



CONSISE

CONSORTIUM FOR THE STANDARDIZATION
OF INFLUENZA SEROEPIDEMIOLOGY



CONSIDE

CONSORTIUM FOR THE STANDARDIZATION
OF INFLUENZA SEROEPIDEMIOLOGY

CONSIDE Activities Overview and Update:

Epidemiology Working Group

Maria D Van Kerkhove, PhD

CONSIDE International Meeting

Cape Town, South Africa, 3-4 September 2013

Aims of CONWISE's Epi Working Group

- **Overall aims**

- Working together with laboratory working group: Recommend best practices and standardize influenza seroepidemiology studies for pandemic, epidemic, zoonotic influenzas and emerging respiratory viruses
- Provide support to countries who wish to carry out seroepidemiology studies for, primarily flu, but also other emerging respiratory pathogens
 - Tools: protocol templates & questionnaires
 - Recommendations on which study to conduct when
 - Guidance on adaptation of tools to meet specific objectives and contexts
 - Guidance and support of implementation of study
 - Coordination of lab support if capacity does not exist in country
 - Analysis and writing up of findings



Just some of the organizations represented within CONSISE's Epidemiology Working Group

Imperial College
London

MRC
Centre for
Outbreak Analysis
and Modelling



Public Health
Agency of Canada



Rijksinstituut voor Volksgezondheid
en Milieu
Ministerie van Volksgezondheid,
Werk en Zorg



中国疾病预防控制中心
CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION



ROBERT KOCH INSTITUT



VIDRL
Victorian Infectious Diseases
Reference Laboratory



Institut national
de la santé et de la recherche médicale

Achievements to date

Shared Protocols and Questionnaires

- **Protocols have been shared by numerous CONSISE members for pandemic, seasonal flu, zoonotic flu and other respiratory viruses**
- **Countries/Institutions providing protocols/questionnaires**
 - WHO, USA, UK, China, Hong Kong, South Africa, the Netherlands, Singapore, Bangladesh, Cambodia, Canada, France, Norway
- **Study designs**
 - FF100-type (PHE, NICD)
 - Outbreak investigations (H5, H7, H1) (the Netherlands, US, Cambodia, Bangladesh, China, Vietnam)
 - Longitudinal Studies (UHK, PHAC, USCDC, Vietnam, Singapore)
 - Cross-sectional serial studies (UHK, PHAC, USCDC, many others)

CONSISE protocol templates

- **Influenza Protocol Working Drafts**
 - Prospective Longitudinal Cohort for Pandemic Influenza
 - Lead: Steven Riley
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 - Leads: Maria Van Kerkhove/Marianne van der Sande
 - Assessment of Health Care Workers
 - Leads: Tony Mounts/Maria Van Kerkhove



Questionnaires

- **Original Aim: To provide questionnaire specific for each protocol**
- **Initial vs. Revised plan**
 - NOW: we have developed a question bank that holds a collection of questions that can be used for surveys in conjunction with serological studies involving respiratory infections
 - Questions are not meant to be exhaustive but should form the critical backbone of any survey instrument
- **Work in progress (*presentation later by Vernon Lee*)**
 - First, will share list of questions with CONSIZE members
 - Then, recommendations need to be made for what questions included for each study
 - Create online interface at consise.tghn.org for users to develop questionnaires



CONSISE in action





Identification of Novel Influenza Virus

Modification of existing materials

CONWISE steering committee to modify CONWISE protocols based on existing knowledge of novel virus

Epidemiology Working Group

Provide recommendations on use of protocols based on research/public health research question

Modification of data sampling and collection methodologies to fit understanding of outbreak; upload information to portal

Generation of data collection form; upload information to portal

Laboratory Working Group

Assess suitability of lab containment for novel virus – upload information

Obtain novel virus; assess suitability of assay methods and work-up assays – upload information

Trouble-shooting on assays using novel virus – forum on global health network CONWISE portal

