Country and global case studies

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DOMAIN 1: Detection and assessment of an emerging or re-emerging respiratory virus

- ## Clinician early warning of SARS in China, 2002

On November 16, 2002, the first case of an atypical pneumonia was reported by clinicians in Guangdong province in the southern part of China (1, 2), prompting local outbreak response activities. Four months later, on March 12th, 2003, the WHO announced a global alert about a severe pneumonia affecting parts of Asia, and on March 24th, 2003, a CDC laboratory analysis suggested that this respiratory disease was caused by a Coronavirus. The new disease was named the severe acute respiratory syndrome (SARS) and a novel coronavirus (SARS-CoV) was identified as the causative agent. Within months after its emergence in Guangdong Province in mainland China, SARS-CoV affected more than 8000 patients and caused 774 deaths in 26 countries on five continents. This example highlights the critical role that organized networks of clinicians may play in global pandemic early warning, and also illustrates how rapid global spread of a novel pathogen may occur due to air travel and globalization.

(1) Viroliegy. J.S.M. Peiris "SARS-COV-1" Paper (2003) 2021 [16/01/2023]. Available from: https://viroliegy.com/2021/10/14/j-s-m-peiris-sars-cov-1-paper-2003/ (accessed 15 Feb 2022)
(2) Zhong NS, Zheng BJ, Li YM, Poon, Xie ZH, Chan KH, et al. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. Lancet. 2003;362(9393):1353-8.

- ## United States Centers for Disease Prevention and Control (CDC) Health Alert Network to monitor for A(H5N1) in the United States, 2022

CDC's Health Alert Network (HAN) is CDC's primary method of sharing cleared information about urgent public health incidents with clinicians, public health laboratories, public information officers and public health practitioners at all jurisdictional levels. CDC's HAN provides health information and the infrastructure to support dissemination at state and local levels and the majority of the state-based HAN programs have more than 90% of their populations covered under the HAN. The HAN messaging system directly and indirectly transmits (e.g. by E-mail) Health Alerts, Advisories, Updates, and Information Services to more than one million recipients. On April 29, 2022 a person tested positive for influenza A(H5N1) in the State of Colorado. This case occurred in a person who had direct exposure to poultry and who was involved in the culling (depopulating) of poultry with presumptive A(H5N1) influenza. The HAN was used to remind clinicians across the country that they should consider the possibility of HPAI A(H5N1) virus infection in persons showing signs or symptoms of respiratory illness who have relevant exposure history. The HAN also sent a reminder to clinicians to contact the state public health department to arrange testing for influenza A(H5N1) virus, to collect respiratory specimens using personal protective equipment (PPE), to consider starting empiric antiviral treatment, and to encourage the patient to isolate at home. The HAN also suggested testing for other potential causes of acute respiratory illness, including SARS-CoV-2, depending on the local circulation of respiratory viruses.

(1) Centers for Disease Control and Prevention. Health Alert Network (HAN) 2022 [13/01/2023]. Available from: https://emergency.cdc.gov/han/index.asp (accessed 15 Feb 2022)
(2) Centers for Disease Control and Prevention. Highly pathogenic avian influenza A(H5N1) virus: recommendations for human health investigations and response 2022 [13/01/2023]. Available from: https://emergency.cdc.gov/han/2022/han00464.asp (accessed 15 Feb 2022)

- Event-Based Surveillance at community and healthcare facilities, Viet Nam

The Ministry of Health of Vietnam implemented a pilot of community and healthcare facility-based event-based surveillance in 2016. The pilot was implemented in four of Vietnam’s 63 provinces. The pilot initiative trained an existing network of village health workers (VHW) and ‘health collaborators’ to increase their awareness to look for and report signals as they appear in the community and to improve their understanding of patterns of disease that could signal the start of an outbreak. Health collaborators were mostly persons with strong community ties, including money lenders, insurance agents, veterinary health staff, landlords, factory managers, community leaders, and others in a good position to directly observe community events. The system did not rely on data reporting, aggregation, and analysis but rather used direct reporting methods to existing district and provincial authorities responsible for outbreak response. This broadened the sources of reporting and resulted in the identification of numerous signals that otherwise would have been missed, such as school absenteeism reported by teachers and the resulting multiple detections of vaccine-preventable diseases (e.g., mumps and chickenpox). In contrast to reporting by clinicians from healthcare facilities, VHWs and health collaborators recognized connections between cases in the community that doctors can miss, such as clusters among neighbors, co-workers, or persons with social connections. In the pilot districts, all events were detected and reported within 48 hours, and response was timely. Before EBS, such a rapid response by District Health Centers would not have been possible because ill persons would have to have been hospitalized to alert the system and, for certain diseases, traditional reporting often bypassed the commune health stations. For example, animal events such as poultry die-offs or rabid dogs previously would have been reported to the Animal Health Department, and human health officials would not always be alerted. During field visits, the District Health Centre staff stated that because of the EBS pilot, multisectoral communication, such as between food safety and public health and human and animal health sectors, improved substantially. The pilot demonstrated that event-based surveillance resulted in early detection and reporting of outbreaks, improved collaboration between the healthcare facilities and preventive sectors of the ministry, and increased community participation in surveillance and reporting. Following this pilot, the Ministry of Health officially adopted EBS as a routine surveillance system and guidance was issues in March 2018 in conjunction with training of provincial and district level staff.

(1) Clara A, Do TT, Dao ATP, Tran PD, Dang TQ, Tran QD, et al. Event-Based Surveillance at Community and Healthcare Facilities, Vietnam, 2016-2017. Emerging infectious diseases. 2018;24(9):1649-58.

- ### Community-based outbreak surveillance identified re-emergence of influenza A(H3N2) during the COVID-19 pandemic in Cambodia, 2020

Global influenza virus circulation decreased during the COVID-19 pandemic. On 18 August 2020, a cluster of respiratory illnesses among residents of a Buddhist pagoda was reported to the Cambodian Ministry of Health via their outbreak reporting system. This outbreak was originally investigated as a possible severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cluster on 20 August 2020, but 34 monks with respiratory symptoms tested negative for SARS-CoV-2, the virus that causes COVID-19. A response team was deployed. People with influenza-like illness (ILI) were asked questions regarding demographics, illness, personal prevention measures, and residential arrangements. Respiratory swabs were tested for influenza and SARS-Cov-2 by real-time reverse transcription PCR, and viruses were sequenced. Sentinel surveillance data were analyzed to assess recent trends in influenza circulation in the community. Among the 362 pagoda residents, 73 (20.2%) ILI cases were identified and 40 were tested, where 33/40 (82.5%) confirmed positive for influenza A (H3N2). All 40 were negative for SARS-CoV-2. Among the 73 residents with ILI, none were vaccinated against influenza, 47 (64%) clustered in 3/8 sleeping quarters, 20 (27%) reported often wearing a mask, 27 (36%) reported often washing hands, and 11 (15%) reported practicing social distancing. All viruses clustered within clade 3c2.A1 close to strains circulating in Australia in 2020. In this situation, community outbreak reporting and trained responders helped identify that influenza viruses began in the community following the relaxation of national COVID-19 mitigation measures.

(1) Sovann LY, Sar B, Kab V, Yann S, Kinzer M, Raftery P, et al. An influenza A (H3N2) virus outbreak in the Kingdom of Cambodia during the COVID-19 pandemic of 2020. Int. J. Infect. Dis. 2021;103:352-7.

