HIGHLIGHTS

FROM **SCIENCE POLICY INTERFACE SESSIONS**

AT THE 7TH ESWI INFLUENZA CONFERENCE
#ESWI2020 VIRTUAL EDITION

THE SEVENTH ESWI INFLUENZA CONFERENCE

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VIRTUAL EDITION
6-9 DECEMBER 2020

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SCIENCE POLICY INTERFACE

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The 7th ESWI Influenza Conference – focus on influenza, RSV and COVID-19 - took place online between 6 December – 9 December 2020. The Conference was organised by ESWI, which summarises here in this Meeting report its interpretation of the key messages from the individual talks at the meeting. The summaries are written entirely by ESWI.

Organized by
European
Scientific
Working group *on*
Influenza

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How to join forces in influenza pandemic preparedness – what can we learn from COVID-19?

The Vaccine R&D Ecosystem After COVID-19: Paradigm shifts or business as usual in tackling future influenza pandemic threats?

MARISSA D MALCHIONE, SABIN VACCINE INSTITUTE, WASHINGTON, DC, USA

A multi-pronged approach to look into the vaccine R&D system post-COVID-19 was developed, including landscaping and cataloguing relevant scientific literature, policy research resources and public reporting. A survey was conducted to capture quantitative and qualitative data from a broad spectrum of experts on novel science & technology, vaccine R&D, and drivers & incentives for COVID-19 vaccine R&D. Interviews were carried out with key stakeholders in vaccine development. Six overarching trends emerged.

A strain of influenza with pandemic potential will appear sooner or later, and our experience with COVID-19 demonstrates that there are vast benefits to preventing an influenza pandemic rather than responding to one. Now is the time to protect the world from influenza, and the COVID-19 experience can inform our efforts in many ways.

Advances in knowledge, methods and platforms related to novel science & technology for COVID-19 vaccine development must be applied to inform and advance the development of next-generation universal influenza vaccines. Collaboration and open data sharing have accelerated progress, but specific incentives will be required for this to persist outside of the context of pandemic response.

COVID-19 has shown the disruption and devastation that viruses can have on the global economy. The case has been made that investments in vaccines pre-pandemic are many times more cost-effective compared to the current situation of response. The financial commitments should continue to be made towards next-generation influenza vaccines with the aim of creating financing mechanisms that decrease risk while enhancing innovation.

COVID-19 has also shown the immense efficiency that exists in product-focused research with a network of partners providing end-to-end support. Applying this to the vaccine discovery development & distribution process will accelerate the development of a more broadly protective influenza vaccine before a pandemic emerges.

COVID-19 has educated regulators on how to prioritize safety while maximizing efficiency. A truly universal influenza vaccine should be produced by distributed manufacturing to ensure equitable access.

The Alliance for Influenza Preparedness: Strategic priorities to enhance our global response to the next pandemic.

JOSEPH BRESEE, US CDC, USA

The influenza burden – which equates with the value of influenza prevention – remains underappreciated in lower-income countries. The WHO has been leading efforts to address this issue through a number of framework activities. At the same time, industry, academic and government partners are all investing in this area because it's clearly seen as key to moving forward with a global response to current and future pandemics.

Access to vaccines remains limited in lower-income countries, and is impeding programme growth and sustainability. The solutions to this problem are complex. They include the need to address small market constraints, to ensure the necessary regulatory streamlining that would make it easier to approve vaccines in a country, to expand the choice of formulations, and to facilitate the correct national budget decisions critical. Multiple solutions are needed, which will vary by income level and country size.

Vaccine hesitancy is a growing problem, especially in middle-income countries. Data that is now available and of a high quality are generally under-communicated, particularly when they refer to the value of vaccination and the link to pandemic preparedness. Consequently, there needs to be a mechanism to develop coordinated, clear messages to a wide variety of stakeholders.

A new initiative Ready2Respond (initially called Alliance for Influenza Preparedness) is a unique global collaboration of partners from the public, private and non-profit sectors committed to augmenting lower-income countries' readiness to respond to influenza and all other emerging respiratory viral pandemics for which vaccines are used. Its mission is to assure the world's readiness to respond to the next pandemic through transformative change in vaccine access and immunization policy in lower-income countries.

The initiative has three initial areas of focus. Working on the health, societal and economic burden of disease of both influenza and COVID-19. Focusing on risk communication, community engagement, and the efficient vaccination of healthcare workers. And ensuring solutions for vaccine access in the areas of approval, affordability and distribution. For these three focus areas, workgroups have been set up and are led by international experts. They aim to identify specific, actionable activities that can be undertaken and funded. This work will begin in the first quarter of 2021.

↘ The Threat of a New Influenza Pandemic: Its certainty, unpredictability (or not?), potential magnitude and speed.

GÜLSAH GABRIEL,
HEINRICH-PETTE-INSTITUTE, LEIBNIZ INSTITUTE FOR EXPERIMENTAL VIROLOGY, HAMBURG, GERMANY

Influenza outbreaks and epidemics pose ongoing risks to global human public health, so it's vitally important to always be in the alert phase and remain vigilant.

The natural reservoir for all influenza viruses are all aquatic birds. Here, influenza viruses are usually apathogenic or lead to low pathogenicity. Some of these bird species can carry the virus over large distances. The Quinghai Lake in China is known to be a large reservoir where different bird species come together during migration and can exchange their viral genome by the faecal-oral route. This could lead to the emergence of new virus strains with the ability to cross species barriers and infect humans, as has been reported for H5N1 avian influenza.

Once influenza viruses gain the ability to cross species barriers and infect humans, they could hit a human population that is immunologically naïve, which could lead to a large pandemic. This was the case with the H1N1 Spanish Influenza of 1918. The first influenza pandemic of the 21st century was in 2009 and was caused by an H1N1 influenza virus hitting an unprotected population. It led to approximately 200,000 respiratory deaths and 80,000 cardiovascular deaths. Risk groups were in children under five and young adults, but the highest mortalities were observed in people with comorbidities. The highest risk factor for hospitalization and death was pregnancy. In 2012 the WHO revised their vaccination recommendations, putting pregnant women as first priority for vaccination against influenza. However, vaccination compliance is very low.

Avian influenza is a continuous pandemic threat. Avian influenza viruses have repeatedly shown an ability to mutate quickly and cross species barriers. Wet markets in China are an important source of transmission and infection of humans. The H7N9 influenza virus is a candidate which has the potential to cause a large influenza pandemic. It emerged in China and has caused five waves of human infections. It peaked during winter and led to a fatality rate of 38% which was highly concerning. However, no sustained human-human transmissions were reported.

H7N9 is low pathogenic or apathogenic for bird species, meaning that large outbreaks do not show up in bird populations. So it could silently spread through the bird population without being observed until transmitted to humans. Countermeasures were taken. Wet markets and poultry markets in China were closed and large disinfection measures were put in place. China also started a massive vaccination campaign against H7N9 in September 2017 which was successful.

↘ Challenges in the Supply of Influenza Vaccines during the COVID-19 Pandemic and Lessons Learned.