Assess need for a new antibody standard

Follow pathway for antibody standard development

Antibody standard available; upload information

Liaise with existing groups (e.g., WHO/ISIARC); feed in laboratory methods developed for novel virus; link research institutions without lab capacity with supporting labs in network

Upload revised materials to CONWISE portal
Provide CONWISE contacts for support

CONSIDE's involvement with H7N9

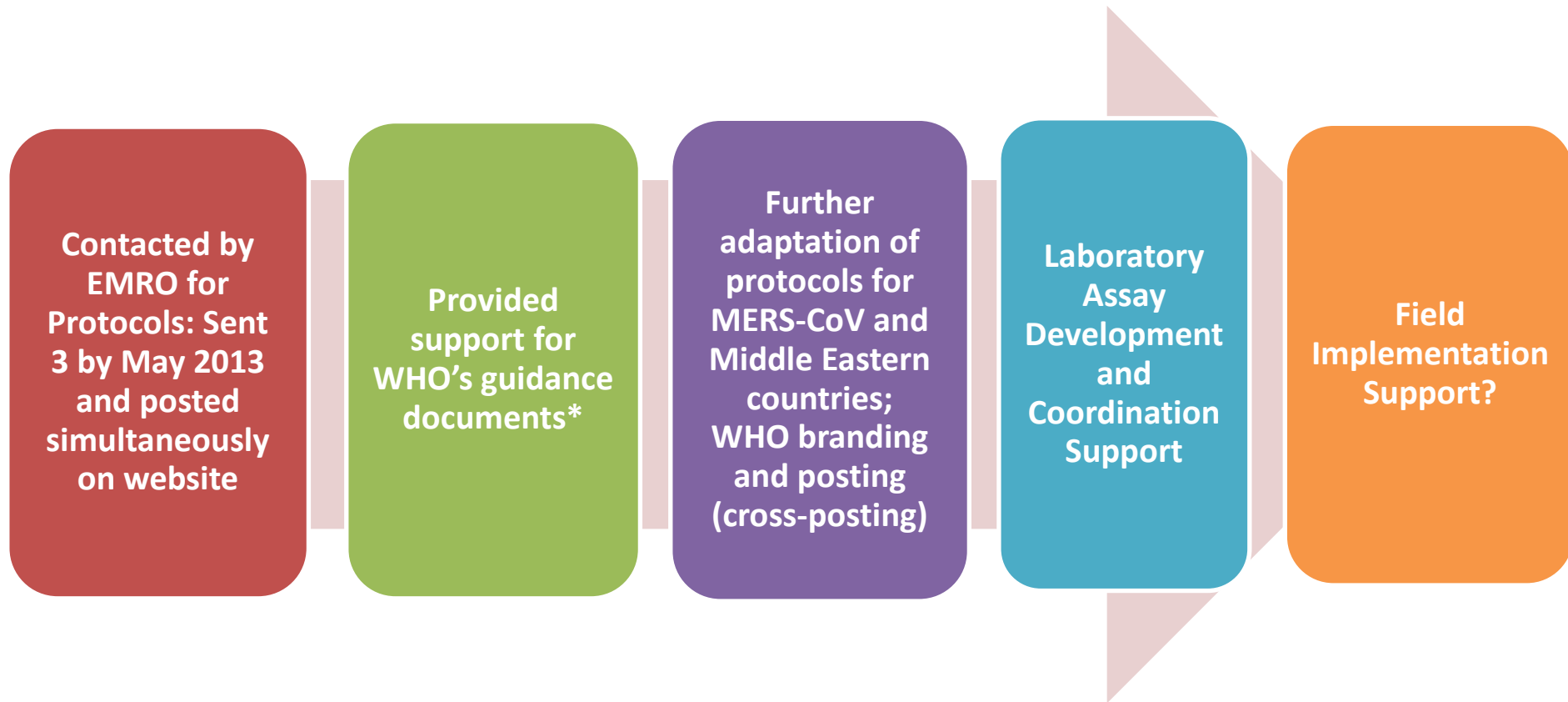
CONSIDE TC in May 2013
to discuss support of
serologic assay
development and study
protocols