- ### Rapid cooperative actions between human and animal health networks in response to the first confirmed human infection of Influenza A (H3N8), 2022

In early April 2022, a child from Henan Province, China, developed respiratory illness and was hospitalized in a critical condition with pneumonia. Samples were collected and tested, and influenza A(H3N8) was detected. Influenza A(H3N8) with all genes of avian origin was confirmed by the National Influenza Center of the Chinese Center for Disease Control and Prevention. The following day the National Health Commission of the People's Republic of China notified WHO of this case, the first ever confirmed case of human infection with an avian influenza A(H3N8) virus. Immediately, the Global Influenza Programme was in communication and collaboration with colleagues in the Global Influenza Surveillance and Response System (GISRS), including the WHO Collaborating Centre for Reference and Research on Influenza in Beijing, and with animal health colleagues in the World Organization for Animal Health (WOAH)/Food and Agriculture Organization (FAO) "Network of expertise on animal influenzas" (OFFLU) to understand the characteristics of this virus, its geographic distribution, and the public health risk of the virus. The week after the case was reported to WHO, influenza experts from GISRS, FAO, OFFLU and WOAH (OIE at the time) virtually convened to formally assess the risk of the virus, especially the risk of human-to-human transmission. On 18 May 2022, a preliminary FAO/OIE/WHO joint rapid risk assessment was published characterizing the risk of further human infections and the likelihood of sustained human-to-human transmission as low (1). At the same time, a second human case of infection with an A(H3N8) virus was reported to WHO from China. The case was also a child, living in a different province, who had exposure to a live poultry market. On 14 June 2022, OFFLU published an H3N8 technical statement on the importance of avian influenza surveillance in poultry and wild bird populations and the importance of rapid sharing of relevant outbreak information and viruses (2). The rapid sequence of cooperative response actions taken following the reporting of the first human case of A(H3N8) virus infection highlights the value of One Health partnerships, including GISRS, and the trust within and among the human and animal health networks to share information and assess risk rapidly and efficiently (1-4).

(1) World Health Organization. Joint FAO/OIE/WHO Preliminary Risk Assessment Associated with Avian Influenza A(H3N8) Virus 2022 [13/01/2023]. Available from: https://www.who.int/publications/m/item/joint-fao-oie-who-preliminary-risk-assessment-associated-with-avian-influenza-a(h3n8)-virus (accessed 15 Feb 2022)
(2) OFFLU. OFFLU statement on H3N8 2022 [13/01/2023]. Available from: https://www.offlu.org/index.php/2022/06/14/human-infection-with-influenza-ah3n8-china-2/.
(3) World Health Organization. Avian Influenza A(H3N2) - China 2022 [14/01/2023]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON378 (accessed 15 Feb 2022)
(4) World Health Organization. Influenza at the human-animal interface summary and assessment, 13 May 2022 2022 [14/01/2023]. Available from: https://www.who.int/publications/m/item/influenza-at-the-human-animal-interface-summary-and-assessment-13-may-2022 (accessed 15 Feb 2022)

• Surveillance and testing for Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Saudi Arabia

Middle East respiratory syndrome coronavirus (MERS-CoV) can cause severe respiratory illness and remains a pandemic threat. Transmission typically occurs through close contact with MERS-CoV–infected patients, particularly in healthcare settings, or through contact with camels. Most cases worldwide have been reported in Saudi Arabia. Since 2015, the Kingdom of Saudi Arabia has mandated all clinicians and health authorities to report all suspected MERS-CoV cases (meeting a clinical case definition) to a national Health Electronic Surveillance Network (HESN). Over a 3-year study period, the Saudi Arabian Ministry of Health tested >65,000 suspected MERS-CoV case-patients per year. Of these, 0.3% were positive for MERS-CoV, representing 0.7 confirmed cases/100,000 population per year. Peaks in percentage positivity corresponded to documented MERS-CoV outbreaks. This system has supported the national MERS-CoV response with to robust testing and contact-tracing efforts and early intervention for healthcare infection control. Continued robust MERS-CoV surveillance, including a more specific case definition implemented since 2018, is pivotal for the early ascertainment of cases and the effective implementation of control measures.

(1) Alzahrani A, Kujawski SA, Abedi GR, Tunkar S, Biggs HM, Alghawi N, et al. Surveillance and Testing for Middle East Respiratory Syndrome Coronavirus, Saudi Arabia, March 2016-March 2019. Emerg Infect Dis. 2020;26(7):1571-4.

• The Canadian Public Health Laboratory Network Best Practices for COVID-19

The Canadian Public Health Laboratory Network developed comprehensive Best Practice Guidelines for detection of SARS-CoV-2. The presence of the laboratory network and its national Respiratory Virus Infections Working Group guided specimen collection, data collection, transportation, testing and biosafety to ensure a consistent approach across the country. During the pandemic these best practices assured standardization of testing and data collection for the purpose of high probability case finding; and for the monitoring of multiple respiratory pathogens in population-based surveillance. To maximize the amount of laboratory testing data, hospitals and other high-complexity laboratories doing testing contributed summary testing data to complement the data from testing at their provincial public health laboratory. These coordinated laboratory data from the network informed local, provincial, and federal snapshots of pandemic activity (1) to help direct the response.

(1) Canadian Public Health Laboratory Network Best Practices for COVID-19. CCDR. 2020;46(5):112-8.

- ## SARS-CoV-2 household transmission investigation in Madagascar for policy decision to respond to the pandemic

Madagascar is one of 32 countries globally to implement a First Few Cases (FFX) or household transmission investigation (HHTI) aligned with WHO's standardised Unity Studies protocol (1). A prospective case-ascertained study of all identified household close contacts of laboratory-confirmed SARS-CoV-2 infections was conducted in Antananarivo immediately following the introduction of SARS-CoV-2 in the country on 19 March 2020, until 30 July 2020. Factors influencing transmission risk were assessed by analyzing the household secondary attack rate (hSAR). The results of the study provided key insights into the epidemiology of the first wave of SARS-CoV-2 in Madagascar. High rates of household transmission were found in Antananarivo (the mean hSAR among close contacts was 38.8% (95% CI [19.5–58.2])), emphasizing the need for preventive measures to reduce community transmission (2).
The investigation team in Madagascar implemented a timely and high-quality study with technical and financial assistance from Institute Pasteur and WHO, which was assessed as having a low risk of bias using a HHTI methodological quality assessment tool (3). Furthermore, excellent collaboration with WHO, including the sharing of early results, in September 2020, almost one year before peer-review publication (in August 2021), allowed for the results to be used to guide regional and global evidence-based response.

(1) World Health Organization. Coronavirus disease (COVID-19) technical guidance: The Unity Studies: Early Investigation Protocols 2022 [15/10/2022]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations (accessed 15 Feb 2022)
(2) Ratovoson R, Razafimahatratra R, Randriamanantsoa L, Raberahona M, Rabarison HJ, Rahaingovahoaka FN, et al. Household transmission of COVID-19 among the earliest cases in Antananarivo, Madagascar. Influenza Other Respir Viruses. 2022;16(1):48-55.
(3) Lewis HC, Marcato AJ, Meagher N, Valenciano M, Villanueva-Cabezas JP, Spirkoska V, et al. Transmission of SARS-CoV-2 in standardised first few X cases and household transmission investigations: A systematic review and meta-analysis. Influenza Other Respir Viruses. 2022;16(5):803-19. doi: 10.1111/irv.13002. Epub 2022 Jun 16.

- ## Burkina Faso implemented timely and high-quality longitudinal SARS-CoV-2 sero-survey

Seroprevalence studies measure antibodies, acquired by natural infection or vaccination, providing a profile of immunity within a population and data on subclinical or under-reported infections that may have been missed by routine diagnostic testing. Findings from these studies are useful to aid public health decision making. Burkina Faso implemented a timely and high-quality WHO supported Unity aligned (1) longitudinal cohort study to estimate the seroprevalence of SARS-COV-2 over time. Data collection ran from March to May 2021 in Ouagadougou and Bobo-Dioulasso. The study determined the proportion of individuals seropositive at baseline and during follow-up visits approximately 21 days apart. An analysis of participants who were seronegative at baseline and had at least one follow-up visit enumerated the incidence rate of SARS-CoV-2 seroconversion per 100 person-weeks. The study compared incidence rate by geographic location and sociodemographic characteristics of respondents. The findings provided useful information to direct policy makers and public health campaigns.