BEVERLY TAYLOR,
INTERNATIONAL FEDERATION OF PHARMACEUTICAL MANUFACTURERS AND ASSOCIATIONS, UK

COVID-19 has had multiple impacts on seasonal influenza. These include a massive reduction in influenza activity globally, significant global logistical challenges, an increase in demand for influenza vaccines, and the potential for a mis-match between circulating viruses and vaccine streams, leading to reduced vaccine confidence.

At the same time, the COVID-19 pandemic has led to significant learnings. The rapid sharing of genetic sequence data (GSD) is critical. The already established Global Influenza Surveillance and Response System (GISRS) was crucial to help COVID-19 surveillance. It was clear that the Seasonal Influenza Programmes enable rapid response to any pandemic. And the COVAX facility highlights the importance of collaboration between multiple stakeholders.

Vaccine manufacturers are playing a central role in the COVID-19 response, building high levels of public trust and helping the development of an improved post-COVID-19 environment for vaccines.

However, vaccine confidence issues must be addressed. People need to have trust in the vaccines, how they are manufactured, and in the healthcare provider who is administering a vaccine. There is a lot of misinformation about vaccines – particularly in social media – which has decreased confidence in vaccines. In 2019, WHO listed vaccine hesitancy as one of the ten top public threats globally.

Vaccine confidence can be addressed in a number of ways. It's essential to demonstrate the highest standards in the development, manufacturing and regulation of vaccines. Transparent communications and working with trusted stakeholders is needed, to promote facts about vaccination and to dispel myths. Improved stakeholder engagement is necessary, including amongst community leaders. Effective tools need to be developed to inform the public of the benefits of immunization.

For improved seasonal and pandemic response, the response needs to be truly global and collaboration between all stakeholders is key. Building expertise and capacity before a pandemic is essential. Established seasonal influenza programmes significantly reduce influenza related morbidity and mortality, and provide the infrastructure to increase preparedness for future pandemics. There is a need for early seasonal influenza vaccines for future campaigns. And clear policies and communications on vaccinations and priority groups are needed.

Benefits of vaccination of healthcare workers

↘ Annual Seasonal Influenza Vaccination of Healthcare Workers.

REBECCA COX, UNIVERSITY OF BERGEN, NORWAY

Each year the WHO recommends annual influenza vaccination, and in many countries healthcare workers are prioritized for influenza vaccination because they can spread the influenza virus in the hospital if they become infected. The WHO recommends that 75% of healthcare workers should be annually vaccinated, especially because the influenza virus strains change almost annually. The three factors influencing whether healthcare workers get vaccinated are knowledge, motivation and availability.

Unfortunately a number of myths surrounding influenza vaccination are circulating the healthcare system, hence the importance of accurate, factual information to enable an informed decision. A study indicated that earlier vaccination influences the decision to choose to be vaccinated each year. It also indicated that healthcare workers vaccinated annually have a shorter duration of side-effects. Moreover, previous vaccination ensured that healthcare workers had higher levels of pre-existing antibodies even during the swine flu pandemic.

Another important finding was that healthcare workers who were not re-vaccinated had a high risk of infection. 67% of healthcare workers who were not vaccinated were infected either with influenza A or influenza B in the space of the 4-year study period. The timing of vaccination is also important. Antibodies fall after a year following vaccination, which also points to the need for annual vaccination. Annual vaccination was also found to increase CD4+ T cells (important for producing antibody responses), whereas no annual vaccination led to a decrease. Annual repeated vaccination increases the protective antibody over a five-year period. Over the course of the 5-year study period, repeated annual vaccination gave the healthcare workers the advantage of maintaining their protective antibody titres over a longer period of time. They also displayed a higher percentage of sero-protection.

Sickness despite vaccination can occur due to a number of respiratory viruses similar to the influenza virus. The use of good role models to increase healthcare worker vaccination is important. One of the most important times for vaccination is during a pandemic. Without the intervention of vaccines there will be high levels of epidemic activity. Once a vaccine is available it will provide protection to the people vaccinated and will flatten the curve. This is particularly important in the healthcare setting, to avoid large numbers of healthcare workers becoming sick at the same time.

↘ Mandatory Vaccination for Healthcare Workers in the US.

LITJEN TAN, NATIONAL ADULT IMMUNIZATION SUMMIT AND NATIONAL INFLUENZA VACCINE SUMMIT, USA

Immunizing healthcare workers is a patient safety issue. Asymptomatic carriers of influenza can infect others, and in a hospital setting this could be immune-compromised patients. In one hospital, increasing the vaccination coverage over 12 years from 4% to 67% led to confirmed influenza cases among healthcare workers decreasing from 42% to 9%. With a safe and effective vaccine, it is clear that the benefits of vaccinating healthcare workers outweigh the limitations of available data. There is also a clear causal transmission pathway for the development of healthcare associated influenza.

Immunization also protects the healthcare workers themselves, as well as their families. Moreover, healthcare workers are role models. A healthcare worker who is not vaccinated is not likely to recommend vaccination to a patient. Indeed, a healthcare worker recommendation is the most important reason why a patient receives influenza immunization. In the US, mandatory influenza vaccination for healthcare workers is also supported by ethical principles and rationale; legal foundations and precedent; and Stage and Federal Power Justifications.

However, despite clear rationale, US healthcare worker coverage rates were not improving, which led to mandates which require strong leadership and good communication among all involved. Hospitals that reached over 90% vaccination coverage were those that implemented vaccination as a condition of employment.

The US Advisory Committee on Immunization Practices recommends influenza vaccination for all healthcare personnel. The US National Vaccine Advisory Committee recommends employer requirements for influenza immunization of healthcare workers. Strong mandatory healthcare worker influenza vaccination rates can significantly help to reduce the mortality rate of influenza. Many facilities in the US already have mandatory healthcare worker influenza vaccination policies and have coverage rates in excess of 90%. The focus is now being turned towards long-term care and assisted living facilities where improvements can be made. Work is also being done to support implementation of mandatory influenza vaccination for healthcare personnel. One incentive is the Immunization Action Coalition's Honor Roll for Patient Safety, which currently involves over 1100 healthcare facilities in the US.

↘ Current Recommendations and Guidelines for Healthcare Worker Vaccination: An overview.

TED VAN ESSEN, GENERAL PRACTICE, THE NETHERLANDS

Since 2012, the WHO gives first priority for influenza vaccination to pregnant women, with healthcare workers and other groups equally second priority (up from fifth priority in 2005). A key reason behind this change of priority is that people are more likely to be vaccinated against influenza if their physician recommends it, especially considering that influenza is the most important infectious disease in Europe.

In Europe, 30 countries recommend influenza vaccination for healthcare workers. In Finland it's recommended for healthcare workers working near patients. In Norway and Slovakia only for those with direct patient contact. In Sweden for healthcare workers caring for severely immunocompromised patients. In Serbia it's mandatory for specific sub-groups. In Austria vaccination has to be documented before employment. No national vaccination policy against influenza exists in Denmark. Mandatory vaccinations for healthcare workers in Europe against other diseases are steadily increasing.

Despite years of effort and recommendation, vaccination uptake among healthcare workers in the world – and particularly in Europe – is still low, with a few notable exceptions.