Led to posting of H7N9
HI/MN assay protocols
from China CDC on
WHO/CONSIDE website
Modification, sharing
and posting of Epi
protocols on CONSIDE
website

Further CONSIDE TC in
July 2013 led to posting
of CDC H7N9 modified HI
assay protocol on
CONSIDE website



CONSISE's involvement with MERS-CoV



*WHO guidelines for investigation of cases of human infection with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (July 2013)



Adaptation of CONWISE protocol templates

- **Influenza A(H7N9)** <http://consise.tghn.org/articles/consise-and-avian-influenza-h7n9/>
 - Cross sectional seroprevalence study
 - Prospective longitudinal cohort study Household transmission studies for pandemic influenza
 - Assessment of Health Care Personnel
 - Investigation of Zoonotic Influenza Infection in Humans
- **MERS-CoV** <http://consise.tghn.org/articles/novel-coronavirus-ncov/>
 - Seroepidemiological Investigation of Contacts of MERS-CoV Patients
 - Cross-sectional seroprevalence study of MERS-CoV infection
 - Case-control study to assess potential risk factors of infection and transmission of MERS-CoV in a health care setting
 - Case-control study to assess potential risk factors related to human illness caused by MERS-CoV



Challenges and opportunities

- **Rapidly responding to fully unknown threat**
 - Unknown source
 - Unknown routes of transmission
- **Getting a “seat” at the table**
- **Setting priorities**
- **Reaching consensus**
 - Is this achievable? Is this necessary?
- **Approval to release documents/open access**
 - Sensitive and tricky
- **Interest and implementation**
 - Biggest hurdle



Website development

- Launched mid-March 2013 on the Global Health network www.tghn.org
- Funded by Imperial College
- Collection of individual websites connected on a shared digital hub
- Built in links with other existing networks “amazonification”
- Quickly generated to provide open access to tools for H7N9 and MERS-CoV
- Will utilize more in the future



Global Health Network

About This Site Contact Us Newsletters Home Register

Select Language Powered by Google Translate

The Global Health Network is a collection of websites that are aiming to support research by sharing knowledge and methods. Each has been established to create a subject specific online community of researchers who can build collaborations, develop documents, share resources and exchange information.

[find out more](#)

The Network

This collection of websites cover varied topics in Global Health and disseminating free content around the world. Click any site to access.



The diagram shows a central yellow circle labeled 'GLOBAL HEALTH NETWORK' connected to several other circles representing different research areas: MICROBIOLOGY, EPIDEMIOLOGY, ENTERICS, DIAGNOSTICS RESEARCH, BIOETHICS, CANCER, MOTHER CHILD LINK, NON-COMMUNICABLE DISEASES, DENGUE RESEARCH, TDRF, CLINICAL TRIALS, REVIEWING RESEARCH, EPIDEMIC RESEARCH, and NEURO INFECTIONS. Each circle is accompanied by a small thumbnail image of a website.

Tweets

GlobalHealthNetwork @Info_TGHN
#PLOSmedicine: Better Reporting of Scientific Studies: Why It Matters
dx.plos.org/10.1371/journal.pmed.1001371
#tghn tghn.org

GlobalHealthNetwork @Info_TGHN
#PLOSmedicine: Reproductive and Maternal Health in the Post-2015 Era: Cervical Cancer Must Be a Priority
dx.plos.org/10.1371/journal.pmed.1001371

GlobalHealthNetwork @Info_TGHN
#PLOSmedicine: Pediatric AIDS in the Elimination Agenda
dx.plos.org/10.1371/journal.pmed.1001371

Tweet to @Info_TGHN

www.consize.tghn.org





The Consortium for the Standardization of Influenza Seroepidemiology (CONSISE) is a global partnership aiming to standardize influenza seroepidemiology and develop comprehensive influenza investigation protocols to inform public health policy.



