

# HIV Molecular Epidemiology

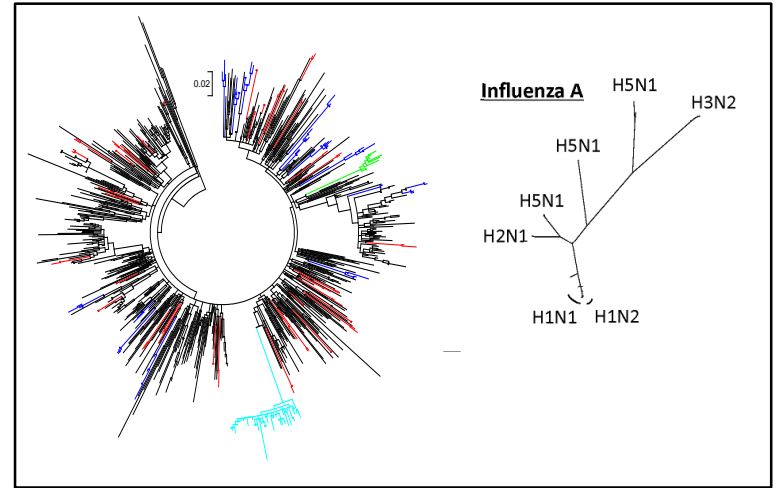
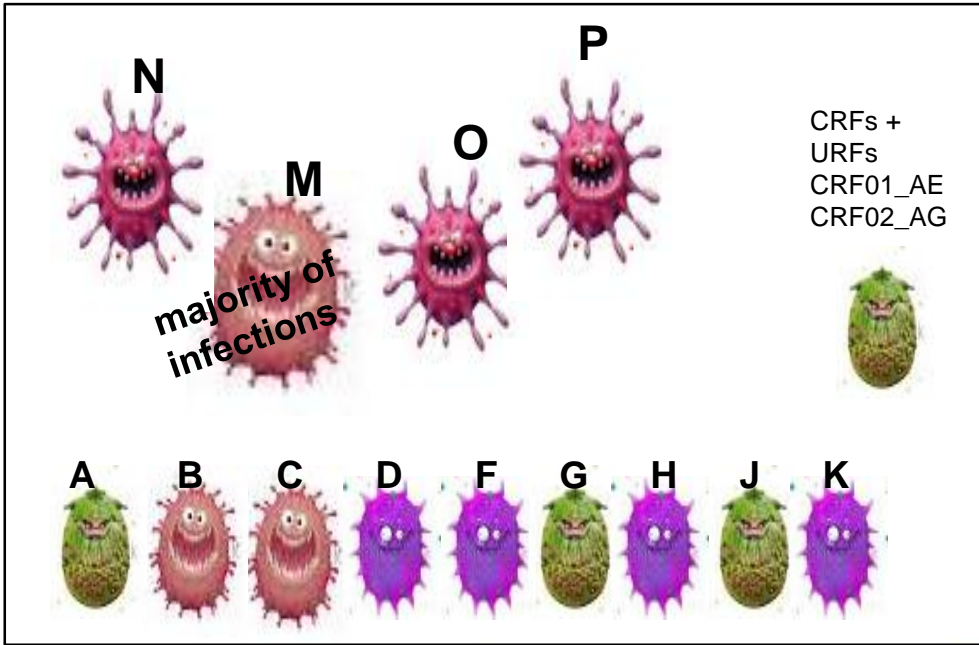
Dr Alison Castley



