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Short Article

The consortium for the standardization of influenza seroepidemiology (CONSISE): a global partnership to standardize influenza seroepidemiology and develop influenza investigation protocols to inform public health policy

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CONSISE – The consortium for the Standardization of Influenza Seroepidemiology – is a global partnership to develop influenza investigation protocols and standardize seroepidemiology to inform health policy. This international partnership was formed in 2011 and was created out of a need, identified during the 2009 H1N1 pandemic, for timely seroepidemiological data to better estimate pandemic virus infection severity and attack rates to inform policy decisions. CONSISE has developed into a consortium of two interactive working groups: epidemiology and laboratory, with a steering committee composed of individuals from several organizations. CONSISE has had two international meetings with more planned for 2013. We seek additional members from public health agencies, academic institutions and other interested parties.

Keywords Health policy, influenza, seroepidemiology, standardization.

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During the 2009 influenza A(H1N1) pandemic (H1N1pdm09), seroepidemiological studies were undertaken to quantify the prevalence of pre-existing antibodies to and cumulative incidence of the new virus in the population, the proportion of infections that were asymptomatic and to estimate rates of infections in specific populations to inform decisions by policy makers on risk groups and the use of mitigation measures[1]. The results of dozens of seroepidemiological studies have become available in the past 2 years.[1–3] However, the majority of studies were performed sub-nationally based on convenience sampling, and many of the results emerged too late to be useful in informing policy-related debates, issues and decisions, specifically those around understanding risk groups for vaccination and age-specific severity of the pandemic virus.[4–6] Additionally, despite many H1N1pdm09 seroepidemiological studies being undertaken, the direct comparability of results was limited due to a lack of standardization in the epidemiological data collected, and the laboratory methods used to assess the presence of cross-reactive antibodies to and cumulative incidence of the H1N1pdm09 virus. Furthermore, there were more general concerns over the difficulties in ensuring quality assurance for seroepidemiological studies in most laboratories.[3,7]

Recognizing these limitations, several institutions including the World Health Organization (WHO), Public Health Agency of Canada (PHAC), European Centre for Disease Prevention and Control (ECDC), US Centers for Disease Control and Prevention (USCDC), Imperial College London (ICL), National Institute for Biological Standards and Control (NIBSC), UK Health Protection Agency (UKHPA), University of Hong Kong (UHK), WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia (WHO CC Melbourne), and others formed

Table 1. CONSISE Protocols under development

Protocol		Primary objectives	Development based on*
Epidemic/pandemic influenza	Longitudinal cohort study of influenza infection during epidemic periods	Determine age-specific cumulative incidence of infection during an influenza epidemic	Longitudinal influenza seroepidemiological protocols from UK, Hong Kong, Singapore, FluScape in Guangzhou[11] and Vietnam[2]
	Cross-sectional seroprevalence study of influenza prior and post-epidemic periods	Determine age-specific cumulative incidence of infection with a novel influenza virus in the population Measure prevalence of cross-reactive antibodies to the novel virus	Numerous cross-sectional seroprevalence studies conducted during the H1N1pdm09 pandemic[2]
	Household transmission studies for pandemic influenza	Estimate household secondary infection risk, and factors associated with variation in the secondary infection risk Characterize secondary cases including clinical presentation and asymptomatic fraction Investigate serological response following confirmed influenza infection	FF100 protocols, household investigations conducted during the H1N1pdm09 pandemic from the UK, US, Hong Kong, South Africa and other countries
	Closed setting outbreak investigation protocol for pandemic influenza	Describe the clinical spectrum of infection including the asymptomatic fraction Estimate overall clinical attack rates (by subgroup and clinical risk group) Describe correlation between infection, disease and serology	Numerous outbreak investigations conducted during the H1N1pdm09 pandemic
Seasonal influenza	Seroepidemiology of human influenza infection using residual sera/convenience samples for establishing baselines and/or monitoring trends over time	Estimate population immune status/susceptibility to relevant influenza viruses Estimate incidence in previous seasons for the different relevant influenza viruses	Protocols from Norway, UK and others
Zoonotic influenza	Outbreak investigation of zoonotic infection in humans exposed to a confirmed source	Measure age-specific infection in relation to zoonotic exposure Identify (modifiable) risk factors for human infection	Zoonotic source outbreak investigations from the Netherlands, China, Cambodia, Thailand and Bangladesh

*This is not an exhaustive list but meant to provide examples of existing and validated protocols used to generate draft detailed generic protocols.

a partnership to develop best practices and standardize seasonal, pandemic and zoonotic influenza seroepidemiological methods. This partnership, now called CONSISE – the Consortium for the Standardization of Influenza Seroepidemiology – (Figure 1) held its first international meeting in Ottawa in January 2011 organized by PHAC.[8]

The participants of the Ottawa meeting decided on a number of areas for improvement in conducting seroepidemiological studies including study design, prior laboratory and methodological standardization and laboratory quality assurance for serological assays.[8] A second international meeting was held in Stockholm in December 2011 hosted by ECDC.[9] Institutions including the WHO, ECDC, ICL, NIBSC, UKHPA, USCDC, UHK and WHOCC Melbourne played and are continuing to play key roles in the development of the work plan of CONSISE.