However, few countries measure vaccination coverage in healthcare workers at all, and even less so by type of work and setting. In general, doctors seem to be more open to getting vaccinated than nurses.

Moreover, evidence for the benefits is not clear-cut, so well-designed, long-term prevention and intervention strategies are needed to maximize the effects of influenza immunization programmes. It will be interesting to see whether COVID-19 changes the opinion of healthcare workers to getting vaccinated.

The obvious question that arises is why is influenza vaccination not mandatory? Mandatory vaccination of healthcare workers against influenza is the situation in the United States and Canada, where there is now good vaccination coverage among healthcare workers.

As long ago as 2008 a study was published into the ethics of mandatory vaccination against influenza for healthcare workers. It concluded that "when uptake falls short, a mandatory programme may be justified". The main justification stems from the duty of care-givers not to harm one's patients when one knows there is a significant risk of harm, and the intervention to reduce this chance has a favourable balance of benefit over burdens and risk.

↘ The Ethics of Influenza Vaccination of Healthcare Workers: A critical appraisal.

SARAH EDWARDS, UNIVERSITY COLLEGE LONDON, UK

The libertarian position on influenza vaccination is that each individual is endowed with an extensive set of strong rights against interference in personal decisions. This gives governments small scope for change. There are three main arguments regarding the ethics of mandatory influenza vaccination of healthcare workers.

1) The government can coerce citizens for their own good. This is a non-starter for libertarians as the government is not justified in imposing conceptions of the good life on adults. Exceptions could be children and non-competent adults.

2) Rights can be over-ridden to avoid "disaster" if rights are not absolute. Libertarians recognize that the spread of disease is bad but not usually bad enough to persuade them to accept mandatory vaccination.

3) Stopping people from wrongly harming each other justifies coercive interference. This is most obvious when an identifiable individual is infected and can be forcibly quarantined. But with influenza there is a conundrum: vaccines are there to prevent people from being infected in the first place, so could involve forcibly vaccinating people who are not a clear or present danger to others. This means looking at "collective action," where individuals participating as a group (e.g. anti-vaxxers) could be perceived as causing harm to others. However, what is regarded as collective risk depends critically on background herd immunity rate, either through natural means or vaccination.

Mandatory policy relating to healthcare workers could take various forms such as contractual obligations from employment, or regulating private health providers. Much work is necessary to show evidence that vaccination of healthcare workers does reduce influenza rates and prevent harm to patients.

All you need to know about influenza, RSV disease and COVID-19

↘ Impact of Influenza Vaccination on Antibiotic Use and Antimicrobial Resistance: A mixed methods study to develop a strategic plan.

LOTTE VAN HEUVEL, NIVEL, NETHERLANDS INSTITUTE FOR HEALTH SERVICES RESEARCH, THE NETHERLANDS

Antimicrobial resistance (AMR) is an increasing threat to global health. For this reason, in 2015 the WHO developed and launched a Global Action Plan on AMR. Its Objective 5 states that investment in vaccines should be increased, and that vaccination as an infection prevention measure should be encouraged. This is because vaccines against viral diseases can reduce the symptom-based prescription of antibiotics, leading to a reduction in AMR.

Research involving a mixed methods study was performed as part of the Global Influenza and RSV Initiative (GIRI) with the aim of developing a strategic plan to integrate influenza vaccination into the global AMR discussion.

Work is ongoing, but some preliminary conclusions have been made. A systematic literature review indicates that influenza vaccination reduces antibiotic use, particularly in infants and children. However, most studies are from high-income western countries, the certainty of scientific studies is low, and there is a data gap. Moreover, while there is high interest in influenza vaccination and AMR amongst scientific studies, this is low in grey literature. The WHO plans to publish a roadmap for strengthening the role of vaccines against AMR. This will likely increase interest in vaccination against AMR.

It was also evident that few National Action Plans include objectives on influenza vaccination, and that implementation of objectives is unclear. However, availability of National Action Plans on AMR in the WHO Library is limited. Also, implementation depends on existing structures per country. For instance, low-income countries face greater challenges to introduce an Influenza Immunization Programme. Furthermore, the COVID-19 pandemic will likely have an impact on the budget and the interest of countries towards vaccination in the coming years.

↘ All you need to know about Influenza, both Epidemic and Pandemic.

AB OSTERHAUS, TIHO, HANNOVER, GERMANY

There are three appearances of influenza: seasonal, avian and pandemic. The large overlap between the symptoms of influenza and those of COVID-19 make it difficult to distinguish between the two in regard to symptoms. Influenza and COVID-19 together may be less severe due to COVID-19 mitigation measures and viral interference. Or they may be more severe due to the cumulative effect of both of them appearing at the same time. Papers are now emerging that are describing simultaneous infection, and are suggesting a more severe net effect.

Annual influenza mortality rates are mainly associated with the elderly, over 65, which is exactly the same as COVID-19. The main pathogen in seasonal influenza is H3N2 virus. In regard to influenza pandemics, four major ones have been seen in the last 100 years or so.

The more recent viruses (and COVID-19) spread much more quickly around the world than the 1918 virus due to more extensive and faster global travel.

An observation from the 2009 pandemic was that the lack of hospital capacity in case of a severe pandemic is not covered in pandemic preparedness plans. The limits of hospital capacity would have been over-stretched if the pandemic would have been worse.

The influenza virus reservoir is migratory aquatic birds. These spread the virus to a number of different species including poultry and pigs.

Seasonal influenza maintains itself in the population by antigenic drift. There are issues of vaccine mismatch and vaccine effectiveness. Vaccination coverage in the high-risk groups is too low. And better vaccines are expected. Avian influenza viruses have shown an unprecedented global spread in the last two decades. They lead to high human case fatality rates. Human-to-human transmission has been limited. Influenza pandemics are unpredictable and intervention strategies are needed along with pandemic preparedness plans and universal vaccines.

Influenza vaccination coverage must be increased (especially for healthcare workers; minimum coverage 70%). Antivirals should be prepared, stocked and used. Extensive surveillance and testing for influenza and other respiratory viruses should be continued.

↘ All you need to know about RSV Disease.

TERHO HEIKKINEN, UNIVERSITY OF TURKU, FINLAND

Respiratory Syncytial Virus (RSV) is one of the major respiratory viruses. It leads to otitis media, sinusitis, bronchiolitis and pneumonia. Outbreaks occur annually in most parts of the world. By the age of two, almost all children have experienced RSV infection, and reinfections are common throughout life. In children younger than five, RSV leads to 33.1 million episodes, culminating in 3.2 million hospital admissions and 118,200 deaths per year, mostly but not only in low-income countries.

RSV is largely transmitted by large droplets but also by aerosols, which may have an impact on ways to prevent transmission. Risk factors for severe RSV disease include prematurity and congenital heart disease, but age is the most significant risk factor; in one study, peak hospitalization occurred at one month.

Recent data also indicates that RSV is an important source of disease in the outpatient setting, where it can commonly lead to complications such as otitis media. RSV is also associated with wheezing and the development of asthma.