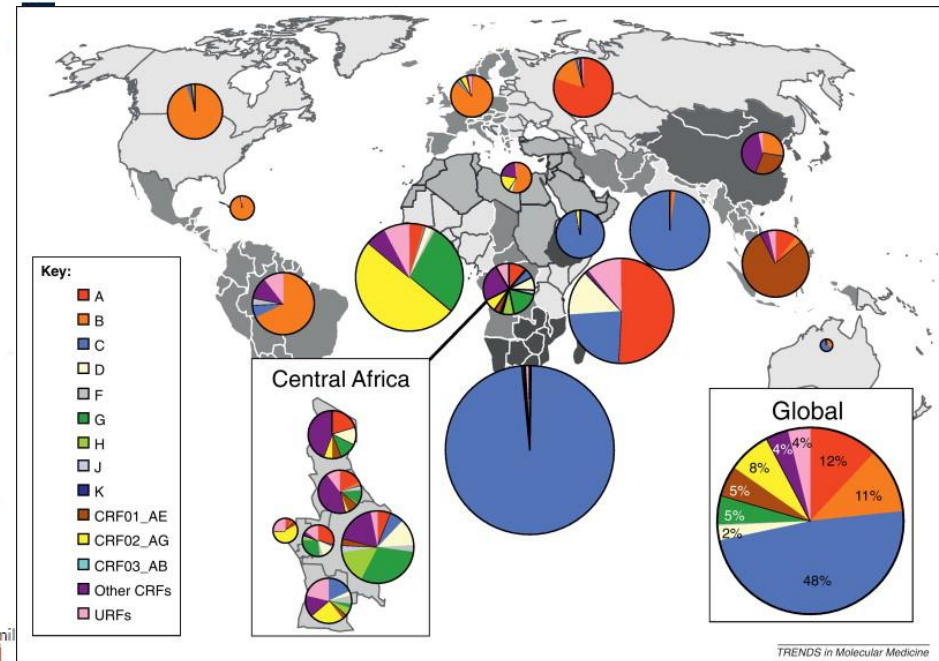
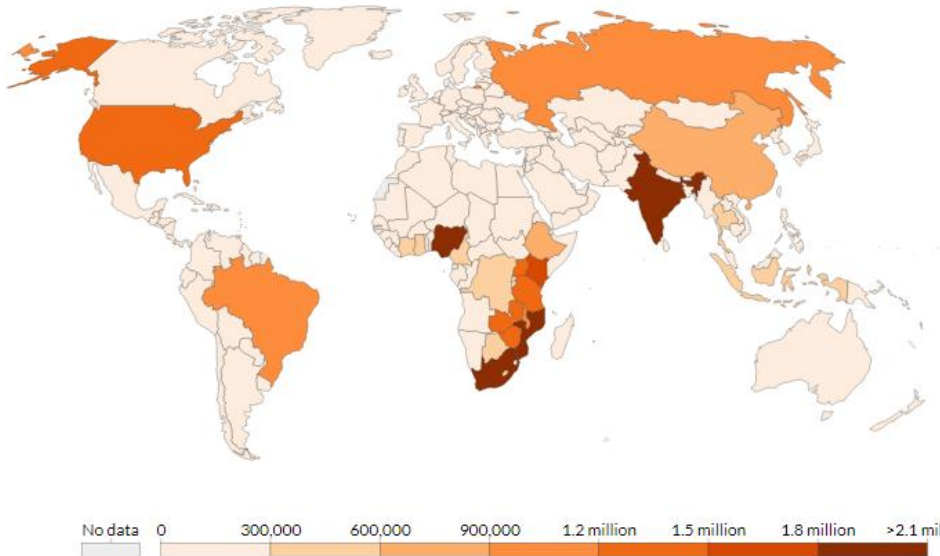
Australian Molecular  
Epidemiology Network



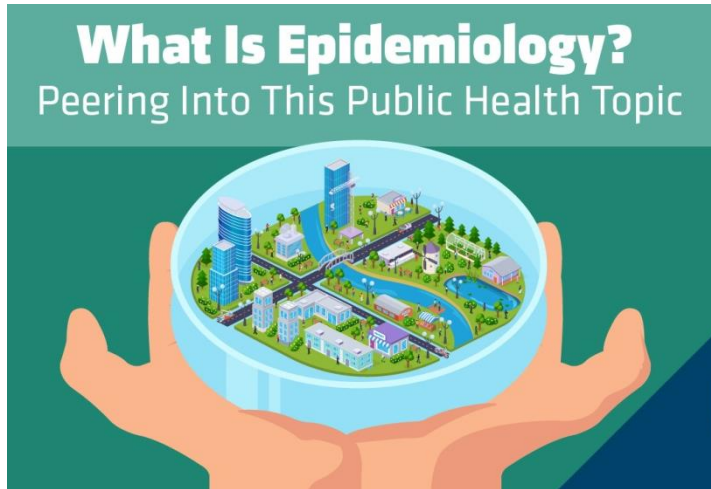
# Background



Number of people living with HIV, 2017  
Total number of people living with HIV/AIDS.