(1) World Health Organization. Coronavirus disease (COVID-19) technical guidance: The Unity Studies: Early Investigation Protocols 2022 [15/10/2022]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations (accessed 15 Feb 2022)

- ### Rapid surveillance using the Public Health Rapid, Emergency, Disease and Syndromic Surveillance system (PHREDSS) in New South Wales, Australia

The New South Wales (NSW) Public Health Rapid, Emergency, Disease and Syndromic Surveillance (PHREDSS) system provides daily monitoring of most unplanned presentations to NSW public hospital emergency departments and all emergency calls to the NSW ambulance service. Emergency hospital presentations and ambulance calls are grouped into related acute illness and injury categories. The number of presentations and calls in each category is monitored over time to quickly identify unusual patterns of illness. Unusual patterns could signify an emerging outbreak of disease or issue of public health importance in the population. PHREDSS is also useful for monitoring the impact of seasonal and known disease outbreaks, such as seasonal influenza or gastroenteritis, on the NSW population. Reports from PHREDSS are regularly included in NSW influenza and communicable disease reports (1).

(1) New South Wales Government. Rapid surveillance using PHREDSS 2022 [05/12/2022]. Available from: https://www.health.nsw.gov.au/epidemiology/Pages/rapid-surveillance-using-PHREDSS.aspx (accessed 15 Feb 2022)

DOMAIN 2: Monitoring epidemiological characteristics of respiratory viruses in interpandemic periods

- ### Sentinel ILI and SARI surveillance in Cote d'Ivoire and Kenya

In Cote d'Ivoire, sentinel surveillance was established in 2003 by the Pasteur Institute Côte d'Ivoire and the National Institute of Public Hygiene/MoH in collaboration with external partners. In this system, sentinel physicians screen all outpatients presenting to the sentinel sites for signs and symptoms of influenza-like illness (ILI). For each ILI case, a case-based surveillance form including clinical and epidemiological data such as date of illness onset, date of sample collection, patient's name, sex, age, clinical symptoms, and vaccination status is completed. A nasopharyngeal (NP) specimen is also collected from each ILI case. Respiratory specimens are tested for influenza, with subsets of specimens tested for multiple respiratory viruses using RT-PCR. During the COVID-19 pandemic, SARS-CoV-2 testing was integrated into the system. This system has been sustained for twenty years and standard data collection from several sentinel facilities has made it possible to interpret trends in influenza activity over time, to interpret patterns of seasonality and disease intensity, and to share these data with WHO GISRS and the international community (1,2).

Beginning in August 2006, The Kenyan Ministry of Health (MOH) with the US CDC in Kenya initiated influenza surveillance at a national referral hospital in Nairobi, multiple provincial general hospitals, selected health centers, and two refugee camps. At each site, surveillance was conducted for influenza-like illness (ILI) and severe acute respiratory illness (SARI). Of note, a trained surveillance officer – either a nurse or a clinical officer – is employed at each of the sites. Officers identify ILI patients at outpatient clinics and emergency rooms, and SARI patients in adult and pediatric in-patient wards in the hospitals. For every consented person with SARI and for the first three consented ILI patients per weekday at each site, a two-page questionnaire with questions about demographics, underlying diseases, influenza vaccine history, signs and symptoms, and exposures, is administered, and a combined nasopharyngeal (NP) swab and oropharyngeal (OP) swab is collected and tested for influenza viruses, as well as other respiratory viruses in selected locations. This successful system, using dedicated and trained staff, was expanded to monitor SARS-CoV-2 during the COVID-19 pandemic using multiplex PCR testing and has also been used to monitor COVID-19 vaccine effectiveness using a test-negative design. Data on both mild and severe illness has been used to publish manuscripts on the national burden of influenza and RSV, and the optimal timing of influenza vaccination campaigns, stimulating the development of a national influenza vaccination policy (3-6).

(1) Kadjo HA, Ekaza E, Coulibaly D, Kouassi DP, Nzussouo NT, Kouakou B, et al. Sentinel surveillance for influenza and other respiratory viruses in Côte d'Ivoire, 2003-2010. Influenza Other Respir Viruses. 2013;7(3):296-303.
(2) Kadjo HA, Adjogoua E, Dia N, Adagba M, Abdoulaye O, Daniel S, et al. Detection of non-influenza viruses in acute respiratory infections in children under five-year-old in cote d'ivoire (january - december 2013). Afr. J. Infect. Dis. 2018;12(2):78-88.
(3) Katz MA, Muthoka P, Emukule GO, Kalani R, Njuguna H, Waiboci LW, et al. Results from the first six years of national sentinel surveillance for influenza in Kenya, July 2007-June 2013. PloS one. 2014;9(6):e98615.
(4) Emukule GO, Paget J, van der Velden K, Mott JA. Influenza-Associated Disease Burden in Kenya: A Systematic Review of Literature. PloS one. 2015;10(9):e0138708.
(5) Emukule GO, Khagayi S, McMorrow ML, Ochola R, Otieno N, Widdowson MA, et al. The burden of influenza and RSV among inpatients and outpatients in rural western Kenya, 2009-2012. PloS one. 2014;9(8):e105543.
(6) Emukule GO, Mott JA, Spreeuwenberg P, Viboud C, Commanday A, Muthoka P, et al. Influenza activity in Kenya, 2007-2013: timing, association with climatic factors, and implications for vaccination campaigns. Influenza Other Respir Viruses. 2016;10(5):375-85.

- ## Integrating laboratory, epidemiologic and clinical surveillance into the ILI and SARI sentinel surveillance system in Costa Rica

Costa Rica, before and during the COVID-19 pandemic, has had an integrated ILI and SARI surveillance system with laboratory, epidemiological, and clinical information. This allows information to be obtained in real time, and analyses to be performed to address questions related to severity of the disease, vaccine effectiveness, and impact in an efficient manner. In Costa Rica, PAHO Flu is the web-based platform used, which allows the collection of demographic, epidemiological, clinical, and laboratory information. To do this, different teams are involved in capturing and entering specific types of information, each with access to this platform in real time. Having a single solid network of trained health centers capable of capturing quality structured information that represents the target population is essential to providing the information needed to guide the implementation of evidence-based public health measures. The platform includes sentinel sites and during the first two years of the COVID-19 pandemic, non-sentinel sites were also included as part of universal surveillance from health services (social security) to achieve this. From this experience Costa Rica has demonstrated that well-designed networks with specifically focused and trained professionals involved; and with interoperable/integrated platforms with the flexibility to be adapted to different surveillance objectives; may be used to form a comprehensive and integrated strategy for respiratory viruses surveillance.

- ## ILI sentinel surveillance provides support for the identification of novel human influenza virus infections and a coordinated One Health response, in Lao People's Democratic Republic

In March 2021, a human infection with avian influenza A(H5N6) virus was identified in a 5-year-old boy in Luang Prabang province in Lao People's Democratic Republic (Laos) through routine sentinel surveillance for influenza-like illness. This was the first time an avian influenza A(H5N6) virus had been detected in humans in Laos, and the first human infection reported outside of China. A multidisciplinary, One Health, investigation undertook contact tracing and enhanced human and animal surveillance in surrounding villages and live bird markets. Seven Muscovy ducks tested positive for highly pathogenic avian influenza A(H5N6) viruses. Sequenced viruses belonged to clade 2.3.4.4h and were closely related to viruses detected in poultry in Vietnam and to previous viruses detected in Laos. In this situation, One Health coordination and established laboratory capacity produced an efficient response to a signal identified in routine human surveillance. This outbreak demonstrates that activities to support the International Health Regulation's core capacities for sentinel and event-based surveillance are essential to public health and pandemic preparedness.

(1) Sengkeopraseuth B, Co KC, Leuangvilay P, Mott JA, Khomgsamphanh B, Somoulay V, et al. First human infection of avian influenza A(H5N6) virus reported in Lao People's Democratic Republic, February-March 2021. Influenza Other Respir Viruses. 2022;16(2):181-5.