LATEST MEMBERS



[Anton](#)

Aug. 22, 2013



[Mario Tristán](#)

Aug. 22, 2013



[wallynso](#)

Aug. 22, 2013



[Anwar M Hashem](#)

Aug. 16, 2013

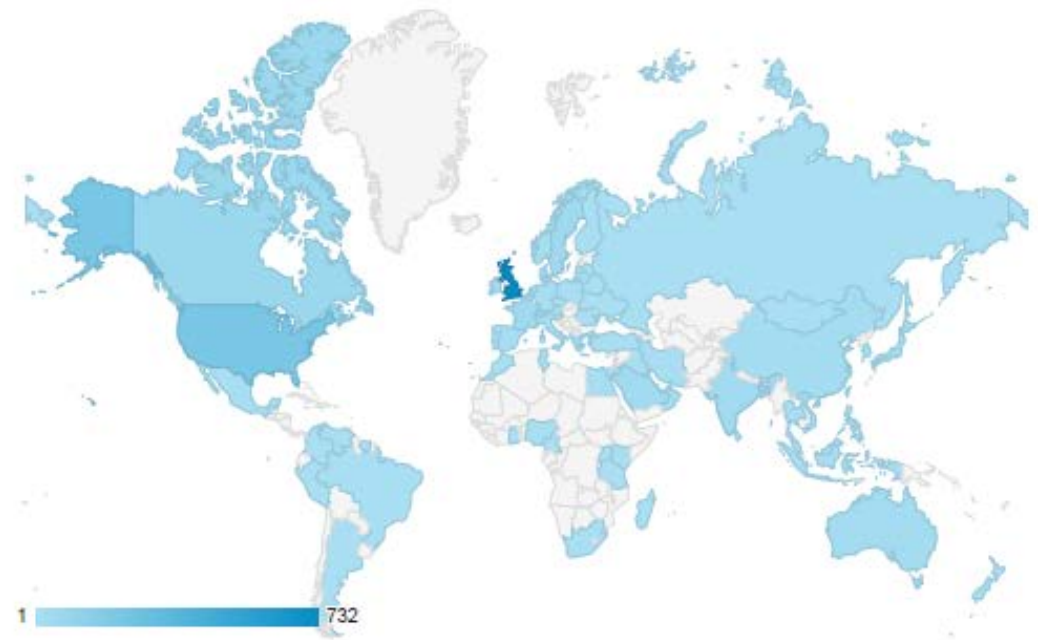


[Hilarious de Jesus](#)

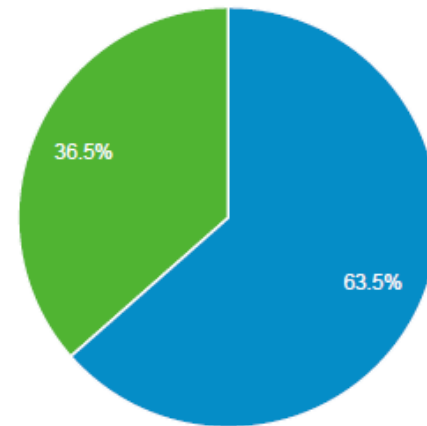
Aug. 15, 2013

Website analytics

- Between 1 April-27 August 13
 - 600 unique visitors to the site
 - >1600 visits from unique IP addresses from 80 countries*
 - 6,435 page views
 - 00:04:36 average visit duration
 - 3.99 pages/visit
 - 58.5% bounce rate
 - Users translated pages into 9 languages
- Fantastic cross-links with other networks
- Functionality is a work in progress



