CONSISE
CONSORTIUM FOR THE STANDARDIZATION
OF INFLUENZA SEROEPIDEMIOLOGY
CONSISE Activities Overview and Update:

*Epidemiology Working Group*

Maria D Van Kerkhove, PhD

CONSISE International Meeting
Cape Town, South Africa, 3-4 September 2013
Aims of CONSISE’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
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
  – Serial Cross-sectional Seroepidemiological Investigation
    • Leads: Tony Mounts/Maria Van Kerkhove/Heath Kelly
  – Household Transmission Study
    • Leads: Ben Cowling/Richard Pebody
  – Closed Setting Transmission study
    • Leads: Peter White/Vernon Lee
  – Routine/Residual Sera
    • Leads: Angus Nicoll/Olav Hungnes/Richard Pebody/Katja Hoschler
  – Close Contact Serologic Investigation for Zoonotic influenza
    • 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 CONSISE 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
Identification of Novel Influenza Virus

Modification of existing materials
CONSISE steering committee to modify CONSISE 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
- 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

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 CONSISE portal
- Assess need for a new antibody standard
- Follow pathway for antibody standard development
- Antibody standard available; upload information

Upload revised materials to CONSISE portal
Provide CONSISE contacts for support
CONSISE’s involvement with H7N9

CONSISE 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/CONSISE website

Modification, sharing and posting of Epi protocols on CONSISE website

Further CONSISE TC in July 2013 led to posting of CDC H7N9 modified HI assay protocol on CONSISE website
CONSISE’s involvement with MERS-CoV

- Contacted by EMRO for Protocols: Sent 3 by May 2013 and posted simultaneously on website
- Provided support for WHO’s guidance documents*
- Further adaptation of protocols for MERS-CoV and Middle Eastern countries; WHO branding and posting (cross-posting)
- Laboratory Assay Development and Coordination Support
- Field Implementation Support?

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

  - 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

  - 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

www.consise.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.
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

*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

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 CONSISE’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 CONSISE**

• **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

www.consise.tghn.org
Session Headings
Epidemiology Working Group Session:

PROTOCOL DEVELOPMENT
CONSISE protocol templates

• Influenza Protocol Working Drafts
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  – Close Contact Serologic Investigation for Zoonotic influenza
    • Leads: Maria Van Kerkhove/Marianne van der Sande
  – Assessment of Health Care Workers
    • Leads: Tony Mounts/Maria Van Kerkhove
Protocols fully drafted and reviewed

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  - Close Contact Serologic Investigation for Zoonotic influenza
    • Leads: Maria Van Kerkhove/Marianne van der Sande

- Ready to be shared
  - Assessment of Health Care Workers
    • Leads: Tony Mounts/Maria Van Kerkhove
Protocols still under development

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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
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 is the impact of infection?

What are the features of the infection?

How can further infections be prevented?

Has the virus drifted?

NOTIFICATIONS

☼
How do we illustrate our recommendations?

<table>
<thead>
<tr>
<th>Public Health Question</th>
<th>Data Needs to address question</th>
<th>Investigation</th>
<th>Protocol template</th>
<th>Examples of published studies</th>
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</table>

But does not address recommendation on WHEN study should be conducted
### Table: Study Design

<table>
<thead>
<tr>
<th>Research Question</th>
<th>Longitudinal Study</th>
<th>Serial cross-sectional study</th>
<th>Transmission studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is the age-specific prevalence of cross-reactive antibodies?</strong></td>
<td>x (pre-pandemic sera)</td>
<td>x (pre-pandemic sera)</td>
<td>somewhat</td>
</tr>
<tr>
<td><strong>What is the age-specific cumulative incidence?</strong></td>
<td>x (ideal - est from paired sera)</td>
<td>x (good, est by taking difference in pre and post sero+)</td>
<td>yes (but in limited numbers)</td>
</tr>
<tr>
<td><strong>What is the age-specific infection severity (e.g., IFR, infection: hospitalization)</strong></td>
<td>x (if can match population with severe cases)</td>
<td>x (more difficult)</td>
<td>x (quick, not necessarily adequate sample size, but informative)</td>
</tr>
<tr>
<td><strong>What proportion of cases are asymptomatic?</strong></td>
<td>very difficult</td>
<td>very difficult</td>
<td>x (ideal study methodology)</td>
</tr>
</tbody>
</table>

*will depend on epidemiology of new virus and country settings

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