- ## Using syndromic surveillance and PISA indicators to monitor COVID-19 pandemic severity in Ireland

The Pandemic influenza severity assessment (PISA) methodology was adapted to assess the severity of the first wave of the COVID-19 pandemic in Ireland. A suite of surveillance parameters were used to assess each of the three severity indicators: transmissibility, impact and seriousness of disease. Age-stratified data were used to compare weekly activity for each parameter with historical data from the previous 5 years and visualised using heat maps.
Out-of-hours cough calls to GPs and COVID-19 ICU admission rates, which used syndromic and influenza-specific historical data respectively for threshold setting, appeared very timely and sensitive for the early detection of COVID-19. Overall, syndromic surveillance data which had previously been used for assessing the severity of influenza were found to be reliable and timely for assessing pandemic severity and were particularly useful when testing capacity was limited or unstable. This work showed that PISA indicators and parameters can be adapted for COVID-19 surveillance, providing a standardised tool for monitoring the severity of pandemics and early detection of elevated activity caused by respiratory viruses. It also identified resilient syndromic surveillance parameters which are informative during both pandemic and inter-pandemic periods.

(1) Domegan L, Garvey P, McEnery M, Fiegenbaum R, Brabazon E, Quintyne KI, et al. Establishing a COVID-19 pandemic severity assessment surveillance system in Ireland. Influenza Other Respir Viruses. 2022;16(1):172-7.

- ## Participatory surveillance tracks community illness through self-reporting, examples from Australia

FluTracking (1) was launched in Australia in 2006 to track community influenza-like illness levels in all jurisdictions and to allow comparison of the timing, attack rates, and seriousness of influenza over time. This is achieved by collecting self-reported data on symptoms of respiratory illness, testing, healthcare-seeking behaviors, and workplace absenteeism through a weekly online survey. The data is analyzed in the context of background demographic and risk-factor data from participants such as vaccination status, age, gender, indigenous status, location and occupational exposure. During the COVID-19 pandemic, data on testing behaviors and results were expanded to include SARS-CoV-2 as well as influenza. In 2021, on average over 60,000 reports per week were received in Australia, and over 40,000 in New Zealand where FluTracking was expanded to in 2018.
Similarly, the InfluenzaNet (2) participatory surveillance system collects weekly online self-reported data from participants in European countries. Since its launch in 2009, it has expanded to receive data from 36% of the 28 member states of the European Union. Demographic and risk factor data are collected alongside symptom and healthcare-seeking reports, with the aim to establish a standardized syndromic surveillance system across European countries. Data collected through InfluenzaNet are reported in FluNews Europe weekly bulletins.

(1) FluTracking. FluTracking - Tracking COVID-19 2023 [14/01/2023]. Available from: https://info.flutracking.net/ (accessed 15 Feb 2022)
(2) InfluenzaNet. InfluenzaNet 2023 [14/01/2023]. Available from: http://www.influenzanet.info/ (accessed 15 Feb 2022)

• Influenza-associated pediatric mortality as a nationally reportable condition in the United States of America

Influenza-associated pediatric mortality became a nationally notifiable condition in the United States of America in 2004. For surveillance purposes, an influenza-associated pediatric death is defined as a death in a person less than 18 years of age, resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory diagnostic test. Demographic and clinical information is collected on each case and reported to the US CDC. The US Influenza-Associated Pediatric Mortality Surveillance System is one of several surveillance systems contributing to influenza surveillance in the United States. It does so by allowing national authorities to (1) monitor and describe the incidence, distribution, and basic epidemiologic characteristics of deaths among children associated with influenza virus infection, (2) provide data to guide future influenza immunization policy, and (3) rapidly recognize influenza seasons during which the impact of influenza may be unusually severe among children. A chart review is conducted for each case by the reporting jurisdiction and a case report form including information on patient demographics and underlying medical conditions, date/place of death, and influenza and invasive bacterial pathogen testing results is submitted to CDC.

(1) Centers for Disease Control and Prevention. U.S. Influenza Surveillance: Purpose and Methods 2022 [15/01/2023]. Available from: https://www.cdc.gov/flu/weekly/overview.htm# (accessed 15 Feb 2022)

• Surveillance of COVID-19 in long-term care facilities in the EU/EEA

The European Centers for Disease Prevention and Control (ECDC) has worked with European Union (EU) and European Economic Authority (EEA) countries to develop a methodology for regular national reporting of national surveillance data on COVID-19 in long-term care facilities (LTCFs). Long-term care facilities (LTCFs) are commonly homes for elderly people with medical and social vulnerabilities. The primary surveillance objectives are to monitor national-level trends in the number/proportion of COVID-19-affected LTCFs; and to monitor trends in the national incidence of cases and fatal cases of COVID-19 among LTCF residents. Austria, Belgium, Croatia, Cyprus, Denmark, France, Germany, Ireland, Italy, Lithuania, Luxembourg, the Netherlands, Norway, Portugal, Slovenia, Spain, and Sweden reported data to this surveillance system. The case facility rate (CFR) in pooled data from a subset of countries demonstrated a decline from 23.2% in Q4-2020 to 13.1% in Q1-2021, 12.0% in Q2, and a slight increase to 13.8% in Q3-2021.

(1) European Centre for Disease Prevention and Control. Surveillance of COVID-19 in long-term care facilities in the EU/EEA 2021 [15/01/2023]. Available from: https://www.ecdc.europa.eu/en/publications-data/surveillance-COVID-19-long-term-care-facilities-EU-EEA (accessed 15 Feb 2022)

- ## Enhancing Respiratory Disease Surveillance to Detect COVID-19 in Shelters for Displaced Persons, Thailand-Myanmar

Refugees and displaced persons are at risk for poor outcomes from acute respiratory infections (ARI) because of overcrowding, suboptimal living conditions, and malnutrition. Adapting and implementing enhanced COVID-19 surveillance measures in temporary camps for displaced persons along the Thailand-Myanmar border were successful in detecting COVID-19 outbreaks and preventing widespread disease during the initial phase of the pandemic in Thailand. Arrangements were made for testing of persons presenting with acute respiratory infection, influenza-like illness, or who met the Thailand national COVID-19 case definition. In addition, testing was performed for persons who had traveled outside of the camps in outbreak-affected areas or who departed Thailand as resettling refugees. All patients receiving inpatient or outpatient services at camp health clinics were screened for respiratory symptoms and history of travel outside the camp. Patients were tested if they met the national case definition for COVID-19 met the existing case definitions for ILI and ARI. Because mobile populations might be more likely to move informally within a country or internationally, establishing surveillance to detect pathogens of international significance and extending national surveillance systems to such vulnerable groups is vital. The enhanced surveillance developed in displaced persons' shelters on the Thailand–Myanmar border is one such example and provided a rapid response to help control the Delta variant surge in this setting.

(1) Knust B, Wongjindanon N, Moe AA, Herath L, Kaloy W, Soe TT, et al. Enhancing Respiratory Disease Surveillance to Detect COVID-19 in Shelters for Displaced Persons, Thailand-Myanmar Border, 2020-2021. Emerg Infect Dis. 2022;28(13):S17-s25.

- ## Hospital Capacity Monitoring undertaken by Public Health Scotland

Public Health Scotland monitors acute hospital activity and National Health Service beds information on an ongoing basis, with quarterly web updates. This hospital capacity monitoring system provides updates on a range of statistics on different aspects of hospital care, sourced from hospital administration systems across Scotland. These include information on trends on outpatient, inpatient and day case activity; and beds statistics.

