responding to specific Governmental needs for scientific guidance about pre-pandemic vaccines, antiviral drugs and antibiotics for stockpiling purposes. I thank NERVTAG members for their input and commitment during what has been a very intensive first year in office. Thanks are also extended to members of the Secretariat (Frances Parry-Ford and Ruth Parry) who have supported our work so effectively.



JS Nguyen-Van-Tam MBE, DM, FFPH, FRCPath, Hon FFPM.

2. Plain English Summary (abstract for lay reader)

The UK National Risk Register says the natural hazards with the greatest likelihood and highest impact are pandemic influenza, and a new and emerging infectious disease.

In the event of a new respiratory virus emerging, the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) advises the Chief Medical Officer and the Department of Health how to minimise risk to the UK population.

NERVTAG monitors respiratory viruses that threaten human health, such as strains of influenza virus or other respiratory viruses with potential to cause an epidemic or pandemic illness. We also include illnesses that may result in a small number of cases but still have a severe impact, such as Middle East Respiratory Syndrome, known as MERS.

MERS was first recognised in 2012 and causes a severe respiratory infection and in many cases death, particularly in older people with underlying medical conditions, such as diabetes and high blood pressure.

The majority of MERS cases have been in people who live or have travelled in the Middle East, but in 2015 there was an outbreak associated with a number of hospitals in South Korea, involving 185 confirmed cases and 36 deaths. This was triggered by an individual who had travelled to the country from the Middle East, and is the only outbreak to date occurring outside the Middle East.

Last year NERVTAG assessed the risk of MERS to the UK, as well as assessing the risk of avian influenza viruses A(H7N9), A(H5N1) and A(H5N8) and enterovirus D-68, with the support of Public Health England.

In addition to these risk assessments, NERVTAG also advised the Department of Health on pre-pandemic influenza vaccine and the influenza antivirals and antibiotics to be used in the event of an influenza pandemic.

As we move forward, NERVTAG has also identified some areas where there are gaps in emerging respiratory infections research, and will provide advice on areas where more research efforts may be needed.

3. Introduction

It is the aspiration of the Department of Health to embed scientific advice in the policy-making process. It is clear that scientific advisory committees must be independent of Government and NERVTAG, being comprised of experts in the field or working in organisations (such as the NHS) which would be in the front line of the response to an emerging new respiratory infection or influenza pandemic, are well placed to advise. The group draws on the expertise of scientists and health care professionals, including clinicians, microbiologists and public health practitioners, and colleagues in related disciplines. The group is supported by a scientific secretariat from Public Health England (PHE), and is scientifically independent.

The terms of reference are found at Annex A. NERVTAG acts as a scientific advisory group to the Chief Medical Officer (CMO) across the range of new and emerging respiratory infections, and related preparedness functions. Outputs from NERVTAG feed into the Department of Health (DH) pandemic preparedness arrangements. It is not the role of NERVTAG to advise directly on matters of policy; instead, to provide scientific and clinical advice that may underpin the formulation of policy by DH.

NERVTAG is comprised of a core membership, with the addition of co-opted members who are included for their input on involvement in day-to-day operational matters. The chair considers the view of core members, co-opted members and observers as being equally welcome, unless a specific scientific consensus is required through a vote which shall apply to core members only (less any members who have disclosed potential conflicts of interest). The terms of reference allow the committee to invite additional members to supplement the core membership where specific expertise is required.

Sub-groups of the main NERVTAG group or subcommittees will be established as necessary with a view to ensuring adequate consideration of detailed technical aspects of the work of the Group. The Chair of each sub-group would sit on the main group, and other members of the sub-groups invited to attend the main Group on an ad hoc basis.

NERVTAG may ask the Strategic Pandemic Influenza sub-committee on modelling (SPI-M) to undertake specific modelling work as necessary. In the event of a pandemic, SPI-M would report independently into the Scientific Advisory Group for Emergencies (SAGE).

NERVTAG is considered to be a committee working under usual inter-pandemic conditions, and will be subsumed by the Health Security Advisory Group (HSAG) in the event of a pandemic or other health emergency related to respiratory viruses, with individual members being drawn from NERVTAG as necessary, at the discretion of the CMO. HSAG would feed scientific advice to inform policy and preparedness into a Scientific Advisory Group for Emergencies (SAGE) which would be co-chaired by the CMO and Chief Scientific Advisor.