There is increasing evidence that RSV impacts the elderly. A study showed that RSV developed in 5% of healthy persons aged 65 or over, and up to 10% of high-risk adults. RSV accounted for 11% of hospitalizations for pneumonia, 11% for chronic obstructive pulmonary disease, 5% for congestive heart failure, and 7% for asthma. This is a similar pattern to that seen for influenza.

Treatment for RSV is currently only symptomatic; no specific antiviral is available. A couple of antivirals are being studied but have not yet come to market. For the prevention of RSV the current hope is on vaccines and monoclonal antibodies; numerous types of both are under development. Most are in the preclinical phase but a couple have reached phases 2 and 3.

Regarding vaccination against RSV, target populations have been defined: pregnant women, young children and the elderly. A phase 3 study on vaccination of pregnant women shows a vaccine efficacy of 44% in preventing hospitalization among infants, which is a significant advance. Another finding is from a study into the use of the monoclonal antibody Nirsevimab for prevention of RSV in pre-term infants. A single injection reduced hospitalization by almost 80%.

↘ COVID-19 Vaccine Development and Approvals in the US: Operation Warp Speed.

ARNOLD MONTO, UNIVERSITY OF MICHIGAN, USA

Vaccine development is a lengthy, risky and expensive process that often takes 15 to 20 years. For COVID-19, many of the platforms have already been established. This, coupled with the heavy investments made, and performing a lot of tasks simultaneously rather than sequentially, has enabled the development time of a COVID-19 vaccination to be significantly shortened.

In the US, Operation Warp Seed involves a conglomeration of various agencies, including the military, and is promoting the development of a number of COVID-19 vaccines.. ACTIV (Accelerating COVID-19 Therapeutic Interventions and Vaccines) is a public-private partnership working on a combined approach to COVID-19 vaccine development. It involves harmonized efficacy trials, collaborating clinical trials networks, collaborating labs, a data and safety monitoring board, and between-trial statistical groups.

The vaccines are being approved for use by the standard methods used in the US. Stringent effectiveness criteria are necessary with robust clinical studies and trials. Vaccine efficacy of at least 50% is required. General expectations for safety are no different than for other preventive vaccines. The safety database for COVID-19 vaccines currently in Phase 3 trials will involve around 50-60,000 subjects, which is much larger than normal.

In the US, Emergency Use Authorization (EUA) for a COVID-19 vaccine may be requested to allow for a vaccine's rapid and widespread deployment for administration to millions of individuals, including healthy people. EUA needs to follow the same guidance for efficacy as for regular licensure. A median of two months is deemed the minimum follow-up duration that could support a favourable risk/benefit determination to issue an EUA for a COVID-19 vaccine. After licensure there will be a lot of follow-up with observational studies to look at continual efficacy and safety considerations, through enhanced studies by the FDA and the CDC.

External reviews and evaluations concerning the safety, effectiveness, and appropriate use of COVID-19 vaccines will be carried out by the Vaccines and Related Biological Products Advisory Committee (VRBPAC). At its October 2020 meeting, VRBPAC stressed the need to keep the general public interested and confident in vaccination, as vaccine hesitancy is considered a major problem, especially considering the speed at which these vaccines are being rolled out.

↘ How Viruses Travel Tricky Routes.

COLIN RUSSELL, ACADEMIC MEDICAL CENTER, UNIVERSITY OF AMSTERDAM, THE NETHERLANDS

For respiratory viruses to survive, they have to establish new infections at the individual and population level. Transmission depends on multiple factors: Are there other people to infect? Are those people susceptible to infection? Do they have prior immunity or have they been vaccinated? And how efficient is disease transmission from one person to the next?

Some viruses are seasonal, which could be related to cool, dry air, time spent indoors, and/or the role of vitamin D. Many hypotheses have been put forward to explain where a virus comes from at the start of the "virus season". One that has been tested showed that the H3N2 influenza virus does not seem to persist locally in between epidemics. On the contrary, it seems to spread in an East & South-East Asian circulation network, epidemic to epidemic, and from there to North America, Europe and Australasia via air travel.

Seasonal influenza however is caused by four distinct viruses (H3N2, H1N1 and two influenza B viruses). A study showed that H3N2 behaves differently from the other three, which might persist locally in between epidemics. The four influenza viruses also move at very different rates, which is related to antigenic evolution. H3N2 has a significantly faster rate compared to the other three, which has a substantial effect on how it spreads around the world. H3N2 causes relatively large epidemics around the world almost every year. H1N1 epidemics are less frequent, and influenza B viruses cause small and infrequent epidemics.

It's also worth considering who travels by air. In a UK study, the majority of air travellers are over the age of 20. The majority of people who get the H1 and B viruses are not getting onto airplanes. People who get H3N2 are probably regularly getting on planes. This suggests a link between antigenic evolution of influenza viruses, behaviour, and the global spread of viruses.

Influenza, RSV disease and COVID-19 intervention strategies: current practice and future strategies

↘ Suppressing COVID-19 Transmission in Three Epidemic Waves in Hong Kong.

PENG WU,
WHO COLLABORATING CENTRE FOR INFECTIOUS DISEASE EPIDEMIOLOGY AND CONTROL, SCHOOL OF PUBLIC HEALTH, LI KA SHING FACULTY OF MEDICINE, THE UNIVERSITY OF HONG KONG, HONG KONG S.A.R. (CHINA)

A variety of interventions have been implemented in Hong Kong to suppress COVID-19 transmission. They are classified as travel-based, case-based, and community-based, depending on the target population and potential impact of the intervention. Three waves of COVID-19 have been experienced in Hong Kong, leading to over 5000 cases. Most cases in the second wave were imported, while the third wave was characterized by local transmission.

In all three waves, travel-based measures were essential to reduce transmission from importation of infections. The measures led to a huge reduction in inbound travellers by 99% and a corresponding reduction in imported infections of 93%. Work-from-home and other physical distancing measures were implemented and were found to be effective in control of local transmission. Work-from-home measures were associated with a 64% and 56% reduction in transmission in the second and third waves respectively.

All confirmed cases in Hong Kong are isolated in hospitals, as are asymptomatic cases. Close contacts are quarantined outside the home for 14 days. Testing capacity has been significantly expanded through the year, up to 10,000 tests per day. Test-and-trace was important but not sufficient to stop spread; a disruption in mid-July was associated with a 30% increase in local transmission. Transmission through mass gatherings, bars and restaurants was particularly important, leading to the phenomenon of super-spreaders.

Multiple potential introductions of COVID-19 into schools did not lead to onward transmission, maybe because younger children could be less efficient spreaders of COVID-19, or because school-based interventions were effective in preventing transmission.

Given the global situation of COVID-19, continuous importation of infections from high-risk areas seems likely. Therefore, travel-based measures will continue, while relaxing border restrictions for travellers from areas with low case numbers (“travel bubbles”). Imported and undetected infections in a community might lead to sporadic local infections and outbreaks from time to time. It’s essential to look for better approaches to identify local cases as early as possible.

↘ Pre-pandemic and Pandemic Vaccines.