(1) Public Health Scotland. Quarterly Acute Hospital Activity and NHS Beds Information 2022 [16/01/2023]. Available from: https://publichealthscotland.scot/media/16579/2022-11-29-acuteactivityquarterly-summary.pdf (accessed 15 Feb 2022)

- ## European mortality monitoring (EuroMOMO) excess mortality monitoring in Europe

Monitoring of excess mortality using weekly mortality data can provide a more comprehensive understanding of the population impact of communicable diseases, including influenza and

COVID-19, and is fundamental to public health decision making. The European mortality monitoring activity (EuroMOMO) (1) is a European network launched in 2008 to assess real-time excess mortality associated with seasonal influenza in Europe. The method on which the EuroMOMO model is based is standardized, making results comparable across countries. Using weekly all-cause mortality data from more than 20 countries in the WHO European region, EuroMOMO has generated pooled, and country specific excess mortality estimates and has promptly detected and quantified mortality associated not only with seasonal influenza, but also with the influenza A(H1N1)pdm09 and COVID-19 pandemics.

(1) EuroMOMO. EuroMOMO 2023 [15/01/2023]. Available from: https://www.euromomo.eu/ (accessed 15 Feb 2022)

- ## South Africa used SARI and ILI sentinel surveillance to assess risk factors for influenza associated hospitalization

South Africa established influenza sentinel surveillance among hospitalized patients with SARI and outpatients with ILI in 2009 and 2011, respectively. ILI sentinel clinics were located in the same catchment areas of selected sentinel hospitals. Detailed demographic, clinical and epidemiological characteristics as well as upper respiratory tract specimens were collected from all enrolled patients with SARI or ILI. Surveillance samples were tested for influenza virus types and subtypes using polymerase chain reaction assays.
Virological and epidemiological data collected during 2012-2015 were used to assess risk factors for influenza associated hospitalization using a case-control study design. The risk factors were assessed using logistic regression by comparing the characteristics of influenza-positive SARI cases (cases) to that of influenza-positive ILI cases (comparison group). Extreme of age, pregnancy, underlying medical conditions, HIV infection and obesity were identified as independent risk factors for influenza-associated hospitalization (1). In addition, the study identified risk factors poorly described in the literature such as prematurity and malnutrition in young children. The investigators of this study highlighted that, if adequately powered, this approach can be used to rapidly assess risk groups.

(1) Tempia S, Walaza S, Moyes J, Cohen AL, von Mollendorf C, Treurnicht FK, et al. Risk Factors for Influenza-Associated Severe Acute Respiratory Illness Hospitalization in South Africa, 2012-2015. Open Forum Infect Dis. 2017;4(1):ofw262.

- ## Assessing risk factors associated with fatal influenza using SARI sentinel surveillance data in Romania

In the winter of 2010 Romania's SARI sentinel surveillance system included 26 hospitals in nine counties. Given the ongoing 2009 A(H1N1)pdm09 pandemic, Romanian officials from the Ministry of Health and National Institutes of Public Health evaluated risk factors for fatal outcomes in patients hospitalized with SARI within the sentinel surveillance system. Laboratory-confirmed infection with influenza A(H1N1)pdm09, A(H3N2), or influenza B as independent risk factors for fatal outcomes in comparison with a reference group of influenza-negative persons. Influenza A(H1N1)pdm09 infection was strongly and independently associated with a fatal outcome. Other variables significantly and independently associated with a fatal outcome were being pregnant, having hepatic disease, increasing age in years, and increasing time from onset to hospital admission. The consistency of findings from these data with other published studies on risk factors for fatal influenza supported the use of ongoing surveillance data to monitor virological trends in the epidemiology of influenza and to serve as a tool to monitor risk factors for complications of influenza virus infections during each influenza season.

(1) Zolotusca L, Jorgensen P, Popovici O, Pistol A, Popovici F, Widdowson MA, et al. Risk factors associated with fatal influenza, Romania, October 2009-May 2011. Influenza Other Respir Viruses. 2014;8(1):8-12.

- Estimating the incidence of pneumonia in rural Thailand using population-based surveillance

In 2002, Thailand began active, population-based surveillance for radiographically confirmed pneumonia in Sa Kaeo Province. Full-time surveillance officers conducted active case ascertainment at every hospital, and routine audits and a community cluster survey promoted complete and accurate reporting. A case of pneumonia was defined as acute infection with signs or symptoms of lower respiratory tract infection and evidence of new infiltrates. An independent panel of radiologists reviewed digital images of all radiographs. Between September 2002 and August 2003, 777 patients met the case definition. The measured minimum incidence was 177/100 000 but the estimated incidence was as high as 580/100 000 with full adjustment for incomplete chest radiography and access to health care. Seventy-two (9%) patients died and 28% were known to be HIV positive. Fifteen (2%) patients had pneumonia twice during the year. The average cost of hospitalization for an episode of pneumonia ranged from US$490.80 to $628.60. The incidence of radiographically confirmed pneumonia requiring hospitalization in rural Thailand was found to be is high, and 1- to 3-fold higher than previous estimates based on passive surveillance. These burden of disease data, combined with etiologic studies, have been used to inform the introduction of new and existing vaccines effective against pneumonia pathogens.

(1) Olsen SJ, Laosiritaworn Y, Siasiriwattana S, Chunsuttiwat S, Dowell SF. The incidence of pneumonia in rural Thailand. Int. J. Infect. Dis. 2006;10(6):439-45.

- ILI and SARI sentinel surveillance to inform influenza burden of disease Lao PDR, Mongolia, and Morocco

In Mongolia routine surveillance for influenza-like illness (ILI), severe acute respiratory infection (SARI) and laboratory-detected influenza is undertaken. Using methods described in the WHO Manual for Estimating Disease Burden Associated with Seasonal Influenza, the Mongolian National Influenza Center, Academy of Medical Sciences and partners used sentinel surveillance data from ILI and SARI sites to estimate the disease burden associated with seasonal influenza from 2013–2018.

SARI and ILI incidence rates associated with influenza virus infections were calculated for the catchment areas of the respective sentinel systems and laboratory data on the percentage of specimens tested that were positive for influenza were analyzed by influenza type or subtype. The estimated incidence of influenza-associated ILI and SARI in Mongolia over five seasons was higher than that in comparable countries and a particular burden in young children was noted, informing potential prevention and control efforts (1,2).

In Lao Peoples Democratic Republic, the National Center for Laboratory and Epidemiology in collaboration with international partners combined epidemiological and virological data from sentinel SARI surveillance with hospital logbook reviews to estimate sentinel site catchment populations to assess the population-based burden of influenza-associated SARI hospitalizations in 2016. The overall influenza-associated SARI hospitalization rate was estimated to be 48/100 000 population (95% confidence interval [CI]: 44–51) or 3097 admissions (95% CI: 2881–3313). Influenza-associated SARI hospitalization rates were highest in children aged <5 years and persons >= 65 years. The burden of hospitalizations for influenza-associated SARI in Lao PDR is comparable to those from other countries and these findings have supported burden of disease and influenza vaccine cost-effectiveness estimates used to inform national policy decisions to procure influenza vaccines (3,4).

In Morocco, virologic sentinel surveillance for influenza virus was initiated in 1996 using a network of private practitioners that collected oropharyngeal and nasopharyngeal swabs from outpatients presenting with influenza-like-illness (ILI). The surveillance network expanded over the years to include inpatients presenting with severe acute respiratory illness (SARI) at hospitals and syndromic surveillance for ILI and acute respiratory infection (ARI). Respiratory samples and structured questionnaires are collected from eligible patients, and samples for influenza viruses. These surveillance data have suggested that influenza viruses affected all age groups and circulate seasonally during the Moroccan winter months of October through April with peak circulation occurring frequently in December. Influenza is responsible for both mild and severe respiratory illness in Morocco and accounted for 4%–9% of SARI hospitalizations. This surveillance system has also generated important baseline data on respiratory illness and the proportion attributable to influenza (5).