At the second international meeting in Stockholm, it was appreciated that considerable work needed to be undertaken to expand the scope of the work to encompass the development of protocols that will cover multiple objectives and functions around influenza and emerging respiratory infections. These objectives are being captured in the development of six generic seroepidemiological protocols for pandemic and epidemic influenza, seasonal influenza and

Table 2. CONSISE Laboratory working group work plan

Topic		Primary objectives	Development based on
Standardization	Haemagglutination inhibition assay†	Based on current knowledge and current best practice, continue to use HI as the primary serology test.	[7]
	Microneutralization assay	Agreement on a standard protocol for microneutralization assay protocols (2-day ELISA endpoint assay (GISRS protocol[12]) and 3-day HA endpoint assay)	[12] and individual laboratory protocols
	Neuraminidase inhibition assay	Establish standard neuraminidase inhibition assay in some of the consortium laboratories	Protocols of Maryna Eichelberger (CBER/FDA)[13,14]
	International serology standards	To discuss the need for development of further influenza international standards for HI assay and to encourage the wider use of the existing standards.	[7]
Quality assessment	Exploration of possibilities for external quality assessment for laboratories performing serological assays for influenza	To explore possibilities for an external quality assessment scheme for serological assays	NA
Cooperation	Laboratory network	To form a laboratory network to actively participate in the standardization work	NA
	Cooperation with those undertaking influenza serology work for regulatory purposes and for evaluation of the response to vaccines	To collaborate with and inform the international actors involved in the regulatory and development work of influenza vaccines about the recommendations of this laboratory working group	NA

NA, not applicable.
†It was concluded at the Stockholm meeting to keep the widely used haemagglutination inhibition assay as the primary serology test in the laboratories.

Figure 1. Logo of CONSISE.

zoonotic influenza (Table 1)[10]. Although generic, these protocols are being designed to be part of a comprehensive approach to include as much useful detail as possible, so that specific protocols for high-quality comparable studies can be produced with the fewest possible modifications. The six CONSISE protocols are based on existing influenza seroepidemiogical protocols, which have been used throughout the world (see Table 1). During both international meetings, it was appreciated that much joint work – both epidemiological and laboratory – is required in the areas of standardization, external quality assurance and cooperation to build on previous work in these areas to improve the quality of serological testing (Table 2).

Under the leadership of an informal steering committee (see acknowledgements), the partnership has organized into laboratory and epidemiological working groups (Tables 1 and 2 outline current activities). The CONSISE steering committee consists of individuals from collaborating institutions in the consortium representing both laboratory and epidemiological influenza expertise and experience. The primary role of the steering committee is to ensure that the agreed work plan is enacted, specifically developing the protocols, undertaking laboratory work and preparing for the Options VIII conference in 2013. Core members of the steering committee are the conveners (EB and AN) together with the leaders of the protocol (MVK) and laboratory development (JW and OGE) aspects. ECDC will serve as the secretariat until the time of the Options VIII meeting in September 2013. There are numerous research institutions

participating as members of the epidemiology and laboratory working groups, and the partnership is growing. Having set out many of the problems and offered some solutions in the first publication,[8] CONSISE has continued meeting via teleconferences and small focused face-to-face meetings. The next checkpoint will be a regional international meeting in Hong Kong in January 2013 with the presentation of the draft protocols from the epidemiological working group and results from the work plan of the laboratory working group. A 4th international meeting of CONSISE is being planned for the Options VIII Conference in September 2013 in Cape Town, South Africa.

Prior to the Options VIII conference, the protocols will undergo extensive revision and iteration with input from our many partners. We plan, at around the time of Options VIII, for the protocols to be made public in a draft format for open discussion, iteration and hopefully adoption with the wider scientific and public health community, with the intention to validate the protocols for seasonal and zoonotic influenza investigations prior to their use in a pandemic or the emergence of respiratory pathogens or emerging zoonoses. The CONSISE partnership welcomes interest in the partnership and comments on the protocols when available.

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