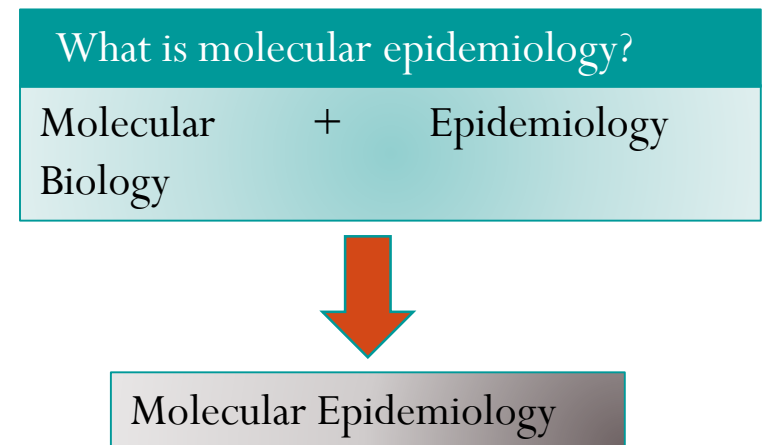
# Principles of Molecular Epidemiology



- The study of the determinants and distribution of health and disease related issues in a population.

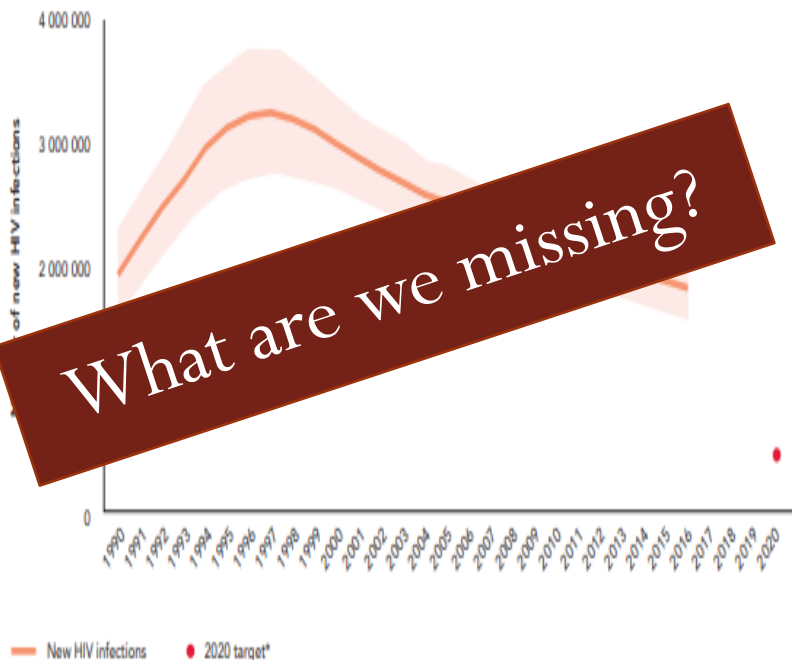
- Investigates genetic sequence variation in virus and other micro-organisms to learn about:

- viral evolution (eg. SHIV -> HIV)
- adaptation to human hosts (changes in virulence)
- emergence of treatment resistance, and
- distribution within a population



# What is the usefulness of HIV epidemiological studies?

- Dynamically assesses new infections
- Monitoring geographical and subtype changes
- Transmission (routes)
- Pathogenesis (disease progression)
- Immune response and escape
- DRMs and response to ART
- Diagnostic tools (ELISA, WB)
- Monitoring tools (HIV-RNA, SBT/NGS)
- VACCINE DEVELOPMENT
- Consider HIV within a global network



Global air travel network

# A number of world wide studies utilising HIV Molecular Epidemiological data.

## Study 1

Western Australian HIV/AIDS epidemic (2000-2014) <sup>1</sup>

Baseline, HIV-1 partial POL sequences (RT)  
Viral subtype  
Patient demographic and clinical data  
(CD4, HIV-RNA)  
Risk factor category (sexual risk factor, IDU)