(1) Darmaa O, Burmaa A, Gantsooj B, Darmaa B, Nymadawa P, Sullivan SG, et al. Influenza epidemiology and burden of disease in Mongolia, 2013-2014 to 2017-2018. Western Pac Surv Response J. 2021;12(2):28-37.
(2) World Health Organization. A Manual for Estimating Disease Burden Associated With Seasonal Influenza 2015 [05/12/2022. Available from: https://www.who.int/publications/i/item/9789241549301 (accessed 15 Feb 2022)
(3) Khamphaphongphane B, Chiew M, Mott JA, Khamphanoulath S, Khanthamaly V, Vilivong K, et al. Estimating the national burden of hospitalizations for influenza-associated severe acute respiratory infection in the Lao People's Democratic Republic, 2016. Western Pac Surv Response J. 2021;12(2):19-27.
(4) Ortega-Sanchez IR, Mott JA, Kittikraisak W, Khanthamaly V, McCarron M, Keokhonenang S, et al. Cost-effectiveness of seasonal influenza vaccination in pregnant women, healthcare workers and adults ≥60 years of age in Lao People's Democratic Republic. Vaccine. 2021;39(52):7633-45.
(5) Barakat A, Ihazmad H, Benkaroum S, Cherkaoui I, Benmamoun A, Youbi M, et al. Influenza surveillance among outpatients and inpatients in Morocco, 1996-2009. PloS one. 2011;6(9):e24579.

- Establishing an ICD-10 code based SARI-surveillance in Germany

Influenza sentinel surveillance in Germany was previously only based on a network of primary care physicians that report consultations for acute respiratory infections (ARI). Weekly reports of ARI activity and corresponding results from virological sentinel surveillance are published year-round and data are sent to ECDC and WHO. However, during the process of pandemic preparedness planning after the influenza pandemic in 2009, the need to implement a routine sentinel surveillance system for severe acute respiratory infections (SARI) was noted. In 2015, the Robert Koch Institute (RKI) set up a collaboration with a private network of 47 hospitals to develop a SARI sentinel surveillance system with cases coded according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). Additional information on relevant procedures, such as ventilation, is also collected. The 47 sentinel sites included 2.4% of all hospitals in Germany, in 13 of the 16 federal states. Over five years the temporal pattern of hospitalized SARI patients corresponded well to the ARI surveillance and the influenza virological results of the traditional German outpatient ARI sentinel system. This work highlights the creative adaptation of country-specific data sources to meet international SARI surveillance recommendations and shows the importance of using different ICD-code case definitions tailored to the objectives of any evaluation. This effort helped create a SARI baseline as a starting point for evaluation of severity of future influenza epidemics or pandemics and future work may also involve analyses of different subgroups of patients with specific risk factors and underlying conditions. The system was leveraged during the COVID-19 pandemic to give robust estimates of severe COVID-19 hospitalization and intensive care incidence (2).

(1) Buda S, Tolksdorf K, Schuler E, Kuhlen R, Haas W. Establishing an ICD-10 code based SARI-surveillance in Germany - description of the system and first results from five recent influenza seasons. BMC public health. 2017;17(1):612.
(2) Tolksdorf K, Haas W, 1, Schuler E et al. ICD-10 based syndromic surveillance enables robust estimation of burden of severe COVID-19 requiring hospitalization and intensive care treatment. MedRxiv. 2022. https://www.medrxiv.org/content/10.1101/2022.02.11.22269594v2 (accessed 15 Feb 2023)

DOMAIN 3: Informing the use of human health interventions

- South Africa uses multiple data sources to assess the effectiveness of the Ad26.COV2.S (Johnson & Johnson) vaccine among health-care workers

During the initial phase of COVID-19 vaccine rollout in South Africa, health-care workers were prioritized for vaccination. Three main data sources were used to assess the effectiveness of the Ad26.COV2.S (Johnson & Johnson) vaccine against severe COVID-19 among health-care workers using a matched cohort design whereby vaccinated health-care workers were matched with an unvaccinated member of the general population. The national online electronic vaccination data system (EVDS) was used to obtain information on vaccination status of all people vaccinated in South Africa, including those who contributed unvaccinated at-risk time to analyses. Any breakthrough SARS-CoV-2 infections, COVID-19-related hospitalizations, and deaths were linked through the COVID-19 Notifiable Medical Conditions Sentinel Surveillance List, the DATCOV database that contained data on individuals admitted to hospital with COVID-19, and the National Population Register. Person-level data for vaccinees and members of the general population were obtained from private and government health-care schemes. Deterministic linkage based on the South African civil identification number or passport number for foreign nationals were used to merge the 3 main databases. Using multiple data sources, it was possible to rapidly estimate the effectiveness of the Ad26.COV2.S vaccine against severe COVID-19 overall and during the epidemic periods dominated by the beta and delta variant of concern (1).

(1) Bekker LG, Garrett N, Goga A, Fairall L, Reddy T, Yende-Zuma N, et al. Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke study): results from a single-arm, open-label, phase 3B, implementation study. Lancet. 2022;399(10330):1141-53.

- ### Case–control study to estimate odds of death within 28 days of positive test for SARS-CoV-2 prior to vaccination for residents of long-term care facilities in England, 2020–2021

Investigators from the UK Health Security Agency in England implemented a case-control study making use of linked demographic and mortality data for cases with confirmed SARS-CoV-2 infection between March 2020 and January 2021 in England. From these data they selected a random sample of 6000 persons who died and 36 000 who did not die within 28 days of a positive test. Based on an address-matching process, the residence type of each case was categorized into one of private home and residential or nursing long term care facility (LTCF). This study found that residents of LTCFs in England had higher odds of death up to 80 years of age. Beyond 80 years, there was no difference in the odds of death for LTCF residents compared with those in the wider community. Increasing age and male gender were also found to be the dominant risk factors for death. The model showed higher odds of death for those in the most deprived areas (IMD deciles 1–4) compared with those in least deprived areas.

- ### Case-control study evaluating risk factors for SARS-CoV-2 outbreak amongst healthcare personnel at a tertiary care center

Investigators in California conducted an outbreak investigation and case-control study to evaluate SARS-CoV-2 transmission risk in an outbreak among health care providers at an academic medical center in California that was confirmed by multiplex PCR and whole genome sequencing. A total of 7/9 cases and 93/182 controls completed a voluntary survey about risk factors. Compared to controls, cases reported significantly more patient contact time. Cases were also significantly more likely to have performed airway procedures on the index patient, particularly placing the patient on high flow nasal cannula, continuous positive airway pressure (CPAP), or bilevel positive airway pressure (BiPAP) (OR = 11.6; 95% CI = 1.7 -132.1). This study also reinforced the risk of SARS-CoV-2 transmission to health care providers due to delayed diagnosis of COVID-19 cases.

(1) Rosser JI, Tayyar R, Giardina R, Kolonoski P, Kenski D, Shen P, et al. Case-control study evaluating risk factors for SARS-CoV-2 outbreak amongst healthcare personnel at a tertiary care center. Am J Infect Control. 2021;49(12):1457-63.

- ## Leveraging SARI surveillance to monitor vaccine effectiveness in Kyrgyzstan and Ghana

For almost a decade, Kyrgyzstan has worked to improve sentinel surveillance of Influenza-like illness (ILI) and SARI to inform policy decisions related to influenza control in the country. Soon after the COVID-19 pandemic began, Kyrgyzstan integrated COVID-19 monitoring into its sentinel influenza surveillance system, as recommended by WHO. In December 2021, Kyrgyzstan began a project to leverage its SARI surveillance system to assess the vaccine effectiveness of COVID-19 and influenza vaccines. Continually assessing vaccine effectiveness is particularly important given the increased risks posed by emerging SARS-CoV-2 variants of concern and the uncertainties about how long vaccine protection lasts, among other things. This can also strengthen routine monitoring of influenza vaccine effectiveness, and data from this system contributes to pooled vaccine effectiveness assessments undertaken by the WHO Regional Office for Europe. Kyrgyzstan's success story is based on harnessing an existing SARI sentinel surveillance system and shows the benefits of ongoing capacity building within sentinel surveillance system to generate essential input to policy decisions related to influenza and now also COVID-19 disease control.