■ Returning Visitor ■ New Visitor



*including UK US, Switzerland, Canada, Sweden, France, India, Saudi Arabia, Australia, China, Netherlands, Italy, Hong Kong, Vietnam, UAE Belgium, South Korea, Egypt, Ireland Norway, Japan Singapore, Spain, Oman Philippines, Bahrain, Germany, Indonesia, Iran, Denmark, Malaysia, Taiwan, Mexico, Brazil, Greece, Poland, Thailand, Austria, Bangladesh, Portugal, Romania, Russia, Turkey, Argentina, Cameroon, Jordan, Kuwait, Lebanon, Mauritius, New Zealand +30 others with 1 hit

Raising the awareness for CONSISE

- **Website and postings**
- **Newsletters, peer-reviewed publications and book chapters**
- **Meetings – posters & presentations**
 - ECDC/EURO Flu meetings; ISIRV meetings; Asia-Pacific Alliance for the Control of Influenza (APACI); Options VIII (Several posters)
 - Innovative Medicines Initiative funding call
 - WHO Surveillance meetings
- **Recommendations/Guidance**
 - WHO guidelines for investigation of cases of human infection with Middle East Respiratory Syndrome Coronavirus (MERS-CoV)*
- **Links with other networks**



*http://www.who.int/csr/disease/coronavirus_infections/MERS_CoV_investigation_guideline_Jul13.pdf

Links with other networks and organizations

- **WHO and GISRIS**
 - Presentations by Tony Mounts/Wenqing Zhang
- **ISARIC**
 - Presentations by Peter Horby
- **TGHN**
- **Institutions/consortiums represented by our members**
- **Networks established for events**
 - MERS-CoV
 - H7N9
 - ??
- **Need to discuss how best to collaborate**



Plan for Cape Town Meeting

- **Status update on protocol templates**
 - Where are in development, review, and validation
 - Progress of the question bank for protocols and discussion of development of online interface for users
 - Recommendations on which to use when
- **Lessons learned thus far from CONWISE's involvement in recent epidemics**
 - MERS-CoV
 - H7N9
- **How have we or can/should we link with other existing networks?**
 - ISARIC/GISRIS/Other
- **Validation of protocols**
 - Experience from the field
 - Future plans to use protocols



Expected outcomes of meeting

- **Plan for field validation**
 - Which protocols can we implement where
- **Consensus statements**
 - Criteria for Seropositivity: Standardization for avian influenza (H5N1)
 - Recommendations on which studies are needed when (possibly in collaboration with ISARIC)
 - Planned web updates
- **Continue to raise the profile of CONSIZE**
- **Future Planning**
 - Fund raising
 - Website feedback and communication with members
 - Coordination and communication with outside networks
 - Identification of new secretariat



Thank you for your interest and active participation

Angus Nicoll, Ben Cowling, Richard Pebody, Steven Riley, Tony Mounts, Marianne van der Sande, Vernon Lee, Peter Horby, Heath Kelly, Tim Uyeki and others in the epi working group

John Wood, Othmar Engelhardt and Eeva Broberg

AFHSC, ECDC and Imperial

Neil Ferguson

Lynne Prior and Integress



Session Headings



Epidemiology Working Group Session:

PROTOCOL DEVELOPMENT



CONSISE protocol templates

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Protocols fully drafted and reviewed

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- **Ready to be shared**
 - Assessment of Health Care Workers
 - Leads: Tony Mounts/Maria Van Kerkhove



Protocols still under development

- **Influenza Protocol Working Drafts**
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 - Closed Setting Transmission study
 - Leads: Peter White/Vernon Lee
 - Routine/Residual Sera
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Discussion Points

- **Sharing and open access**

- CONSISE has adopted the Creative Common License

LICENSE

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- **Revision – how do we reach consensus?**

- Is it possible and do we want to aim for consensus?
- If not, how do we finalize to post?

- **For discussion – what is the best way to provide these templates?**

- Post templates online for users to download and modify
- Post outlines and suggest CONSISE members help draft?