**De-identified**

## Study 2

Australian HIV/AIDS epidemic AMEN (2005-2012) <sup>2</sup>

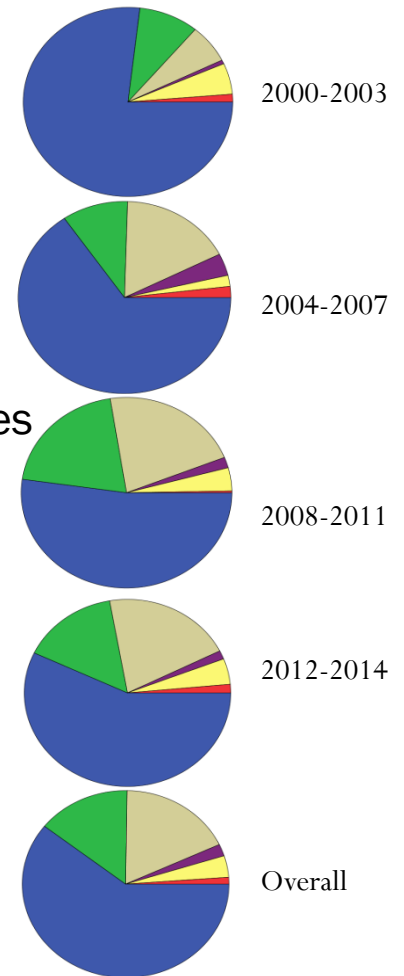
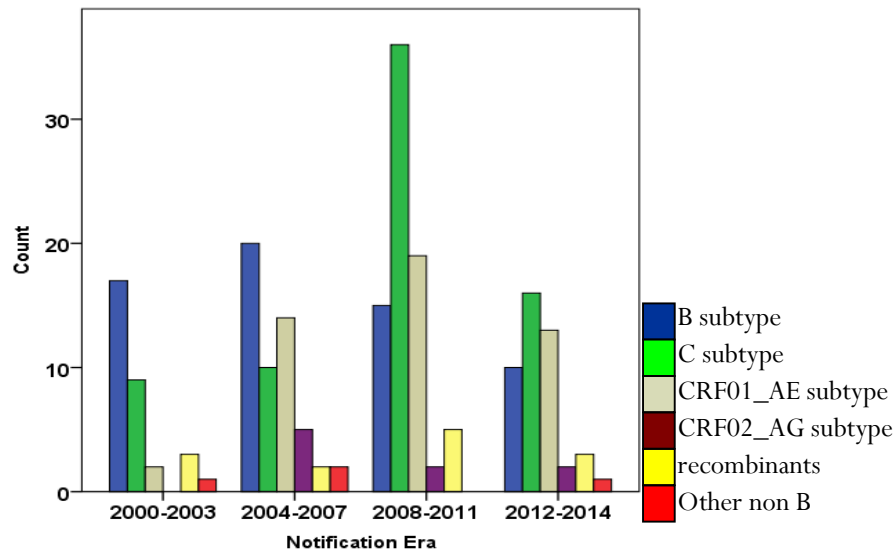
A collaboration of labs across jurisdictions  
WA/SA/VIC/w NSW  
Large scale, HIV-1 partial sequences (PR+RT)  
Patient demographic and clinical data  
(state, year of acquisition, sex)

**De-identified**

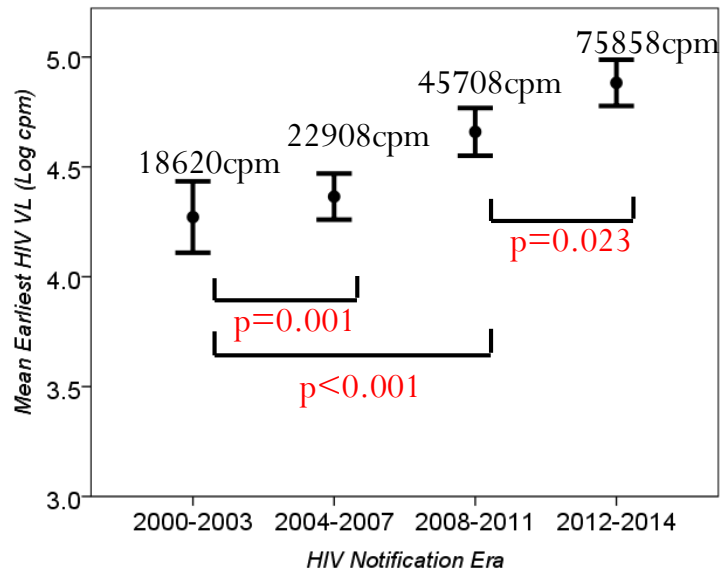
1.Castley A et al AIDS RHR, 2015: Longitudinal trends in Western Australian, HIV-1 sequence diversity and viral transmission networks and their influence on clinical parameters: 2000 – 2014.  
2.Castley A et al PlosOne 2017; A national study of the molecular epidemiology of HIV-1 in Australia 2005-2012.