FLORIAN KRAMMER, ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, USA

The many different sub-types of influenza virus and the different host species they infect make it very difficult to predict which viruses are going to transmit to humans and cause an epidemic or pandemic. Surveillance and monitoring of animal reservoirs and of zoonotic infections in humans is therefore continuously ongoing.

Influenza virus vaccines can be inactivated vaccines, live-attenuated cold-adapted vaccines, or recombinant protein vaccines. Technology exists to make them quickly, and to measure them to ascertain that they are actually working – without doing large efficacy trials.

However, it still takes a long time to make a matched vaccine, such as six months for the pandemic H1N1 in 2009. This needs to be shortened, ideally to three months. One way to be better prepared is through stockpiling of vaccines. A challenge with this approach is antigenic drift and immunogenicity. Solutions include the use of adjutants, prime boost strategies, and better vaccine platforms (e.g. mRNA and viral vectors). Another way to improve preparedness is by making universal vaccines, a number of which are under development.

Other issues regarding pandemic preparedness need to be addressed. These include production capacity and speed, global distribution of vaccines, vaccine hesitancy, the need for two vaccinations, unknown immunogenicity of emerging pandemic sub-types, and safety.

While producing an influenza vaccine in three months may be possible, it's clearly not currently possible to make a vaccine against other viruses in such a short timeframe, although this should be the ultimate goal. One way ahead would be to select 50-100 strains of virus that have the potential to cause a pandemic, and start to make vaccines now. They could be tested in phase 1 and 2 trials. In parallel, the correlates of protection of related viruses that are already circulating in humans could be studied (e.g. the human coronaviruses that cause the common cold). When a new virus emerges then it could be identified to identify the closest vaccine available. Phase 3 trials could be started up and manufacturing could begin within a short time; even three months.

↘ Antivirals Influenza, RSV, COVID-19: Key recent developments.

FREDERICK HAYDEN, PROFESSOR EMERITUS OF MEDICINE, USA

A number of antivirals are being investigated and/or used against respiratory viral pathogens.

A key advance in the prevention of RSV in infants is the development of Nirsevimab, an anti-F IgG1 monoclonal antibody which enables season-long protection.

Regarding influenza, the approval in 2019 by the BMA of the intravenous Zanamivr was a major advance. It was approved for the treatment of complicated and life-threatening influenza A or B virus infection in adult and paediatric patients when resistance to other anti-influenza products is known or suspected. This is an option for serious influenza B infection.

Another key development is the availability of Baloxavir Marboxil, a potent inhibitor of influenza A and B viruses. It is approved for influenza treatment in Japan and USA. A single dose therapy is effective in uncomplicated influenza.

A disappointment was the recent announcement that two Phase 3 trials of Pimodivir in high-risk and hospitalizing influenza were being stopped following interim analysis of results.

Turning to COVID-19, early anti-viral intervention is essential to maximize therapeutic benefits. Studies of Remdesivir do not show a decreased need for mechanical ventilation, nor for a reduced hospital stay.

An active area of investigation has been the development of monoclonal antibodies to the COVID-19 spike protein. One of these – Bamlanivimab – has been granted Emergency Use Authorization by the FDA for treatment of COVID-19 out-patients.

Interferon-based treatments are receiving increasing study, and initial investigations are showing positive signs. Molunpiravir is undergoing Phase 3 testing for COVID-19 in hospitalized patients and out-patients.

↘ Non-medical Interventions.

ANGELIKI MELIDOU, EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL, SWEDEN

In September 2020 the ECDC published guidelines for the implementation of non-pharmaceutical interventions (NPIs) against COVID-19. These are grouped into personal protection measures (e.g. hand hygiene, respiratory etiquette, facemasks), environmental measures (e.g. surface cleaning, ventilation), social distancing measures (e.g. isolation, quarantine, mass gathering restrictions), and travel measures (e.g. entry/exit screening, border closures).

In the absence of effective, safe and widely available vaccines or antiviral drugs, a combination of NPIs is necessary to protect vulnerable groups. Each intervention might have imperfections, but together they improve the chances of success.

It is difficult to calculate the effectiveness of each intervention as many are used in combination, and each country has differing epidemiological conditions, demographics, density and age of population as well as different behaviours and lifestyle. However, there is sufficient evidence that NPIs are effective health interventions.

Interesting is that the NPIs have also had a positive effect on the circulation of the influenza virus. In the southern hemisphere there was virtually no influenza in the 2020 influenza season. In the northern hemisphere it's too early to report, but a similar decline in circulating influenza viruses could also be anticipated due to the use of NPIs.

In the event of widespread community transmission, the most important NPIs are physical distancing in all settings; self-isolating of the ill; easy access to testing and rapid contact tracing; advice on social bubbles; consistently limiting size of indoor/outdoor gatherings; promoting teleworking where possible; wider use of facemasks, especially in closed settings; closing selected businesses where people have limited possibility for physical distancing; and stay-at-home measures.

NPIs have been effective in reducing COVID-19 although countries need to implement stricter NPIs to mitigate the second wave. Timely and targeted decisions need to be made, guided by data on local epidemiological situations.

↘ Regulatory Requirements of (Pre)pandemic Vaccines.

MARCO CAVALERI, EUROPEAN MEDICINES AGENCY, THE NETHERLANDS

During an inter-pandemic period, "pandemic preparedness vaccines" can be authorized for a strain that has potential to cause a pandemic and for which the majority of people are immunologically naïve. Data is provided on the safety and immunogenicity of the vaccine. Such a platform should already be validated for seasonal influenza. The actual strain causing the pandemic will then replace this potential strain. Approval could take place fairly rapidly. This is in parallel to ongoing work on seasonal vaccines, zoonotic vaccines, and novel pandemic vaccines.

The EMA has also developed an updated Health Threat Plan to address any bio-health threat. It is applicable to various acute hazards including threats of chemical, environmental and unknown origin, with a focus on human medicines.

The EMA COVID-19 pandemic task force was set up to become involved in early interactions with manufacturers and various health bodies, organisations and partners in Europe and elsewhere. It explores and reviews current investigational products for treatment or prevention of emergent disease; identifies the most appropriate regulatory pathways to ensure swift availability of vaccines; gives rapid scientific advice; interacts with academia; and sponsors clinical trials not funded by industry.

One of the bases for approval of a vaccine is the conditional marketing authorisation which is based on less comprehensive data than normal and is subject to specific obligations and criteria. One important criterion is that the benefit to the public health of the immediate availability of the medicinal product outweighs the risk in the fact that additional data are still required.

Regarding the compressed development plans for COVID-19 vaccines, the EMA followed development very closely and has been clear about which clinical studies have been able to be conducted in parallel and the minimal evidence that will be sufficient in order to start larger trials.

The EMA has issued a reflection paper around the preclinical data that could support the approval of COVID-19 vaccines, while ensuring convergence with international regulators and streamlining early development. The EMA is also assessing the considerable amount of robust data produced on efficacy and safety in order to produce timely regulatory decisions. The EMA has also commissioned independent research to prepare for real-world monitoring of COVID-19 vaccines.

Influenza, RSV disease and COVID-19 from a global health perspective, including underserved communities

↘ PEDSIDEA Community: Real-time Mapping of Influenza/RSV/COVID Incidence & Severity in Underserved Communities in the United States.