When NERVTAG was established, the intention was for meetings to be held every 6-12 months, unless otherwise required. Members are encouraged to raise concerns about threats or observations coming out of their own virus horizon scanning to raise these at meetings or to contact the chair and secretariat, in between meetings, if they have concerns regarding any specific topic within the NERVTAG remit, so that the committee can respond appropriately. From time to time DH may raise issues that require more immediate attention, and when this occurs NERVTAG will hold additional meetings in person or virtually.

Minutes of NERVTAG meetings are made publicly available and published in full, unless they contain confidential or commercially sensitive information, in which case the relevant sections will be redacted. These, and other outputs from meetings, can be found through a link embedded in the NERVTAG page on gov.uk

Members are asked to declare all their interests at the time of their appointment and are asked to notify promptly the Secretariat of any changes. Before or at the start of every meeting, members are asked to declare any changes to their interests and the minutes of each meeting will include interests that are declared and how they have been handled.

A register of members' interests is found at:

<https://www.gov.uk/government/groups/new-and-emerging-respiratory-virus-threats-advisory-group>

4. Meetings

NERVTAG held full meetings on two occasions in its first year. In addition, two subcommittees met in 2015 to consider -

- 1) pandemic vaccines;
- 2) the antibiotics stockpiled for use in the event of an influenza pandemic.

Two other subcommittees were convened, (but did not meet until 2016) to consider -

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- 1) the personal protective equipment (PPE), particularly facial/respiratory protection, such as facemasks and respirators, stockpiled for use in the event of an influenza pandemic;
- 2) the clinical algorithms underpinning the National Pandemic Flu Service (NPFPS) which would be re-activated in the event of an influenza pandemic.

NERVTAG meeting 19 December 2014

As this was the first meeting of the group the Terms of Reference were agreed and any gaps in representation in the group identified. Behavioural sciences and animal health expertise were areas highlighted where representation was needed but currently absent.

Situation reports on avian influenza viruses A(H5N1), A(H5N8) and A(H7N9), MERS-CoV and Enterovirus D-68 were reviewed.

DH indicated that they were seeking advice on the re-procurement of influenza pre-pandemic vaccine (PPV).

Recommendations/outputs

- The committee agreed that a substantive written risk assessment of avian influenza A(H7N9) would be beneficial, and that this could be combined with risk assessments of avian influenza A(H5N1) and A(H5N8) viruses, identifying the avian influenza viruses of most concern.
- The committee recommended that work is undertaken to assess potential methods for raising the profile of MERS-CoV amongst clinicians, and re-enforcing the importance of obtaining a travel history, and generalised infection control as standards across UK clinical practice.
- The committee suggested possible gaps in research on infectious respiratory diseases.
- In response to the request from DH the committee suggested that a vaccine sub-group is established, and that representation from the National Institute of Biological Standards and Control (NIBSC) would be appropriate.

NERVTAG meeting 27 November 2015

The NERVTAG code of practice was agreed and any new conflicts of interest raised.

NERVTAG had been asked to provide DH and the CMO with expert advice on the continued appropriateness of the current UK policy of stockpiling antivirals for use in an influenza pandemic. A significant proportion of the oseltamivir stockpile will expire in 2016/17. NERVTAG's advice will be used to inform the CMO and Ministers on the options relating to the replenishment of the current stockpile as well as the procurement of future antiviral stockpiles. The committee therefore discussed the issues around provision of a stockpile of antivirals in general as well as the modelling assumptions upon which decisions are based. Part of the discussion included consideration of the findings detailed in the Academy of Medical Sciences report on the use of neuraminidase inhibitors for influenza, and their interpretation of the evidence with respect to pandemic influenza.

The recommendations of the NERVTAG subcommittee on pandemic influenza vaccines were discussed and ratified, subject to some minor changes

The recommendations of the NERVTAG subcommittee on antibiotics were reviewed and ratified.

DH requested that NERVTAG establish a short life sub-group to provide it with scientific and clinical advice to inform decisions on the facemask and respirators stockpile for UK use in an influenza pandemic.

