Serum biobanking for serosurveillance of emerging infectious diseases

Kylie Carville and Miranda Smith
The Doherty Institute for Infection and Immunity

15 08 2017

A joint venture between The University of Melbourne and The Royal Melbourne Hospital

Introduction to serosurveillance

- Less biased than other forms of surveillance that are limited by underreporting and under-ascertainment and do not measure asymptomatic infection[1]
- Gold standard: prospective population-based sampling
  - Detailed epidemiological data, oversampling
  - Costly, decreasing response rates
- Residual sera (retrospective) or blood bank samples (retrospective or prospective)
  - Convenient, much less costly, potential for prospective blood bank collection
  - Limited epi data, challenges accessing at-risk populations, representativeness of blood donors (healthy donors)
- Global efforts to standardise methodologies (CONCISE[2]) - benchmarking

[1]Gibbons et al BMC Public Health 2014;[2]Horby Influenza Other Respir Viruses 2017

Scoping exercise

- **Rapid literature review**
- **Consulted experts**
  - Kristine Macartney (NCIRS)
  - Frank Beard (NCIRS)
  - Peter McIntyre (NCIRS)
  - David Irving (Red Cross Blood Bank)
  - Helen Faddy (Red Cross Blood Bank)
  - Kanta Subbarao (WHO Collaborating Centre for Reference and Research on Influenza)
  - Ian Barr (WHO Collaborating Centre for Reference and Research on Influenza)
  - Jodie McVernon (Doherty Institute)
  - Dominic Dwyer (Pathology West - ICPMR Westmead)
  - Linda Hueston (Pathology West - ICPMR Westmead)
  - Ezra Linley (Public Health England)

International approaches

- Prospective population-based serosurveys
  - Dutch national serum bank
  - US CDC for influenza
- Residual sera
  - European Sero-Epidemiology Network (1996-2005)
  - The US Department of Defence Serum Repository
  - Public Health England (PHE) collect sera from laboratories on an ongoing basis (ethics)
- Biobanks
  - Can have a range of specimen types, may be purposive or house specimens from individual studies, generally have some epidemiological information

Existing Australian systems

- Focused on enhancing current resources, given existing infrastructure, as opposed to establishment of a new national mechanism
- Vaccine Preventable Diseases (VPDs) serosurveillance system (NCIRS/ICPMR)
  - Objectives relate to estimating immunity to VPDs
  - Population representative
  - Residual sera: ICPMR staff travel to diagnostic laboratories, identify samples, collect as large as possible volumes of sera, aliquot and package specimens and send to ICPMR for storage until testing.
- Australian Red Cross Blood Service (ARCBS)
  - Store residual plasma from screening samples for 3 years post collection
  - Also conduct purposive sampling of (healthy) donors

Key gaps in utilising existing systems for EIDs 1

	VPD serosurveillance program	Red Cross Blood Service	Key gaps
Validity of use	Nationally representative sample (each age group and gender sampled proportionally to population size). This means some jurisdictions are relatively under-represented. Sera are obtained from hospital and community-based laboratories, which should improve external study validity relative to hospital specimens only.	Not representative. Healthy donors 16-70 years only, no pregnant women, exclusions related to specific diseases, travel history, sexual activity. Plasma.	Under-represented jurisdictions: serosurveillance program could be expanded to obtain specimens sufficient for regional studies (subject to funding). Paediatric samples are scarce from laboratories in certain age groups e.g. infants and adolescents. Collection could be expanded. Not available through blood bank. No oversampling of key populations e.g. pregnant women, Aboriginal and Torres Strait Islander people, people working at the animal/human interface. No epi/risk factor/comorbidity/ vaccination info for residual sera, limited for residual plasma from blood bank.