# Study 1: Western Australian HIV/AIDS epidemic (2000–2014)

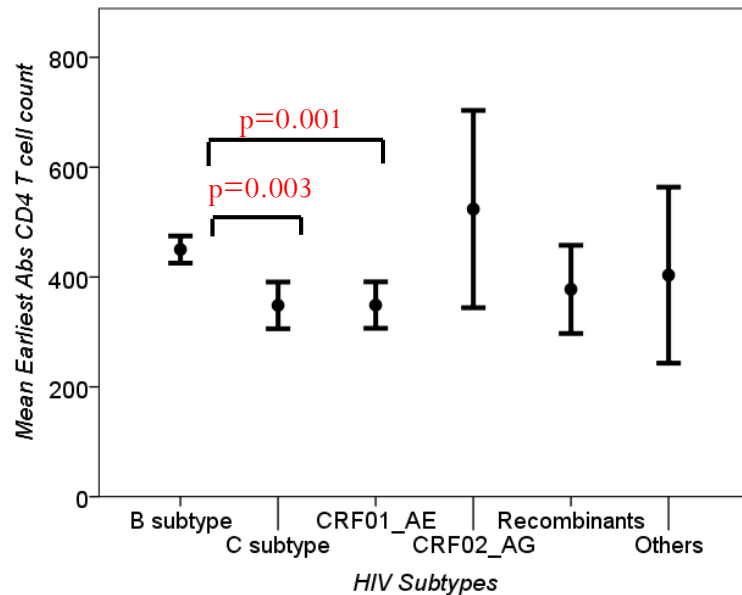
- Baseline HIV-1 sequencing at diagnosis: 1021 individuals
- 20% female (average age 35 years females cf 45 years for males)
- Subtype diversity changed over time
- More viral diversity in females (↑ over time)
- Lower baseline viral load in B subtype
- Lower CD4 T cell counts in non-B subtypes (ie later diagnosis)
- More Australian-born males acquire non-B subtype HIV-1 O/S cf females
- More overseas born males and females acquire HIV overseas.



# Earliest viral load and CD4 assessment



- Strong influence of notification era ( $p < 0.001$ ).
- Higher viral load associated with HIV-1 sequences in large cluster ( $n=53$ ,  $p=0.01$ ; data not shown)
- No association between HIV-1 subtype and viral load ( $p=0.31$ ).
- Possible evidence of viral adaptation over time



- No significant association between notification era and CD4 T cell count ( $p=0.1$ ) or CD4:CD8 ratio ( $p=0.2$ ).
- HIV-1 subtypes C and AE associated with lower CD4 count ( $p < 0.01$ ): **later diagnosis**
- Higher CD4 count associated with large cluster of highly similar HIV-1 sequences: **earlier diagnosis**

# Study 2: Australian HIV/AIDS epidemic (2005-2012)

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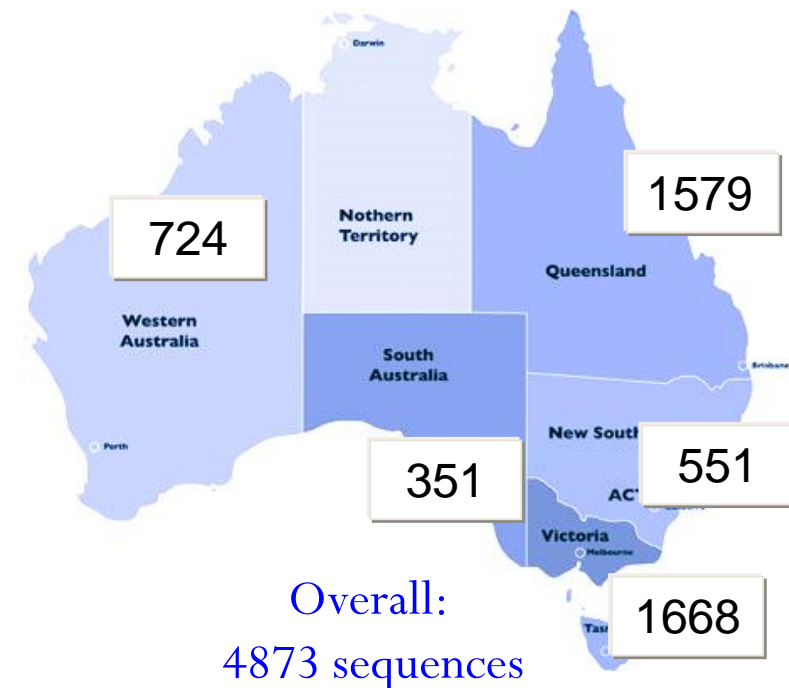
- New rates of HIV-1 on the increase in Australia
- Some jurisdictions had shown an increase in Non B subtypes
- No current Australian Epidemiological data
- AIM: to define HIV-1 subtype diversity patterns and to assess network patterns across Australia from 2005-2012.