BARBARA RATH, VIENNA VACCINE SAFETY INITIATIVE, GERMANY

Defining the severity of influenza or indeed any disease is notoriously difficult, as so many parameters are involved. A quality improvement programme was developed for standardized disease severity assessments and standardized risk factor assessments using a mobile app at the point of care. This enabled the VIVI Disease Severity Score which was also correlated with antibiotic use. The app was then extended to cover different viruses that contribute to disease severity and thus help to disentangle "incidence" from "severity".

The mobile app was used in multiple sites simultaneously to study disease severity under the project PEPSIDEA (Partnering for Enhanced Digital Surveillance of Influenza Disease and the Effect of Antivirals and Vaccines in Europe). The initial focus was on tertiary hospitals in Berlin and Athens. Both the severity score and the prescribing behaviour were found to differ across the sites. The severity scores were highly predictive of ICU admission and of antibiotic/antiviral use.

The researchers moved on to study influenza and RSV disease severity outside the hospital, by implementing the app in New Orleans. The aim was to work with community clinics across the city to try and understand how to provide assistance to them by introducing modern ways to assess individual level disease incidence and severity at the point of care and in real time.

The app leads to multi-dimensional mapping of influenza and influenza-like illness (ILI) incidence and severity in real time in different centres. It also gathers information on the behaviour and the preferences of the clinical teams doing routine care, as well as on the use of antibiotics and antivirals. The app takes only three minutes to make a diagnosis.

↘ What is the Impact of COVID-19 in Underserved Communities?

OLIVIA TULLOCH, ANTHROLOGICA, UK

Underserved communities are populations that are disadvantaged because of a reduced ability to pay and access care and healthcare. This could be for a variety of reasons and disparities. These communities face an unequal burden of COVID-19 across social groups and settings. Restrictive measures have severely disrupted delivery of healthcare services. Public health measures have left people without resources to address other health problems. Quarantine can lead to loss of security, income and social support. Job losses have increased the care burden. Income losses make it harder to afford healthcare.

There are additional hardships in low/middle-income countries (LMICs) which suffer disproportionately from high burdens of diseases. Lockdown measures have made it difficult for both patients and healthcare workers to travel to access and provide care. Under-resourced health systems in some LMICs are struggling to sustain essential health services. Most people in these countries have "informal" livelihoods and now face a disturbing lack of access to social protection and an inability to earn money.

The specific social groups experiencing heightened baseline vulnerabilities include people living with disabilities; elderly people; women and girls; refugees, displaced people and migrant workers; people in conflict-affected areas; and racial, ethnic and religious minorities. All these groups face a number of significant impacts in various areas of service delivery.

To reach and support the underserved communities that are affected not only by COVID-19 but other infections too, social science research is essential to engage and facilitate integrated and multidisciplinary analysis. It could cover such topics as outbreak analytics, analysis of health service data, social and behavioural data, and impacts response measures. Good data exists but has not always been optimally used.

Questions have to be asked which matter to women, adolescents, gender non-binary people as well as diverse ethnic and cultural groups. Data has to be collected that represents those most likely to need, but are least likely to access, care.

Policymaker decisions must be informed by a "whole of health" perspective that considers the potential trade-off between addressing COVID-19 and the broader health impact. It's important to think how to integrate infectious disease response within existing health system infrastructures and programmes across sectors, including social protection and education.

↘ Unique Features of the Epidemiology of Influenza and COVID-19 in Low- and Middle-Income Countries: Implications for policy.

CHERYL COHEN, UNIVERSITY OF THE WITWATERSRAND, SOUTH AFRICA

COVID-19 reached South Africa relatively late, with the first case reported on 5th March 2020. On 28th March an early national lockdown was implemented along with travel restrictions, despite low case numbers, in order to give the health system time to prepare. The epidemic reached 18,000 cases per day before numbers declined, and remained low even when society was re-opened. This is quite an unusual epidemic trajectory compared to that seen in higher-income countries.

The question was thus posed as to whether COVID-19 behaves differently in low/middle-income countries (LMICs) compared to high-income countries. In South Africa the disease came down without seemingly overwhelming the health system but there is limited data available from elsewhere in Africa so it's difficult to make conclusions about other parts of the world.

In South Africa, immunity appears to have played an important role in observed reductions in incidence. There are reports of high seroprevalence in other settings such as Brazil and India, but data is lacking on the role of immunity in bringing down COVID-19 epidemics. However, it does seem to be a phenomenon that is not just limited to South Africa.

NPIs have played an important role despite imperfect implementation particularly in LMICs that lack running water, toilets etc.

Very high COVID-19 attack rates have been seen, mainly asymptomatic, and it's unclear whether these confer immunity. The young age distribution in South Africa may play a role, as might the climate.

The important message is that understanding the local epidemiology and immunity may have important implications for policy on control of COVID-19 and how vaccines are used in LMICs when they become available. It's critical to have in-depth data from such countries to fully understand what's happening with COVID-19.

↘ Global Access to Vaccines for LMICs: Challenges and opportunities.

NITEEN WAIRAGKAR, VACCINES FOR ALL, USA

Vaccine access depends on multiple issues such as disease burden, vaccine development, sustainable finance, and regulatory pathways. There is a particularly high disease burden and unmet public health need for vaccines against RSV, pandemic influenza and COVID-19.

The RSV virus kills around 118,000 children per year; 99% of them in low/middle-income countries (LMICs). Despite the RSV virus being discovered 60 years ago, no vaccine exists and only one antiviral (Palivizumab monoclonal antibody) is available – but only in a few high-income countries. There is a development pipeline of over 60 vaccine and antiviral candidates, but multiple challenges exist in technology, regulation, manufacturing capacity, and funding.

A challenge with developing influenza A vaccines is that the virus constantly evolves, and thus it's difficult to develop and stockpile pandemic strain specific vaccines. Alternative new products are needed against a possible influenza pandemic such as a universal flu vaccine and long-acting universal monoclonal antibodies. These need to be developed with global private-public partnerships to ensure access of these products to LMICs. However, at the same time there are existing challenges with ensuring access of existing seasonal influenza vaccines to LMICs.

Huge global coordination of efforts to develop a vaccine against COVID-19 are proving successful, but again, LMICs are facing significant challenges. LMIC manufacturing facilities are not approved by high-resource regulators. LMIC systems are under-prepared for new technology vaccines, and vaccine logistics are challenging in view of the low storage temperatures required. In addition, fast-track development, with perceptions of cutting corners, may erode vaccine confidence in LMICs.

Consequently, when considering the above common themes and challenges, particularly from an LMIC perspective, there is a strong need for a renewed global vaccine architecture. This should consist of a global development organisation, a global manufacturing organisation and mechanism, a global procurement/delivery organisation and mechanism, and a global sustained finance mechanism. Ultimately these will enable a global strategy for vaccines for all.

Risk evaluation and communication strategies in influenza and COVID-19: lessons learned

↘ Cross-sectoral Collaboration and Communication during an Infodemic.