(1) Mirage News. Kyrgyzstan: leveraging SARI surveillance to monitor vaccine effectiveness 2022 [15/01/2023]. Available from: https://www.miragenews.com/kyrgyzstan-leveraging-sari-surveillance-to-792905/#:~:text=Kyrgyzstan%3A%20leveraging%20SARI%20surveillance%20to%20monitor%20vaccine%20effectiveness,the%20vaccine%20effectiveness%20of%20COVID-19%20and%20influenza%20vaccines (accessed 15 Feb 2023)

Leveraging the existing sentinel SARI surveillance system established by Noguchi Memorial Institute for Medical Research and Ghana Health Service in 2017, the Kintampo Health Research Centre and Ghana Health Service and collaborating partners in Ghana (University of Health and allied sciences, University of Ghana, Public health directorate, World Health Organization Country Office Ghana) designed and implemented a test-negative design VE study with recruitment starting in June 2022. Data is being collected from SARI patients from 18 sentinel sites in Ghana in order to estimate COVID-19 VE (overall and product-specific) against laboratory-confirmed SARS-CoV-2 patients requiring hospitalisation in target vaccination groups. Data has been successfully captured since June 2022, covering COVID-19 activity in June and July 2022 in Ghana. As part of a multi-pronged approach, significant progress has been achieved towards strengthening integrated respiratory disease surveillance, monitoring vaccine effectiveness, and regulatory capacities in Ghana. Systems for monitoring disease burden and VE are important to support the introduction of new products in the region and this study forms the basis as a sustainable platform for estimating VE against severe disease for COVID-19 and other respiratory viruses.

- Influenza and SARS-CoV-2 Incidence and Vaccine effectiveness of COVID-19 vaccines in Chile

In Chile, health care providers enter patient SARS-CoV-2 and influenza vaccination status when completing the lab requisition for reverse transcription–polymerase chain reaction respiratory virus RNA testing as part of routine clinical management. Patients vaccination status, molecular and sequencing laboratory results, and public and private hospitalization discharge diagnoses are all stored in encrypted nominal electronic databases which the Ministry of Health uses to monitor viral activity, vaccine coverage, and vaccine effectiveness as part of their efforts to optimize their programs mitigation efforts. Specifically, the Ministry determines the number of persons discharged from all hospitals with International Classification of Diseases, Tenth Revision (ICD-10) pneumonia and influenza (P&I) discharge diagnoses codes J09–18, and estimates the proportion attributable to SARS-CoV-2 or influenza. They make these estimates by assuming that a similar proportion of persons with P&I discharge diagnoses would have tested positive for these viruses as those of the same age group who tested positive for these viruses during the same epidemic week as part of routine clinical practice. This fraction of P&I hospitalizations attributable to SARS-CoV-2 or influenza is then divided by Chile's population to estimate the risk of hospitalizations with COVID-19 or influenza by age group. As part of the REVELAC/SARINET Network to estimate the effectiveness of COVID-19 vaccines through existing SARI sentinel surveillance networks for influenza and SARS-CoV-2, Chile uses a test-negative design. This estimates the effectiveness of current vaccine products and schedules by modelling the odds that a person partially or fully vaccinated with a specific combination of vaccines will be hospitalized and subsequently test positive for SARS-CoV-2 (1-3, 4) or influenza. As leaders in respiratory virus surveillance and vaccine effectiveness, the Chilean Ministry of Health shares all information about respiratory virus molecular and genetic test results, near real time, with PAHO and WHO through the SARINet and GISRS plus networks. Chile also shares estimates of the cumulative risk of SARS-CoV-2, influenza, and vaccine effectiveness periodically (e.g., mid- and end-of-influenza-season), as part their collaboration in PAHO REVELAC and their contribution to the GIVE report to guide influenza strain selection.

(1) Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, et al. Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. N Engl J Med. 2021;385(10):875-84

(2) Jara A, Undurraga EA, Zubizarreta JR, González C, Pizarro A, Acevedo J, et al. Effectiveness of homologous and heterologous booster doses for an inactivated SARS-CoV-2 vaccine: a large-scale prospective cohort study. The Lancet Glob Health. 2022;10(6):e798-e806.

(3) Jara A, Undurraga EA, Zubizarreta JR, González C, Acevedo J, Pizarro A, et al. Effectiveness of CoronaVac in children 3-5 years of age during the SARS-CoV-2 Omicron outbreak in Chile. Nature medicine. 2022;28(7):1377-80.

(4) Evaluación de la efectividad de la vacuna contra la COVID-19 en Chile, 2021 https://www.paho.org/es/node/86651 (accessed 15 Feb 2022)

- WHO Clinical platform for COVID-19 informs treatment practices, characterizes co-infection with HIV, and the impact of omicron variant on disease severity

To expand the understanding of clinical characteristics and prognostic factors among patients hospitalized with suspected or confirmed COVID-19, and to inform optimal clinical management and interventions, the World Health Organization (WHO) established the Global Clinical Platform (1). The platform is secure web-based database which collects individual-level, anonymized, clinical data of hospitalized patients with suspected or confirmed COVID-19 from health facilities across the globe. The WHO Global Clinical Platform is intended to provide Member States with a standardized clinical data collection system to characterize the natural history of COVID-19; identify risk factors for severe disease and poor outcomes; and describe treatment interventions and outcomes among adults, children, and subpopulations, including pregnant women and people living with HIV. Examples of its impact are the publication of two major reports and their respective findings. One report "Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 infection" showed that HIV appears to be a significant independent risk factor for severe or critical illness at hospital admission and in-hospital mortality (2). The second report demonstrated a lower risk of developing severe disease as well as a lower risk of mortality among patients infected with the Omicron variant as compared with the Delta variant (3).

Early in the COVID-19 pandemic, clinicians also questioned whether corticosteroids might be a useful treatment for COVID-19. Recognizing the urgency of getting reliable data on the efficacy of corticosteroids, the WHO developed a protocol for a prospective meta-analysis of seven ongoing randomized clinical trials. It was unprecedented in its size and collaborative effort. More than 1700 critically ill patients with COVID-19 were recruited from countries on five continents. Meeting attendees were regularly encouraged to contribute data. Pooling of unpublished data from the trials demonstrated that administration of corticosteroid therapy was associated with lower mortality in critically ill patients with COVID-19. Simultaneously, clinical guidelines for corticosteroid use were developed and published in parallel with peer-reviewed primary data. This was published by the WHO REACT (Rapid Evidence Appraisal for COVID-19 Therapeutics) working group in JAMA (4): and the first lifesaving intervention for COVID-19: corticosteroids published as WHO strong recommendation for severe or critical patients with COVID-19 as early as September 2022, V1 of the WHO Living guideline for COVID-19 and Therapeutics (5). This demonstrated the importance of collaboration between WHO and clinicians in a crisis, leading to shared unpublished data and the generation of a high-impact scientific analysis that was able to urgently inform international guidance on COVID-19 treatments.

(1) World Health Organization. The WHO Global Clinical Platform for COVID-19 2022 [15/10/2022]. Available from: https://www.who.int/teams/health-care-readiness/covid-19/data-platform (accessed 15 Feb 2022)
(2) World Health Organization. Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 infection 2021 [15/01/2023]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical-HIV-2021.1 (accessed 15 Feb 2022)
(3) World Health Organization. Severity of disease associated with Omicron variant as compared with Delta variant in hospitalized patients with suspected or confirmed SARS-CoV-2 infection 2022 [15/01/2023]. Available from: https://www.who.int/publications/i/item/9789240051829 (accessed 15 Feb 2022)
(4) Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, Angus DC, et al. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA. 2020;324(13):1330-41.
(5) World Health Organization. Therapeutics and COVID-19: living guideline 2022 [15/01/2023]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.4 (accessed 15 Feb 2022)

- ### Integration of Surveillance for Antiviral Resistance in health interventions in the United States of America

The emergence and spread of viruses with reduced susceptibility to antivirals can diminish the usefulness of drugs for controlling influenza infections during epidemics or future pandemics. This necessitates continuous monitoring of antiviral susceptibility among circulating viruses. Antiviral testing has become an integral part of influenza virologic surveillance conducted by laboratories of the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS). It is also monitored and supported by the WHO GISRS Expert Working Group on Antiviral Surveillance (AVWG).