# Study 2: Background and Methods

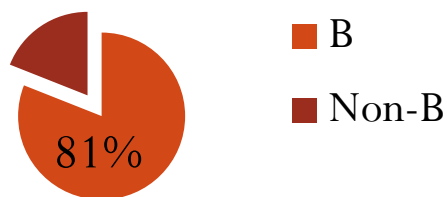
- Australian Molecular Epidemiology Network (AMEN) formed December 2013
  - All states and territories represented (NT + Tas → Vic)
  - Ethics and governance framework established
    - De-identified HIV-1 sequence results
      - Gender, age, state
      - Year of sequencing
    - HIV-1 sequences (RT + PR)
      - 2005 – 2012
      - 4 sequence eras (2005-06, 2007-08, 2009-10 and 2011-12)
    - Data analysis at one site
      - Sequence alignments checked
      - Duplicate sequences checked
      - Phylogenetic analysis
    - Complete dataset other than NSW



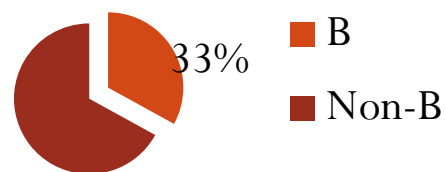
# Study 2: HIV-1 subtypes and distribution

| State        | Method        | Year      | Sequence (n) |                | SUBTYPE ID       |            |                  |           |                   |                | Hospital/Service      |
|--------------|---------------|-----------|--------------|----------------|------------------|------------|------------------|-----------|-------------------|----------------|-----------------------|
|              |               |           | B Subtype    | Other Subtypes | CRF01_AE Subtype | C Subtype  | CRF02_AG Subtype | D Subtype | Recombinant Forms | Other Subtypes |                       |
| WA           | Stanford dB   | 2005-2012 | 724          | 427            | 139              | 109        | 17               | 5         | 23                | 4              | RPH-DCI               |
| SA           | Stanford dB   | 2005-2012 | 351          | 240            | 38               | 35         | 20               | 1         | 9                 | 8              | SA Health             |
| VIC          | Los Alamos dB | 2005-2012 | 1668         | 1261           | 174              | 153        | 10               | 4         | 49                | 17             | VIDRL                 |
| W-NSW        | Stanford dB   | 2005-2011 | 551          | 407            | 43               | 54         | 21               | 3         | 13                | 10             | Westmead              |
| QLD          | Stanford dB   | 2007-2012 | 1579         | 1296           | 90               | 124        | 20               | 8         | 34                | 7              | QLD HIV Reference Lab |
| <b>Total</b> |               |           | <b>4873</b>  | <b>3631</b>    | <b>484</b>       | <b>475</b> | <b>88</b>        | <b>21</b> | <b>128</b>        | <b>46</b>      |                       |