Epidemiology Working Group Session:

QUESTION BANK



Epidemiology Working Group Session:

FIELD VALIDATION – EXPERIENCE FROM THE FIELD



Epidemiology Working Group Session:

**FIELD VALIDATION – ADAPTATION OF
GENERIC PROTOCOLS FOR FLU/MERS-COV**



Examples

- **China**
- **South Africa**
- **Mongolia**
- **Others?**



Epidemiology Working Group Session:

SIMULATION STUDIES



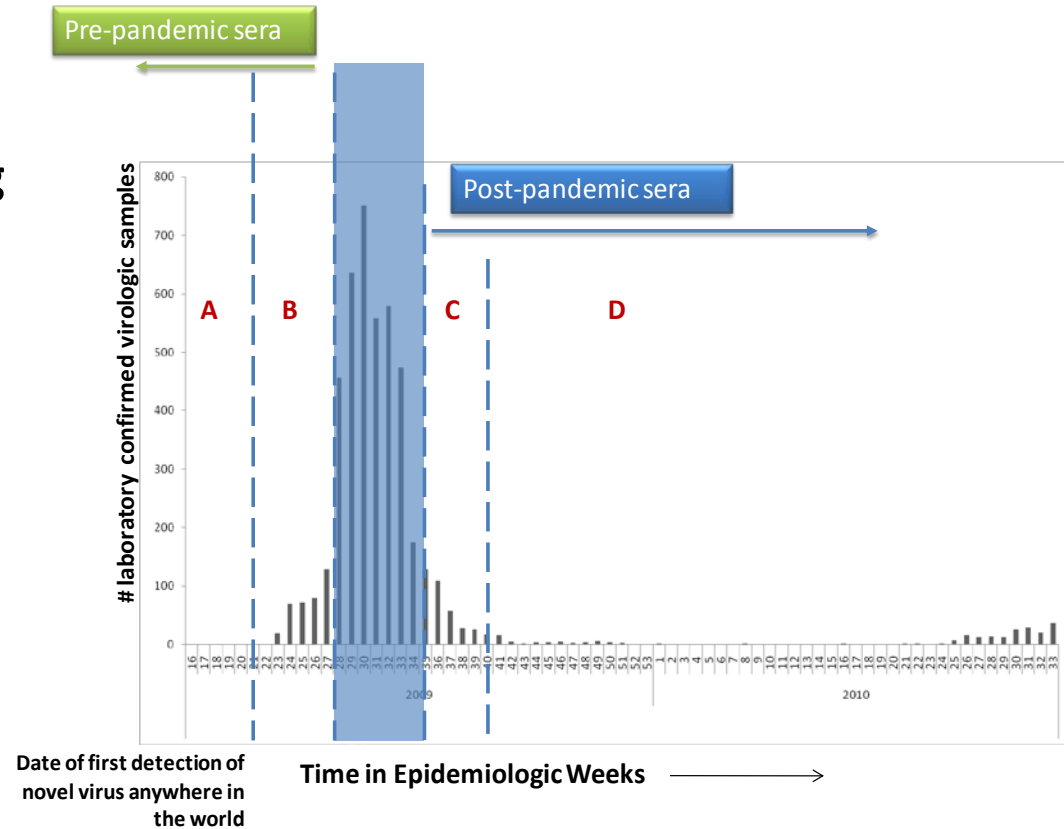
Epidemiology Working Group Session:

TIMELINE OF PROTOCOL RECOMMENDATIONS DURING AN OUTBREAK



Background

- Each Protocol has specific objectives and an ideal timing to be implemented with respect to an epidemic
 - Will be virus specific
 - Will be context specific
 - Feasibility
- Recommendations needed
 - Timing vs public health question or both
- Links with ISARIC