Key gaps in utilising existing systems for EIDs 2

	VPD serosurveillance program	Red Cross Blood Service	Key gaps
High risk populations	Unlikely as sample collection is currently based on nationally representative and subgroups may not be able to be identified (have only age, gender and location data) and sample sizes would be small.	Unlikely as specimens from healthy donors	May depend on the context and who is at high risk, but in general not covered. Capacity may exist to access residual sera for some populations (subject to funding). Collection of residual sera can be structured to maximize representation of all age groups.
Lookback potential	As primary objective is VPD serosurveillance the bulk of specimens are used for this purpose. However, in the 2012-3 serosurvey biochemistry specimens were collected with larger volumes, and sera from adult subjects are in storage.	Keep residual plasma for 3 years.	May be satisfactory if longer term historical data are not required. Capacity to increase storage would need to be investigated if more specimens or more frequent collections were desired.

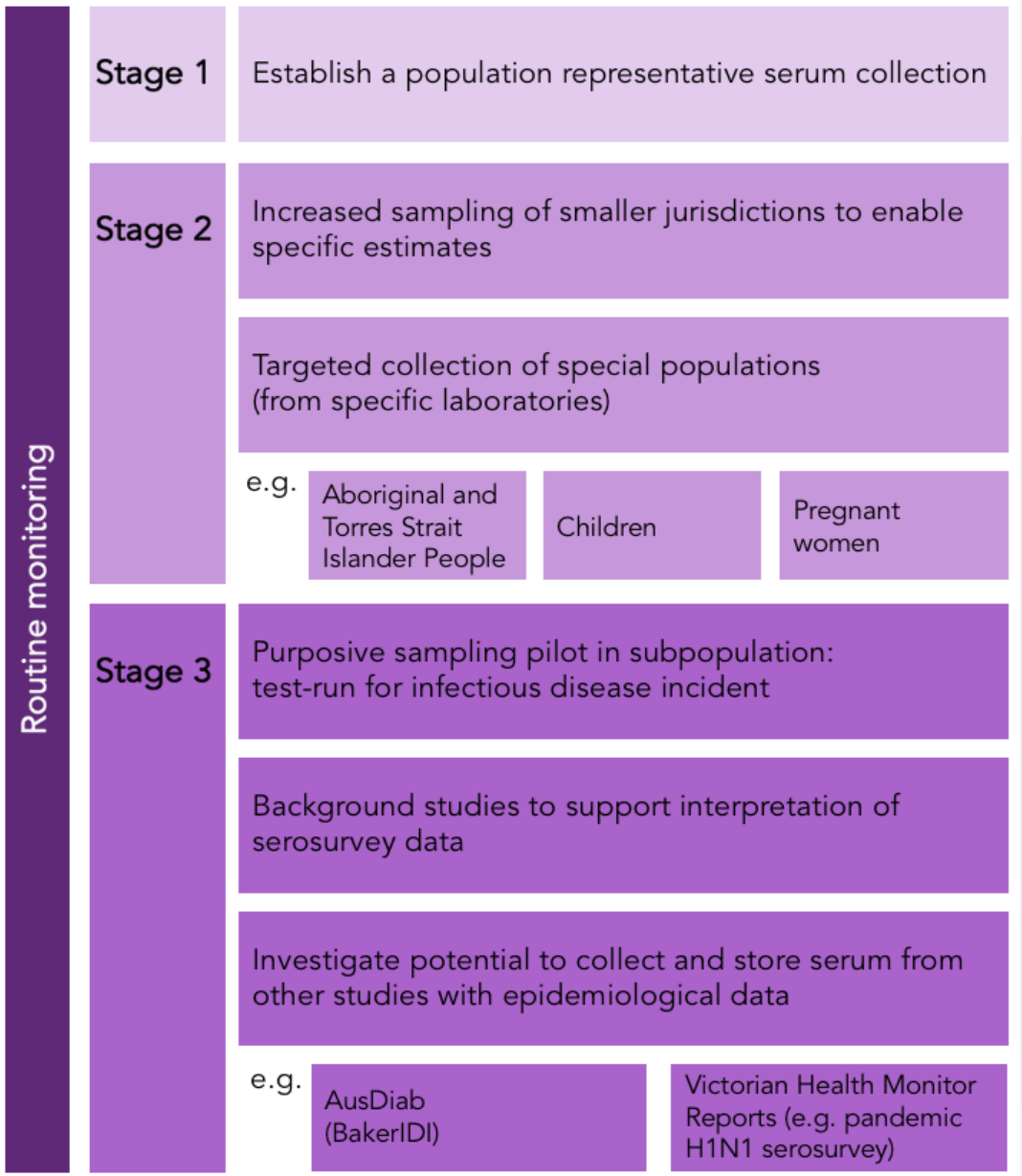
Key gaps in utilising existing systems for EIDs 3