TIM NGUYEN, WORLD HEALTH ORGANISATION, SWITZERLAND

An infodemic is an overabundance of information – some accurate and some not – that makes it difficult for people to make informed decisions for their health. Misinformation, disinformation and fake news can cause real harm to health, public trust, social cohesion and emergency response. Examples abound worldwide of people ingesting methanol, bleach and other products because they heard somewhere that they might kill the virus. Moreover, in the COVID-19 pandemic, technology has changed the way information is produced, distributed and consumed. Managing the infodemic is thus critical to managing the pandemic. This requires an evidence-based systematic frame culminating in interventions to address the infodemic.

The WHO has started looking at the rising narratives about what people are talking about and what questions they are asking. This helps to push out better information and guidance to counter misinformation or answer certain questions, for example on the WHO website or elsewhere.

Another concept concerns cross-sector communication and looking beyond the traditional geographic communities to communities that share common values and activities. The WHO is, for example, engaging with the faith community to share best practices and experiences that can support COVID-19 education, preparedness and response. Another direction is to collaborate with young people to design creative, engaging and relevant communication content around reducing transmission of COVID-19. This can include creative posters, social media, gifs etc. The third group is the world of work through working with professional organisations, unions, employers, employees and customers etc.

The WHO has also recently published a framework with 50 actions for cross-sector collaboration during an infodemic. It aims to strengthen the scanning, review and verification of evidence and information, as well as the interpretation and explanation of what is known. At the same time it serves to strengthen the amplification of messages and actions from trusted actors to individuals and communities that need the information.

↘ The Role of Experts in Guiding Policy.

PETER OPENSHAW, IMPERIAL COLLEGE LONDON, UK

Scientists working in a publicly funded role are obliged to inform and educate in ways that benefit public health – and in this respect, vaccines are among the most cost-effective health interventions. Direct advice is not the only way to influence policy; experts can also engage with the media. The trajectory of policy starts by identifying a need and then building the evidence, which is where scientists have a huge role to play. It is vital that policy is evidence-based, and that the evidence is carefully and critically examined. Experts are less involved in the later stages of creating policy, implementation, and monitoring & evaluation.

Governments should respect the academic freedom and expertise of its independent scientific advisors, who in turn should respect the democratic mandate of governments. Scientific advisors should remain free from political interference; be free to publish and present their research; be free to communicate publicly their advice to governments; have the right to engage with the media and the public; and say in what capacity there are communicating.

Mainstream scientific advice pertaining to COVID-19 covers multiple areas. It is not practical to isolate the vulnerable from carers, relatives etc. Herd immunity is unlikely to be reached by natural infection, which has a totally unacceptable lethality of about 1%. The risk of long-term COVID-19 is unknown but significant. Treatment methods are improving weekly, and there are real prospects of safe and effective vaccines.

A survey was conducted to ask whether people thought that policymakers have taken the mainstream scientific advice on COVID-19 that is available. The countries where less than 30% of people think that policymakers listen to scientists are also those countries where the highest death rates are being experienced, namely Spain, Russia, UK, Brazil, and USA.

Experts can contribute in multiple ways. They have specialist knowledge, whereas most within governments are generalists and may not have any significant scientific education or training. Experts can maintain a level of objectivity by evaluating the evidence and seeking balance, while being aware of the bigger picture with credibility and without getting emotional or bullying politicians into following their advice. Realism and consistency are required, along with communicating with brevity by highlighting the key points.

↘ Reaching Out to People at Risk: Focus on the elderly – why and how.

JANET MCELHANEY, NORTHERN ONTARIO SCHOOL OF MEDICINE, USA

The burden of influenza and COVID-19 is usually considered over short time horizons. It's important to consider the longer-term impact of complications of influenza and COVID-19 in older patients.

Multiple chronic conditions increase the risk for serious complications of influenza and COVID-19. It's important to account for the effects of frailty and risk for disability due to influenza and COVID-19.

Influenza and COVID-19 can contribute to worsening frailty, functional decline and the need for long-term care. This means that society must do all it can to avoid frailty.

From non-frail through pre-frail, mildly frail and moderately to severely frail categories of aging people, vaccination rates increase. Despite this, the death rates increase. In the ICU setting, particularly in the 50-64 age group, survival (and functional outcomes) worsen with increasing Clinical Frailty Scale scores, independent of age. This impacts the ability of 50-64 year olds to return to work following an influenza illness. Vaccination can help prevent this from happening.

Catastrophic disability is defined as a loss of independence in at least two basic activities of daily living. It was found that 18.3% of older adults experience catastrophic outcomes following influenza hospitalization. This relates to dysregulated immune responses, which are described as the "geriatric giant" of chronic diseases, leading to strokes, CHF, pneumonia, ischemic heart disease, cancer, and hip fracture.

For all these reasons, it's important to effectively and efficiently communicate the benefits of influenza vaccination. This includes full-throttle activation of vaccine initiative programmes, and safe accessibility to vaccination for underserved populations and aging adults. Vaccination at point of care for adults with chronic health conditions is essential. Greater awareness about public health and disease prevention should be utilized to broadcast the benefits of influenza vaccination. And there needs to be greater accessibility to vaccination for underserved populations.

↘ Talking Vaccines is Risky Business: Challenges in the post-trust environment.

FREDERIC BOUDER, UNIVERSITY OF STAVANGER, NORWAY

Recommendations concerning vaccination have been communicated for decades, but their implementation is not common practice, while distrust is growing. This is becoming increasingly apparent the closer a COVID-19 vaccine comes to reality.

Risk communication is about providing good information to support good decisions. It involves interactively sharing risk and benefit information with the public to enable people to make informed, independent decisions. It starts with the understanding of risk perception. Here there are frequently many factors that have contrasting impacts. These include natural vs technological; control vs non-control; the risk of vaccination vs the risk of illness; freeloading vs altruism; patients vs experts.

The prevalence of a disease also has an impact, as does trust in institutions. All these lead to significant challenges facing those who seek to build trust in vaccination. Bad management may have a negative effect on people's perception, such as a regulatory failure in the swine flu pandemic which led to a loss of trust.

There are a number of examples of how risk communication science has been applied to vaccines. A good doctor-patient relationship is linked to higher acceptance. The ambiguity of giving a jab to a healthy patient has to be addressed. Most patients have no understanding of how a vaccine works. Complex and contradictory concerns exist as people have mixed feelings about the medical profession and the media.

Healthcare professionals have a key role to play. Patients are more likely to be compliant with vaccine recommendations when the doctor has also been vaccinated, yet this is far from being always the case.

Communicators need to be science-informed, and risk communication should be based on accurate, scientific data. However, big data can be a blessing and a curse; more information needs to be presented in a more intelligible way. Doctors need to be accessible, which is challenging in an environment of more automated communication. Patients should be encouraged to present their reasons for vaccine hesitancy.

Communications need to be understandable. A solid, evidence-based message must be provided consistently to re-emphasize key messages in repeated interactions and with an ongoing dialogue with the patient. Narratives and metaphors have been shown to work.

Burden of influenza, RSV disease and COVID-19 and impact on society

↘ Monitoring the Fitness of Mutant Strains of COVID-19 and Influenza.