Timing is critical

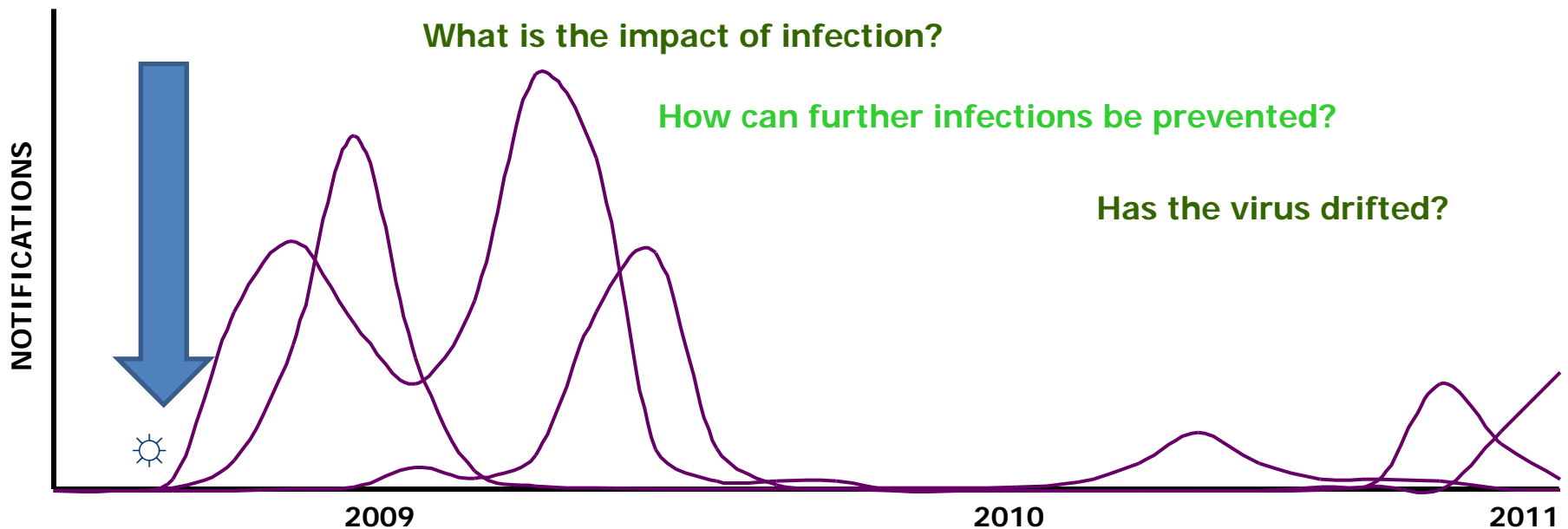
- During a pandemic/severe epidemic, the availability of data will not match the information needs of policy makers, meaning key decisions will be made using limited data

What are the features of the infection?

