

The challenges of diversity: HIV-1 subtype distribution and transmission networks within the Australian Molecular Epidemiology Network-HIV 2005-2012

Castley A, Sawleshwarkar S, Varma R, Herring B, Thapa K, Chibo D, Nguyen N, Hawke K, Ratcliff R, Dwyer DE, Nolan D: The Australian Molecular Epidemiology Network-HIV (AMEN-HIV).

Australian Molecular Epidemiology Network



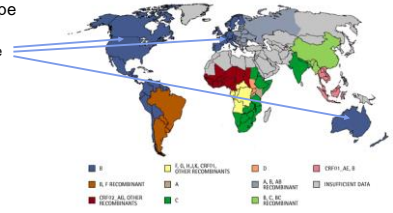
Australian Molecular Epidemiology Network

Background



- HIV-1 is a genetically variable and rapidly mutating virus
 - HIV-1 sequencing has been performed in routine HIV laboratories throughout Australia for >10 years
 - Drug resistance testing
 - HIV-1 subtype

B subtype



Australian Molecular Epidemiology Network



Background



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B subtype
C subtype



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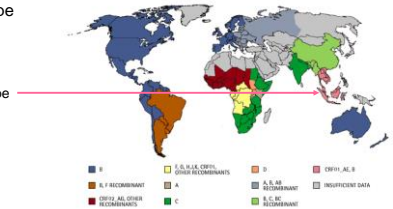


Background



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 - Drug resistance testing
 - HIV-1 subtype

B subtype
C subtype
AE subtype



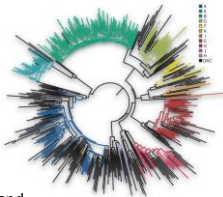
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Background



- HIV-1 is a genetically variable and rapidly mutating virus
 - Phylogenetic analysis: statistical approach, used globally.
 - Viral sequence similarity:
 - More likely from a transmission chain/network (does not infer direct transmission)
 - More likely to be found in early versus long-term infection (host factors)
 - Dependent on sequence quality and length of HIV-1 sequence assessed



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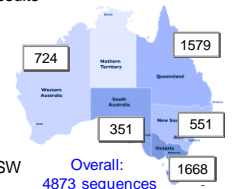
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Methods



- 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
 - Data analysis at one site
 - Sequence alignments checked
 - Duplicate sequences checked
 - Complete dataset other than NSW



Phylogenetic analysis



Evidence of phylogenetic cluster (similar HIV-1 sequences)

CLUSTERING CRITERIA
 Bootstrap ≥98%
 Genetic distance ≤1.5%

- MEGA provides the *Bootstrap test* -reliability of Phylogenetic tree
- Nucleotide sequences are re-sampled 100 times.
- Maximum-Likelihood branch lengths are computed.

How likely is it that sequences will cluster together statistically in repeated analyses? (≥ 98 out of 100 times)

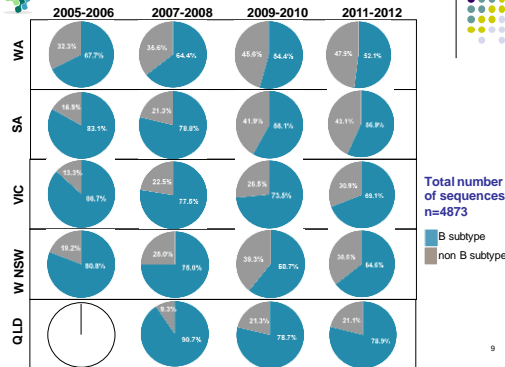
How genetically similar are the sequences? (≥ 98.5% identical)

Results: Proportion of HIV-1 sequences committed per State to the AMEN study

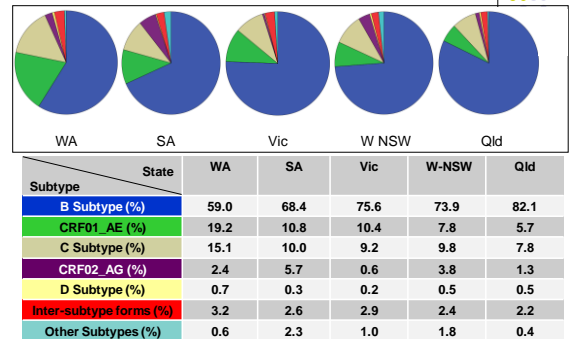


State	Non B (%)	B (%)	Total
QLD	283 (17.9%)	1296 (82.1%)	1579
SA	111 (31.6%)	240 (68.4%)	351
VIC	407 (24.4%)	1261 (75.6%)	1668
WA	297 (41.0%)	427 (59.0%)	724
W NSW	144 (26.1%)	407 (73.9%)	551
TOTAL	1242 (25.5%)	3631 (74.5%)	4873

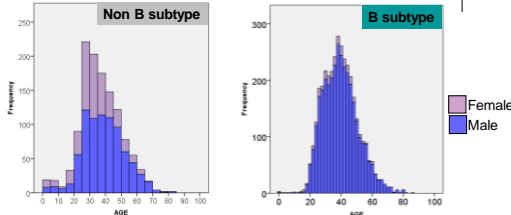
Results: HIV-1 subtype distribution over time