The group considered the risk assessment update on new and emerging respiratory virus threats and broadly agreed with PHEs assessment of the risk from avian influenza viruses A(H7N9) and A(H5N1), MERS-CoV and Enterovirus D-68

Recommendations/outputs

- The Committee agreed that the current evidence continues to support a UK policy of maintaining an antiviral stockpile of oseltamivir and zanamivir for use in an influenza pandemic in order to be able to treat all cases of influenza within the reasonable worst case (RWC) pandemic scenario, regardless of risk group or severity of complications.
- The committee recommended that the current H5N1 vaccine stockpile is not replenished once it expires, and that there should be no further investment in any new vaccine stockpile at the current time. However, the committee did agree with the subcommittee recommendation to investigate the potential for re-investment in the development of improved vaccine technologies and other preparatory work.
- The committee accepted the recommendations of the subcommittee on antibiotics. The committee recommended that the Department of Health commission an update to the 2007 Pandemic Flu Clinical Guideline to take into account the latest available evidence. In the meantime, the committee recommended that the composition of the antibiotic stockpile should be re-considered in the light of suggested changes in the recommended indications for the use of antibiotics. In particular the committee agreed that there should be no further recommendation for use of preventive/precautionary antibiotics.
- It was agreed to form a sub-committee to consider the facemask and respirators stockpile issues and that the subgroup would be chaired by Dr Ben Killingley, who is NERVTAG's influenza transmission expert. It was anticipated that recommendations would be made by March 2016.

Subcommittees:

Joint NERVTAG and Joint Committee on Vaccination and Immunisation (JCVI) pandemic vaccine subcommittee (meetings 20 Feb and 23 April, 2015)

The committee suggested that DH consider the short, mid and long-term options in developing a pandemic vaccine strategy.

Short term

The committee recommends that potency testing of the current H5N1 PPV stockpile is undertaken as a priority. The results of this testing would inform further testing e.g. cross-reactivity testing against other newly emerged H5 sub-type viruses, and help plan if and how the existing stockpile could be used in a future pandemic.

The committee recommended that further clarity is required on the adequacy of current Advanced Purchase Agreement (APA) contracts and the reliance on one manufacturer, which is in sharp contrast to the US Biomedical Advanced Research and Development Authority

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(BARDA) approach. The committee advised that consideration is given to the current contract in time for possible variations during renewal.

Mid-term

There is support for the UK to develop a risk-assessment based approach to prioritising investment in future pandemic vaccines. This approach could be used to determine the level of investment in developing a national library of viruses suitable for rapid use in vaccine manufacture (seed lots).

The committee noted that currently they do not have enough information on the benefits of seed lots vs. larger amounts of ready-made vaccine to make firm recommendations around the establishment and composition of a national seed lot library. The committee considered that exploring seed lots, and if funding allows, some larger batches and trials would be a good investment.

The committee felt there would be merit in learning more about BARDA arrangements to help identify any gaps that would benefit from UK investment.

In terms of technology, the committee agreed that the range of viable commercial partners with the ability to deliver commercial –scale quantities of pandemic vaccine is currently confined to the existing EU influenza vaccine manufacturers. The committee also acknowledged that there is potential for development in the area of live attenuated influenza vaccine (LAIV).

A discussion may be required between NIBSC/Medicines and Healthcare products Regulatory Agency (MHRA) around the new European Medicines Agency (EMA) licensure regulations and the impact for developing future pandemic vaccines.

Long Term

The committee agreed there is a strong need for a research agenda and a long term UK strategy.

As a long-term strategy, the committee believed it would be advantageous for the UK government to develop plans for inward investment in vaccine development, including universal influenza vaccines.

Such a strategy should be aligned with work that is being led by the CMO around vaccine technologies that is following the Ebola outbreak.

This would ensure the UK can be more reactive and responsive to future vaccine preventable threats, including influenza.

Antibiotic stockpile subcommittee (meetings 4 and 25 September, 2015)

The recommendations of the subcommittee are as follows -

1. In offering an expert view to the Department of Health on the issue raised, the Committee noted that the recommendations are offered in the absence of an updated Pandemic Flu Clinical Guideline and recommended that its advice should be reviewed once an update is completed.
2. The Committee recommended that the Department of Health commission an update to the 2007 Pandemic Flu Clinical Guideline to take into account the latest available evidence.
3. In the meantime, the Committee recommended that the composition of the antibiotic stockpile should be re-considered in the light of suggested changes in the recommended indications for the use of antibiotics, as detailed.

4. One suggested change to the indications for antibiotic use was to no longer offer 'prophylactic' treatment with antibiotics to certain adult high-risk groups presenting with acute bronchitis or symptoms of an uncomplicated influenza-like illness alone. Implementing this approach would mean that the antibiotic stockpile would reduce in size.
5. The Committee recommended that the Department of Health liaise with Public Health England on an annual basis regarding changes in antimicrobial resistance or trends in pathogens, and call a review of the appropriateness of the antibiotic stockpile if any cause for concern emerges. A review should be conducted in 3 years' time in the absence of any intervening review.
6. The Committee suggested that any savings made by a reduction in the antibiotic stockpile could be reinvested into supporting an update of the Pandemic Flu Clinical Guideline and addressing the limitations in the current surveillance systems for respiratory pathogens.