	VPD serosurveillance program	Red Cross Blood Service	Key gaps
Logistics – collection	ICPMR staff visit labs to collect samples. 60% of required 2012 sample size collected in 6 weeks targeting five laboratories.	Specimens are collected, and residual plasma stored, as part of routine activity.	ICPMR confident of their approach to collecting specimens and relationships with labs. Sample size may not be met for youngest paediatric specimens.
Logistics – storage	Sufficient storage for current specimen volume	Retention of specimens for three years.	Need for better, dedicated systems for storage and cataloguing of residual specimens was identified.
Funding	Sufficient for sample collection and storage but not testing. Funding through the 4-year funding agreement cycle with Department of Health, being re-negotiated for 2018-21.	Residual sera are stored as part of routine activity.	Source of funding for a combined VPD/EID system with more frequent collection of samples. More funding required for studies of regional and high risk populations.

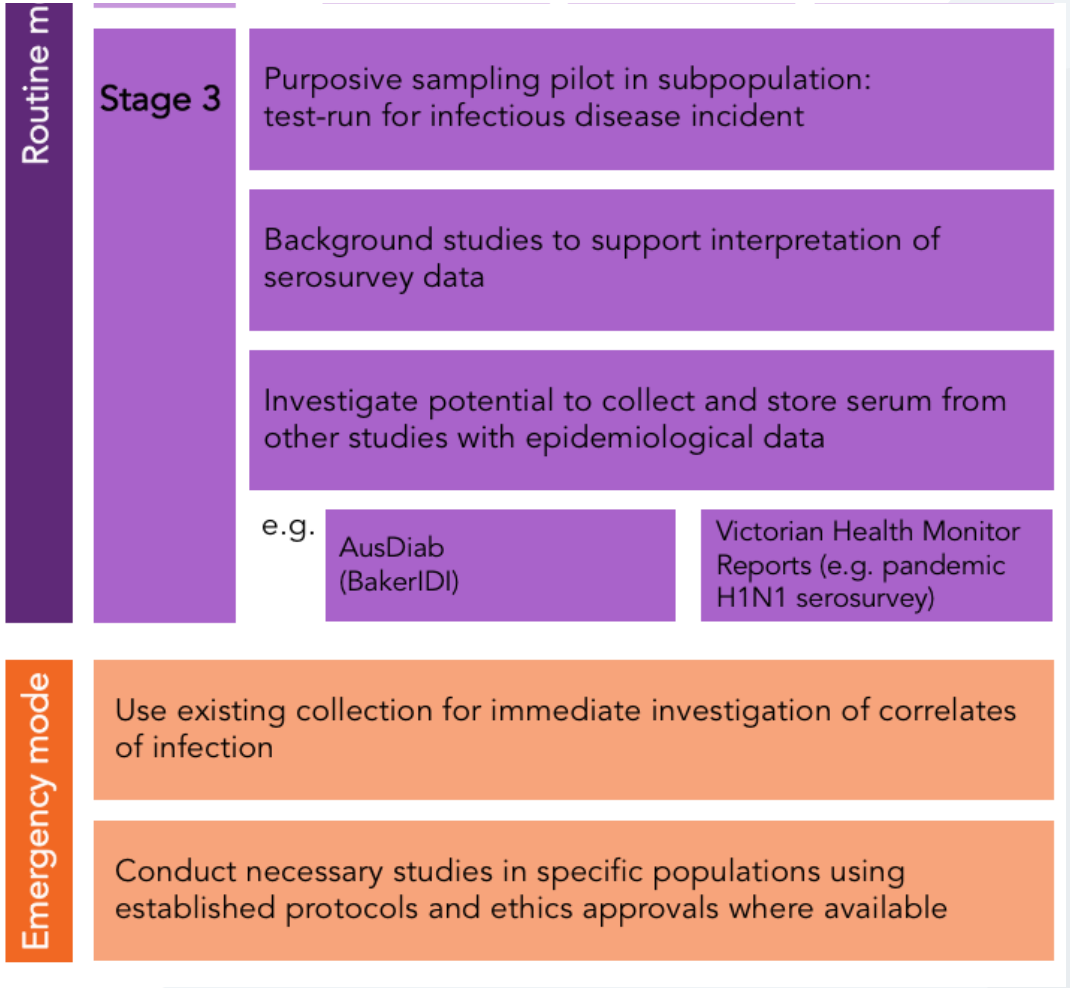
Building on existing systems

- Red Cross Blood Service
  - Utilise samples in 3 year storage
  - Store additional samples at end of 3 year period
  - Prepare for post-emergence studies (additional specimens and data collection)
- VPD serosurveillance system
  - More frequent specimen collection (5 yearly) for required volumes and timeliness in the advent of an emergent infection
  - Samples split between VPD and EID requirements (?permit high-value research access to any surplus specimens on a cost recovery basis)
  - Requires physical infrastructure, cataloguing, personnel to identify, collect, store, and curate samples, and to retrieve, package and send out for studies
- Approaches
  - Ongoing collection and management of the collection (PHE model)
  - Two-yearly sample collection
  - A modular approach to development of the collection

Proposed modular development of serum collection



Proposed modular development of serum collection



Other opportunities

- With a staged establishment of a serum collection objectives could expand over time
- Serosurveillance of people working at the animal-human interface
- Collaboration of APPRISE with NCIRS/ICPMR, ARCBS, the Communicable Diseases Network of Australia (CDNA) and the Public Health Laboratory Network (PHLN) to push for prioritization and funding of an EID serosurveillance collection that is part of an overall national biobanking effort.
- Development of protocols and methodologies for collection of serum specimens (and epidemiological data) in advance of an EID (consider international standards in protocol development such as CONSISE)