In the United States of America, Centers for Disease Control and Prevention (CDC) continually improves its ability to rapidly detect influenza viruses with antiviral reduced susceptibility and antiviral resistance through improvements in laboratory methods; increasing the number of surveillance sites domestically; and increasing the number of laboratories that can test for viruses with reduced susceptibility to antivirals. Enhanced surveillance efforts have provided CDC with the capability to detect resistant viruses more quickly, and enabled CDC to monitor for changing trends over time. The capacity to do both genotypic and phenotypic testing helps identify new mutations consistent with antiviral resistance or reduced susceptibility to already licensed or new drugs. Genotypic testing alone has a shortfall of only identifying already known mutations but is not able to identify new mutations. Accordingly, both laboratory methods are essential for such work. Monitoring trends on the global level requires such integration by all countries.

Integration of such components into national virologic surveillance of respiratory viruses with epidemic or pandemic potential contributes to the global public health response to such threats.

(1) Govorkova EA, Takashita E, Daniels RS, Fujisaki S, Presser LD, Patel MC, et al. Global update on the susceptibilities of human influenza viruses to neuraminidase inhibitors and the cap-dependent endonuclease inhibitor baloxavir, 2018-2020. Antiviral research. 2022;200:105281.

CROSS-CUTTING

- ### Integrated Outbreak Analytics for contextualizing surveillance data

Contextual information may also be integrated into surveillance dashboards to further inform public health risk assessment and response measures. The Integrated Outbreak Analytics (IOA) network (1) has considered these issues in more detail and applies a multidisciplinary approach to understanding outbreak dynamics and to inform outbreak response (2). IOA aim to support effective public health and clinical strategies by enabling communities and national and subnational health authorities to use data for operational decision-making. Through this approach, coordinating surveillance authorities may map, leverage and integrate vertical surveillance systems and health information, interpret surveillance data, and promote the integration of multisectoral expertise (including sociocultural, political, economic, environmental, biomedical and epidemiological expertise) to support risk assessments and public health decisions.

(1) Integrated Outbreak Analytics. Geneva: World Health Organization; 2022 (https://integratedoutbreakanalytics.org (accessed 21 January 2023).
(2) Global Outbreak Alert and Response Network. Integrated Outbreak Analytics delivers holistic understanding of outbreak dynamics. Geneva: World Health Organization; 2022 (https://extranet.who.int/goarn/content/integrated-outbreak-analytics-delivers-holistic-understanding-outbreak-dynamics (accessed 21 January 2023).

- ## Estimating the effective reproductive number for SARS-CoV-2 variants using globally pooled sequencing data

Investigators evaluated 1,722,652 SARS-CoV-2 sequences uploaded to the Global Initiative On Sharing All Influenza Data (GISAID) hCoV-19 database from around the world to estimate the effective reproduction number (Rt) of variants of interest and variants of concern relative to the non-variant viral population. Similar patterns were exhibited across different countries, with new variants of concern rapidly becoming dominant. The increase in all-country pooled mean effective reproduction number ranged from 29% for B1.1.7 to 97% for B1.617.2. These estimates were used to predict that the B.1.617.2 variant was likely to outcompete others and become the dominant circulating virus. Although estimating Rt relies on several assumptions, the potential for using sequence data to understand transmissibility underscores the importance of ensuring that this data is geographically representative and shared in a timely manner. Estimates for the effective reproduction number are useful not only for comparing the transmissibility of variants but also for estimating pandemic trajectory and generating forecasts of future activity. For instance, the Epiforecasts tool (1) has shown that COVID-19 case and death notification data can be used to generate daily estimates of the reproduction number globally, regionally, nationally, and sub-nationally and to forecast future activity (1-3).

(1) Epiforecasts. Temporal variation in transmission during the COVID-19 outbreak 2023 [15/01/2023]. Available from: https://epiforecasts.io/covid/ (accessed 15 Feb 2022)
(2) Campbell F, Archer B, Laurenson-Schafer H, Jinnai Y, Konings F, Batra N, et al. Increased transmissibility and global spread of SARS-CoV-2 variants of concern as at June 2021. EuroSurveillance. 2021;26(24).
(3) Abbott S, Hellewell J, Thompson R, Sherratt K, Gibbs H, Bosse N, et al. Estimating the time-varying reproduction number of SARS-CoV-2 using national and subnational case counts [version 2; peer review: 1 approved, 1 approved with reservations]. Wellcome Open Research. 2020;5(112).

- ## Use of clinical networks to monitor 'long covid'.

As the COVID-19 pandemic progressed in early 2020, WHO Clinical Network meeting attendees began to report neurological problems in patients who had recovered from the disease. Fatigue was commonly reported globally, while members from Spain and the United States highlighted an increase in cases of depression, insomnia, and delirium in recovered patients. This kind of information was helpful for identifying future pathways of care and the potential longer-term health issues that may need specific treatments and guidelines. WHO responded with the development of recommendations for clinical care after acute illness as early as May 2020, included in the 2nd version of the "WHO Living guideline for clinical management and COVID-19" (1), followed by the development of the "WHO Clinical case definition" (2) and the "Clinical case record form on the Clinical Platform" (3). From these exchanges, WHO recommendations fitted the needs of the field because WHO staff had this interaction with clinicians who could tell us what was happening, and what they needed at those critical moments.

(1) World Health Organization. Clinical management of COVID-19: Living guideline, 23 June 2022 2022 [15/01/2023]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2022-1 (accessed 15 Feb 2022)
(2) World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021 2021 [15/01/2023]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1 (accessed 15 Feb 2022)
(3) World Health Organization. The WHO Global Clinical Platform for COVID-19 2022 [15/10/2022]. Available from: https://www.who.int/teams/health-care-readiness/covid-19/data-platform (accessed 15 Feb 2022)

- National and international data pooling to enable identification of risk factors for severe disease in the influenza A(H1N1)pdm09 and COVID-19 pandemics

During the 2009 influenza H1N1 pandemic, the World Health Organization (WHO) and its member states collected data to characterize the clinical severity of influenza A(H1N1)pdm09 infection and identify risk factors for severe disease. On behalf of the WHO Working Group for Risk Factors for Severe H1N1pdm Infection, pooled data from 19 countries and administrative regions was analyzed to assess the risk of hospitalization, ICU admission and death for different risk groups (1). The investigators compared the distribution of risk factors across 70,000 laboratory-confirmed hospitalized influenza A(H1N1)pdm09 patients, 9,700 patients admitted to intensive care units (ICUs), and 2,500 deaths. Hospitalization rates were highest in the youngest age groups, while the highest risk of death was observed for the oldest age groups and the death to hospitalization ratio increased with age. Pregnancy was also associated with increased rates of hospitalization and death, as well as the presence of one or more chronic condition, including obesity which had not previously been described as a risk factor for seasonal influenza.
During the COVID-19 pandemic, the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) WHO Clinical Characterization Protocol UK (CCP-UK) study was activated to investigate risk factors for in-hospital mortality for COVID-19 in 208 acute care hospitals in England, Wales, and Scotland (2). Increasing age, male sex, and chronic comorbidity were identified as risk factors early in the pandemic, demonstrating the value of having standard data collection protocols which can be activated quickly and implemented across countries during outbreaks and pandemics.

(1) Van Kerkhove MD, Vandemaele KA, Shinde V, Jaramillo-Gutierrez G, Koukounari A, Donnelly CA, et al. Risk factors for severe outcomes following 2009 influenza A (H1N1) infection: a global pooled analysis. PLoS medicine. 2011;8(7):e1001053.
(2) Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ (Clinical research ed). 2020;369:m1985.