KATHY LEUNG, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF HONG KONG

Influenza viruses constantly change through antigenic drift, antigenic shift and the process of adaptation. This can lead to seasonal influenza epidemics that may differ in severity or age groups affected, vaccine mismatch or even influenza pandemics.

Coronaviruses mutate slower than influenza viruses. One of the most notable mutations is the G614 mutation of the spike protein. Its rapid spread suggests that G614 may have a transmission advantage. It's important to discover why it spreads so quickly.

G614 has been found to enhance replication on human epithelial cells and primary human airway tissues through an improved infectivity of virions. Mathematical epidemiological modelling to estimate the fitness of the G614 mutant has been performed. It was found to be 31% more transmissible than D614 and that R0 of the G614 strain would be approximately 1.3 times higher than the D614 wildtype strain. This would suggest more stringent control measures are required, as well as higher critical vaccination coverage.

An alternative but less probable explanation for the faster doubling time of the G614 strain is that there was no change in R0 but the mean generation time of the G614 mutant was around 20% shorter than that of the D614 wildtype. This would indicate the same critical vaccination coverage but more rapid response in contact tracing and testing.

↘ Mortality Associated with Seasonal Influenza Epidemics in the European Union: Overall estimates based on respiratory mortality from 2002-2011.

JOHN PAGET, NIVEL, UTRECHT, THE NETHERLANDS

The WHO estimates that seasonal influenza causes about 290,000 to 650,000 deaths annually around the world. The GLaMOR II project, funded by WHO in 2016, came to a global number of 389,000 respiratory deaths attributable to influenza each season during the study period of 2002-2011. Of these, two-thirds were among people aged 65 years and older.

Estimates were then calculated for the WHO European Region (53 countries with over 800 million inhabitants) and the European Union (including the UK), a region with a population of roughly 500 million.

The GLaMOR estimate of seasonal influenza-associated mortality in the EU is roughly 27,000 per year. This is similar to the CDC estimate of 28,200 (1999-2015). However, it's 2.5 fold lower than a recent FluMOMO estimate based on all-cause mortality conducted during 2012-2018.

Important differences in the average rates of influenza-associated mortality across EU countries were found. One question to ask is why do mortality differences appear across Europe? These range from 21.6% in Portugal to 36.7% in Malta.

Vaccination uptake rates certainly vary considerably, from 2% in Lithuania and 9% in Poland, to 75% in UK and 82% in the Netherlands. However, no correlation between the two was found. Further research is needed to determine explanations for these differences (e.g. age structures, comorbidities and vaccination).

Robust estimates of the mortality burden in Europe are important for communicating with the public (presenting the burden of disease pyramid), cost analyses to support prevention measures, and for comparing the mortality impact of other diseases – such as the COVID-19 pandemic – with seasonal influenza.

↘ Excess Mortality and Healthcare Resource Use Attributed to Influenza in People at High Risk for Developing Complications: Real-world evidence from a US managed care population.

SUSAN C. BOLGE, JANSSEN GLOBAL SERVICES, LLC, RARITAN, USA

The WHO has identified groups who are at elevated risk of complications from influenza, including young children, pregnant women, older adults, and individuals with specific medical conditions. Globally it is estimated that there are around 290,000 to 645,000 seasonal influenza associated respiratory deaths annually.

Substantial direct costs of medical care and indirect costs such as productivity losses are associated with influenza. While the burden of influenza is well documented, there is limited real-world evidence specifically focusing on patients at high risk of developing complications.

A study was performed to quantify excess mortality and healthcare resource use attributed to influenza in people at high risk of developing complications in a US managed care population. Real-world retrospective data from January 2014 to July 2019 were obtained, and inclusion criteria for patients at high risk of developing complications from influenza were defined.

Data were collected from a US administrative claims database, which enabled a retrospective analysis of a very large cohort of patients. However, these data do not include confirmatory diagnostics of influenza. Therefore it's possible that there are influenza patients who are not included in the data as well as patients who may have a diagnostic code for influenza but do not have a confirmatory diagnostic test for influenza. Also, the data do not measure the severity of comorbid conditions which would be expected to affect outcomes.

It was found that influenza increases risk of mortality and leads to greater healthcare resource use and direct medical costs. The data showed the magnitude of this among people at high risk of influenza complications due to the age and/or comorbid conditions. These effects are seen as early as within the first 30 days after diagnosis, but their impact continues throughout a year of follow-up.

↘ Respiratory Syncytial Virus (RSV) Burden of Disease in Adults over 60 years of age: A systematic literature review and meta-analysis.

MILOJE SAVIC, GSK, WAVRE, BELGIUM

The burden of RSV disease differs with age. In children it is a major cause of respiratory illness leading to hospitalization in infants older than two. In healthy young adults it is generally associated with common cold-like symptoms. In older and immunocompromised adults RSV is associated with an increase in disease severity that more frequently leads to hospitalization.

Amongst adults aged over 65, in 2015 in industrialized countries there were around 1.5 million cases of RSV-ARI, 214,000 hospitalizations and 3.300 deaths. However, mortality and morbidity could easily have been underestimated.

Due to immune-senescence and the presence of comorbidities, older adults are at higher risk of RSV and related complications. While RSV incidence is lower than that of influenza, complications and mortality may occur as often in older adults with RSV as in those with influenza.

A systematic literature review and meta-analysis showed a high burden of RSV disease in adults aged 65 or over in industrialized countries. This translates to around 2.9 million RSV-ARI (acute respiratory infection) cases per year, around 360,000 hospitalizations, and around 24,000 in-hospital deaths annually. The risk factors are frailty and underlying comorbidities in the population. Complications leading to community-acquired pneumonia were in the range of 4-10%.

↘ The Disease Burden of Respiratory Syncytial Virus Infection in Young Children in Primary Care: Results from the RSV ComNet pilot in Italy and the Netherlands.

JOJANNEKE JGT VAN SUMMEREN,
NIVEL, NETHERLANDS INSTITUTE FOR HEALTH SERVICES RESEARCH, UTRECHT, THE NETHERLANDS

Respiratory Syncytial Virus (RSV) is the most common pathogen causing respiratory diseases in young children. Nearly all children have an RSV infection before two years of age. In temperate climates it is a highly seasonal disease.

Knowledge on disease burden is important to make informed decisions regarding new interventions, but there is little information available on the socio-economic burden of RSV. The RSV ComNet study was developed to measure the disease burden of RSV in children younger than five in the winter of 2019/20 in Italy and the Netherlands.

Children were eligible if they were under five years of old, had consulted a general practitioner or paediatrician, displayed symptoms of acute respiratory infection, and showed a positive lab test to RSV. The study assessed 119 RSV positive children in Italy and 32 in the Netherlands.

The study showed that the clinical burden, healthcare utilisation and societal impact of RSV can be measured in a primary care setting.

The data collection procedure is important: a separate research network of general practitioners or paediatricians may lead to more efficient data collection than by collecting data via an existing influenza surveillance network.

The disease burden study protocol has been updated and will be applied in three countries with large sample sizes during the 2020/21 winter.

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