- Obtain an over-arching ethical approval for the collection and use of residual sera (potentially linked to additional data where samples are from a hospital laboratory) and blood bank specimens

Summary

- Potential to build on existing systems to develop capacity to survey for emerging infections
- Limited capacity for (recent) lookback within existing systems
- High-risk populations are not currently targeted by the existing VPD serosurveillance system collection or the blood bank
- Residual sera are currently not collected frequently enough (five-yearly) to be of use in an emergent event
- There is capacity in both systems to collect samples in an emergency situation, although this would require additional funding and pre-specified protocols, and time to collect specimens.
- With an established collection protocol, look-back studies could be conducted in a timely fashion, special population groups could be targeted, and research during periods of routine monitoring would be facilitated.

Key decisions to be made

1. Objectives of the serosurveillance and serum banking program
2. Use of residual specimens (retrospective or prospective) versus prospective purposive collection (or both, assessing suitability, cost and timeliness)
3. Combination of residual sera and healthy donor specimens
4. The frequency and method of sample collection
5. Sample storage/cataloguing
6. Structure of residual serum collection – staged development regarding special populations
7. Governance - custodianship, responsibility for decisions re: access to specimens, develop a hierarchy of needs
8. Two modes of operation
   - Routine monitoring: establish systems and collection, background studies
   - Infectious disease incident mode: target specific populations
9. Development of documentation e.g. obtain ethics approval in advance, protocols for collection from special populations etc.

Brief from Public Health pillar of APPRISE

- Scoping assessment of opportunities to develop a nationally representative serosurveillance collection, with reference to the following issues
- Validity of using retained routine diagnostic specimens;
- Validity of using routinely collected screening samples from healthy blood donor populations
- Opportunities for surveillance of populations at high risk of severe disease outcomes and/or exposure, including at the animal human interface
- Ability to scale up collection/lookback activities in the context of an infectious diseases emergency (including historical examples)