5. Work programme and future areas to be covered

See Annex C

Annexes

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Annex A

NERVTAG TERMS OF REFERENCE AND MEMBERSHIP

Role and establishment

The role of NERVTAG is to act as an Advisory Group to provide the Chief Medical Officer (CMO) and, through the CMO, ministers, the Department of Health (DH) and other Government departments, with scientific risk assessment and mitigation advice on the threat posed by new and emerging respiratory virus threats and on options for their management.

The group will draw on the expertise of scientists and health care professionals, including clinicians, microbiologists and public health practitioners, and colleagues in related disciplines. The group is supported by a scientific secretariat from Public Health England (PHE), and is scientifically independent. Members of the Group are expected to adhere to the Code of Practice adopted by the Advisory Committee on Dangerous Pathogens (ACDP).

The scope of the group would include new and emerging respiratory virus threats to human health including strains of influenza virus (regardless of origin), and other respiratory viruses with potential to cause epidemic or pandemic illness, or severe illness in a smaller number of cases.

Core membership

Chair: external independent health scientist, formally appointed through an independent process

- Public Health
 - Surveillance and epidemiology (national)
 - Public health microbiology (national)
- Academic infectious disease epidemiology
- Academic microbiology
- Virology
- Clinical respiratory medicine
- Emergency preparedness/response
- Modelling
- Behavioural Sciences (to be appointed)

Co-opted

Nominee on NHS England emergency preparedness

Nominee on NHS England Pandemic influenza resilience

Nominee from DEFRA /Animal Health

Observers

Nominees from DH, other UK Health Departments

Nominees from Other Government Departments

Additional members as required (depending on nature of threat)

Public health local (PHEC and/or DPH)

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PHE Field Epidemiology

PHE public health microbiology local

Public health ethics

PHE travel and migrant health

Secretariat: The secretariat is provided by Public Health England.

Annex B

Membership

Current members of NERVTAG are:

Professor Jonathan Nguyen-Van-Tam, **Chair**: Professor of Health Protection in the Health Protection and Influenza Research Group, University of Nottingham; Honorary consultant epidemiologist, Public Health England

Professor Peter Openshaw, **Deputy Chair**: Professor of Experimental Medicine at the National Heart and Lung Institute, Imperial College London and President of the British Society for Immunology

Professor Wendy Barclay: Chair in Influenza Virology, Department of Virology, Imperial College London

Dr Matthew Donati: Consultant Medical Virologist/Clinical Service Director, Public Health England, Bristol Public Health Laboratory and University Hospitals Trust

Professor John Edmunds: Dean of the Faculty of Epidemiology and Population Health at the London School of Hygiene and Tropical Medicine

Professor Neil Ferguson: Director, Medical Research Council Centre for Outbreak Analysis and Modelling, Imperial College London

Professor Andrew Hayward: Head, Department of Infectious Disease Informatics, Farr Institute at University College London

Professor Peter Horby: Public health physician and clinical academic; Director of the Epidemic Diseases Research Group at the University of Oxford

Dr Ben Killingley: Consultant in Infectious diseases and acute medicine at Whittington Health NHS Trust, with a research interest in the transmission of infection

Professor Wei Shen Lim: Consultant respiratory physician in a large teaching hospital (Nottingham University Hospitals NHS Trust) and Honorary Professor of Medicine (University of Nottingham) with a special interest in respiratory infections

Dr Jim McMenamin: Strategic lead for the respiratory viral team within Health Protection Scotland, responsible for seasonal and pandemic influenza

Dr Malcolm Semple: Senior lecturer in Child Health, University of Liverpool and Consultant in Paediatric Respiratory Medicine, Alder Hey Children's Hospital Liverpool – with research interest in severe acute respiratory infections

Dr Chloe Sellwood: Co-opted Member, National Lead, Pandemic Influenza, NHS England, within the Emergency Preparedness, Resilience and Response (EPRR) team

Dr Bob Winter: Co-opted Member, National Clinical Director for Emergency Preparedness and Critical Care for NHS England.