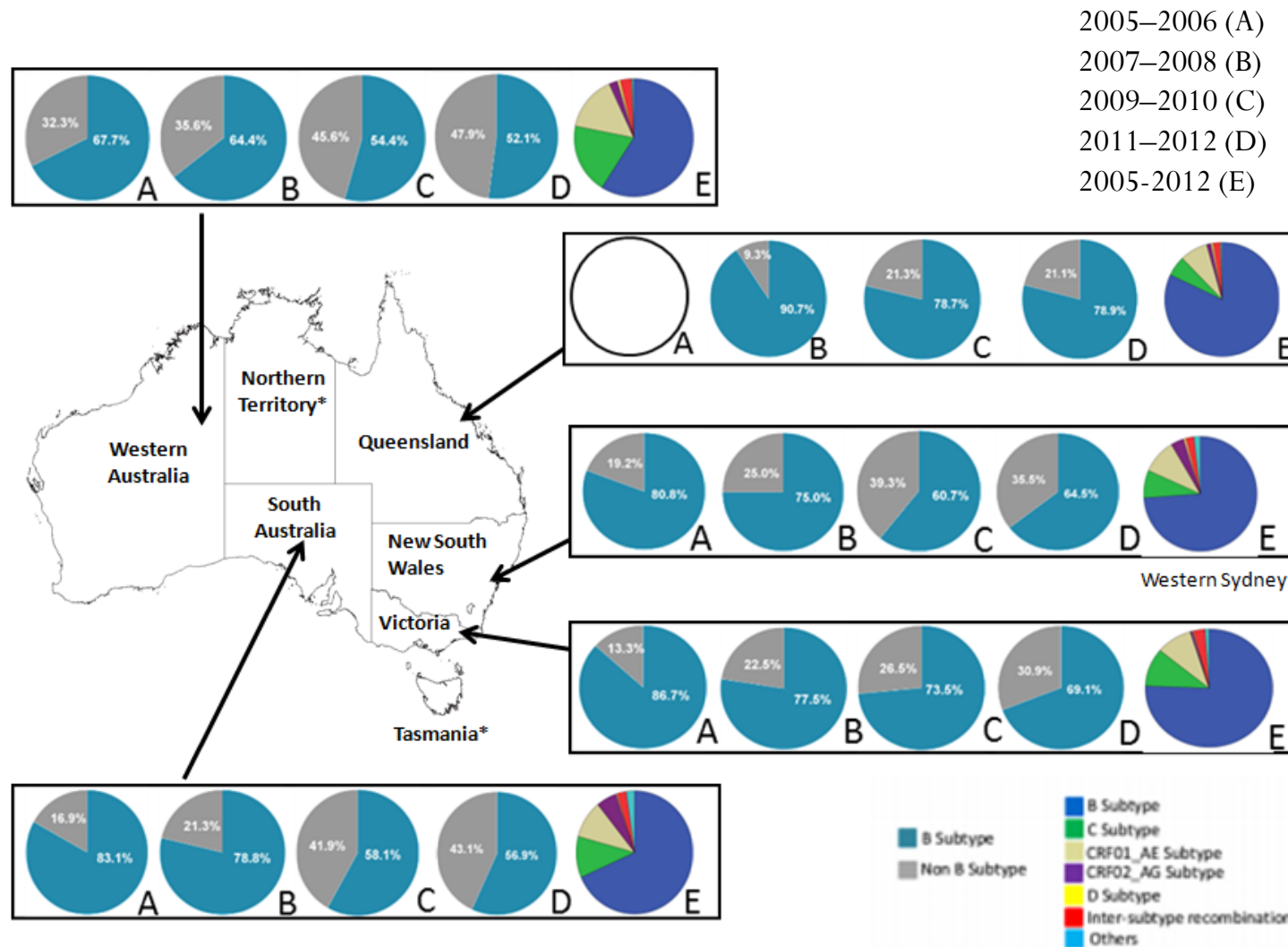
HIV-1 subtypes  
(4189 males)