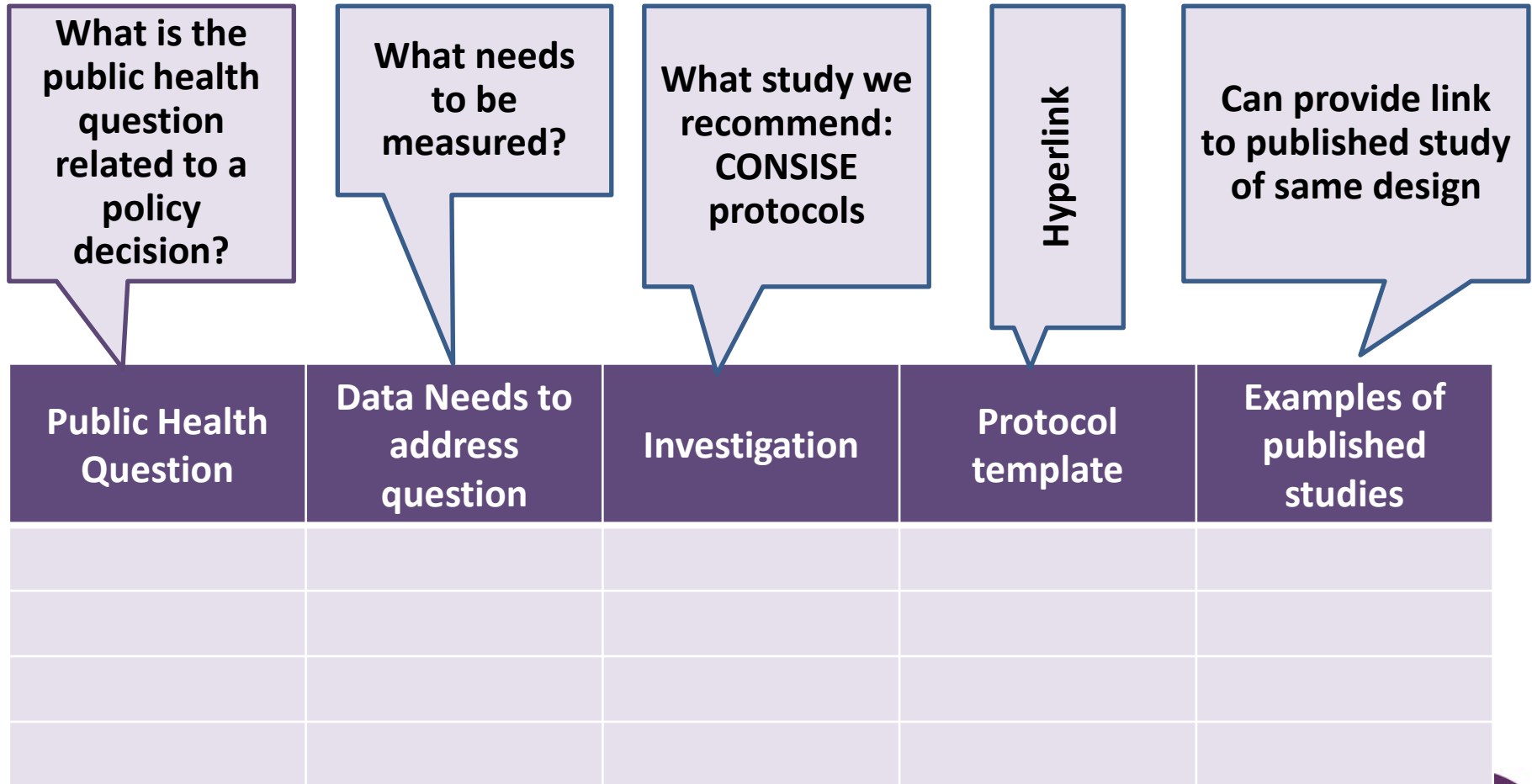
What is the impact of infection?

How can further infections be prevented?

Has the virus drifted?



How do we illustrate our recommendations?



But does not address recommendation on WHEN study should be conducted



Research Question	Study Design				
	Longitudinal Study	Serial cross-sectional study	Transmission studies		
			Households	Schools	Others*
What is the age-specific prevalence of cross-reactive antibodies?	x (pre-pandemic sera)	x (pre-pandemic sera)	somewhat	no	
What is the age-specific cumulative incidence?	x (ideal - est from paired sera)	x (good, est by taking difference in pre and post sero+)	yes (but in limited numbers)	somewhat	
What is the age-specific infection severity (e.g., IFR, infection: hospitalization)	x (if can match population with severe cases)	x (more difficult)	x (quick, not necessarily adequate sample size, but informative)	x (potentially useful but limited to school age children)	
What proportion of cases are asymptomatic?	very difficult	very difficult	x (ideal study methodology)	x (potentially useful but limited to school age children)	

*will depend on epidemiology of new virus and country settings

This table was based on a 2009-like virus; but could and should be developed for a more severe scenario

Solution?



Epidemiology Working Group Session:

ETHICAL PRE-APPROVAL



Ideas

- **Support users to obtain pre-ethical approval?**
- **Work with ISARIC and their methods for pre-ethical approval?**
- **WHO ethical approval for templates?**