Members' biographies are available at:

<https://www.gov.uk/government/groups/new-and-emerging-respiratory-virus-threats-advisory-group>

Attendees and participants at the joint NERVTAG and JCVI pandemic vaccine subcommittee meetings were:

13 March 2015

Professor Jonathan Nguyen-Van-Tam, Chair of subcommittee and Chair of NERVTAG:
University of Nottingham

Professor Peter Openshaw: Imperial College London

Dr Peter Grove: Department of Health Analytical Team

Dr Wendy Howard: National Institute for Biological Standards and Controls

Professor Andrew Pollard: (Chair JCVI), University of Oxford

Professor Richard Pebody: Respiratory Diseases Department, Public Health England

Invited - Mr Alan Russell: Commercial Medicines Unit

23 April, 2015

Professor Jonathan Nguyen-Van-Tam, Chair of subcommittee and Chair of NERVTAG:
University of Nottingham

Professor Peter Openshaw: Imperial College London

Dr Peter Grove: Department of Health Analytical Team

Dr Wendy Howard: National Institute for Biological Standards and Controls (NIBSC)

Professor Andrew Pollard: (Chair JCVI), University of Oxford

Professor Richard Pebody: Respiratory Diseases Department, Public Health England

Professor Maria Zambon: Reference Microbiology, Public Health England

Invited- Dr Othmar Engelhardt: NIBSC

Dr Rick Bright: BARDA (by telephone)

Attendees and participants at antibiotic subcommittee meetings were:

4 September, 2015

Professor Wei Shen Lim (Chair): Nottingham University Hospitals NHS Trust

Professor Jonathan Nguyen-Van-Tam (Chair of NERVTAG): University of Nottingham

Professor Peter Openshaw: Imperial College London

Dr Malcolm Semple: University of Liverpool

Dr Meera Chand: Public Health England

Dr Simon Stockley: Principal in General Practice, Eaglescliffe Medical Practice

Dr Steven Searle; Western Sussex Hospitals NHS Trust

Dr Bob Winter: NHS England

Mr Alan Russell: Commercial Medicines Unit

25 September 2015

Professor Wei Shen Lim (Chair): Nottingham University Hospitals NHS Trust

Professor Jonathan Nguyen-Van-Tam (Chair of NERVTAG): University of Nottingham

Martyn Underdown: Clinical Countermeasures Procurement, Public Health England

Invited - Geoff Wooton, Analytical Team, DH

**Annex C- NERVTAG forward work plan –
areas/future subcommittees**

Ongoing work areas commenced upon in 2015

- A standing request to continue to operate responsively, providing expert advice in a timely and flexible manner, and provide expert input to inform the wider government response in incidents/emergencies involving emerging respiratory viruses, as required by the Chief Medical Officer.
- A standing request to continue to monitor emerging respiratory viruses globally and provide scientific risk assessments and advice over a wide range of subjects relevant to the threats posed by new and emerging respiratory viruses, whilst maintaining engagement with the Advisory Committee on Dangerous Pathogens (ACDP) to ensure joint working in areas of concern to both committees.
- NERVTAG was asked to review its advice on the stockpiling of antivirals following consideration of the most recent available evidence on the use of antivirals in a pandemic (including the Academy of Medical Sciences and the Wellcome Trust report). This topic was covered in the November 2015 meeting, recommendations made to DH and, acting on that advice, Ministers have agreed to the replenishment of the remaining 'Tamiflu' stock expiring in 2016/17. This continues to be an ongoing or "live" issue as DH will review the position again in 2018/19 in advance of a planned major replenishment of both the Tamiflu and Relenza stockpiles.
- NERVTAG was asked to review the appropriateness of the antibiotics currently held in the UK stockpile for use in an influenza pandemic and make recommendations for future procurements from 2017 onwards. A subcommittee was formed and recommendations made to DH. Ministers accepted the advice and the stockpile will be reduced accordingly. The subcommittee agreed to review advice periodically to take account of changes in antimicrobial resistance, making this an ongoing issue for the committee.

New work areas identified for 2016

- A request to form a subcommittee to consider various questions posed by DH with regard to procurement/re-procurement of items of Personal Protective Equipment (PPE), particularly facemasks and respirators, which form part of the pandemic influenza preparedness stockpile.
- A request to form a virtual subcommittee comprised of NERVTAG members who are practicing clinicians as well as relevant experts co-opted by the Chair. The subcommittee will be asked to aid the updating of the algorithms behind the National Pandemic Flu Survey (NPFs) by advising on the wording of clinical questions.
- NERVTAG was tasked to provide clinical advice to support work being progressed by DH and PHE to develop a new Pandemic Specific Vaccine (PSV) strategy and vaccination policy for pandemic influenza.