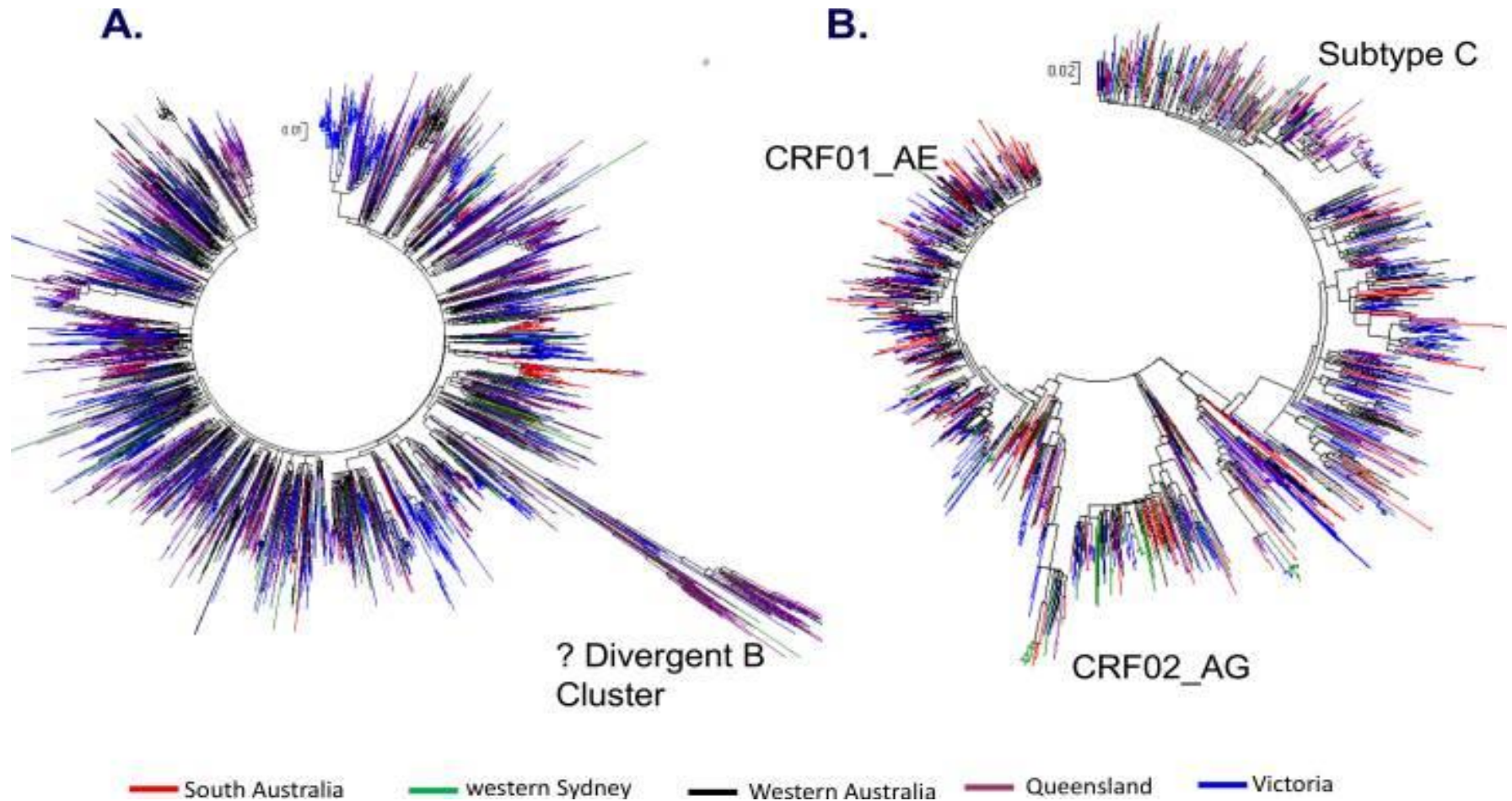
HIV-1 subtypes  
(648 females)



# Study 2: HIV-1 subtypes and distribution



# Study 2: HIV-1 subtypes and distribution



Of 4873 sequences, 23% were within a pair or cluster (no difference between B and Non B subtypes)  
286 pairs, 115x 3 to 5 sequences, 17 x 6-13 sequences and 1x large group of 29 sequences.

# Discussion (1)

- 1. Growing diversity in HIV-1 sequences in Australia over time, including HIV-1 subtypes historically linked to Africa and SE Asia**
  - Likely to reflect increasing impact of travel and migration
    - Highlights value of regional engagement
    - Strong role in 'ending HIV' strategy in Australia
  - Similar patterns identified throughout Australia
    - Highlights value of national approach
  - Higher levels of HIV-1 subtype diversity among women living with HIV in Australia
    - Highlights diverse origins of HIV transmission for women living with HIV in Australia
  - High rates of circulating recombinant forms of HIV-1, indicating ongoing evolution of viral subtypes
    - Highlights need to evaluate local/national sequence diversity when developing/testing viral load and resistance testing assays
- 2. Investigated baseline (pre-treatment) HIV-1 sequence diversity only – has not evaluated drug resistance at a national level**

# Discussion (2)

## 1. National collaboration of HIV-1 sequencing laboratories

- Forms a basis for monitoring drug resistance, with national coordination
  - Particularly valuable in PrEP era – will inform evolution of treatment strategies
- Data sharing to support evaluation and implementation of viral load and HIV-1 sequencing assays
  - Valuable both nationally and regionally
- Has provided a model for ethics/governance framework nationally, as well as highlighting challenges of current state-based approach

## 2. Future direction uncertain – no existing funding to support national approach, or to engage regionally

- Need to separate national collaborative strategy from discussion of HIV criminalisation
  - HIV-1 sequencing from routine laboratory cannot legally infer transmission (although can exclude that possibility)
- Requires dedicated and sustainable support, underpinned by existing collaborative goodwill

# Acknowledgements

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