Results: HIV-1 subtype distribution per state in more detail



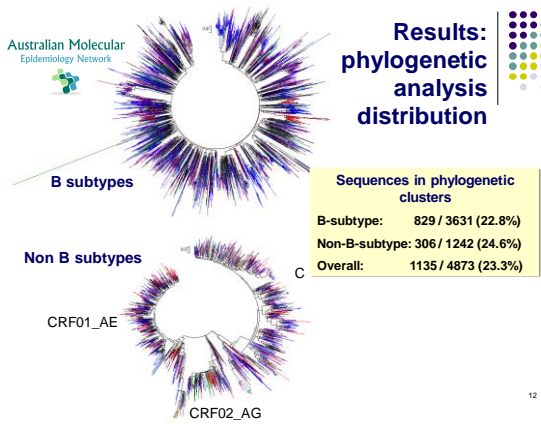
Results: Age and gender according to HIV-1 subtype



	Non B subtype (p<0.001)			B subtype (p<0.001)		
	Mean	Std	N	Mean	Std	n
Female	32.5	11.9	434	36.3	11.6	214
Male	38.5	13.2	796	39.2	11.2	3393

p=0.001
p=0.12 ¹¹

Results: phylogenetic analysis distribution



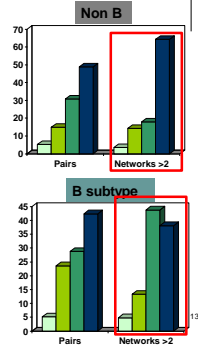
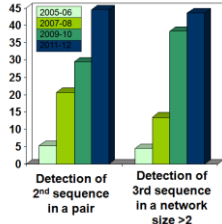
Sequences in phylogenetic clusters
B-subtype: 829 / 3631 (22.8%)
Non-B-subtype: 306 / 1242 (24.6%)
Overall: 1135 / 4873 (23.3%)

¹²

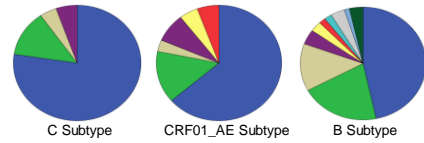
Results: Detection of HIV subtype pairs and networks over time



National results - All sequences



Results: Distribution of network size for a given HIV subtype



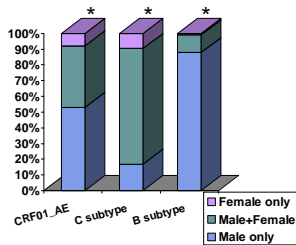
Sequences	C subtype (%)	CRF01_AE subtype (%)	B subtype (%)
2 Pairs	77.4	63.7	46.7
3 Network of 3	12.9	14.5	20.4
4 Network of 4	4.3	3.2	13.6
5-7 Network of ≥5-7	5.4	18.4	8.8
8-11 Network of ≥8	0	0	10.3

Significantly more non B pairs than non B larger networks (p=0.003)
Larger network size (>2) with B subtypes than the non B subtypes (p=0.021).

Results: Gender distribution in HIV networks for a given subtype

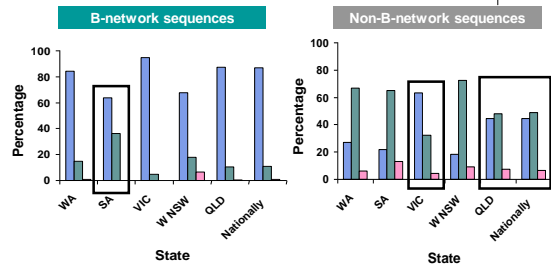


- 76% of male only groups
- 88% B subtype groups are only males
- 53% AE subtype groups are only males
- 17% C subtype groups are only males



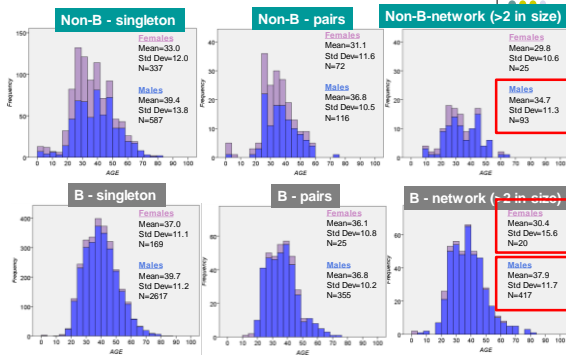
* Anova: p<0.001

Results: Proportion of B and Non-B sub-type networks according to gender

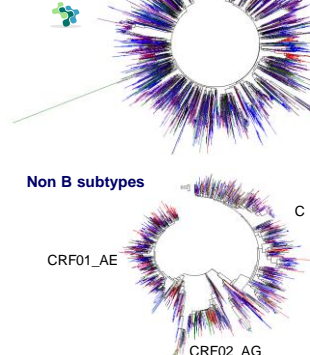


Male only Male+Female Female only

Results: Age and gender according to HIV-1 subtype and network size



Results: comparison of interstate vs intra-state clusters



Sequences in interstate versus 'intra-state' clusters (>2 in size)
B-subtype: 190 / 438 (43.4%)
Non-B-subtype: 52 / 115 (45.2%)
Overall: 242 / 553 (43.8%)

Sequences in interstate versus 'intra-state' clusters (pairs)
B-subtype: 78 / 384 (20.3%)
Non-B-subtype: 34 / 186 (18.3%)
Overall: 112 / 570 (19.6%)

Conclusions



- AMEN collaboration has established a national approach to HIV-1 molecular epidemiology studies
 - Ethics and Governance frameworks are in place
 - National database: prospective as well as retrospective dataset
 - Inclusion of NSW data underway
 - Platform for research collaboration: non-affiliated.
- Not a contact tracing analysis
 - De-identified baseline viral sequencing data

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Conclusions



- HIV-1 subtypes in Australia
 - Overall ~25% of sequences are non-B-subtype
 - Increasing proportions across all states, with a broad range of subtypes reflecting geographic origins.
 - Reflects a growing influence of migration and travel
 - Wide age distribution for both B- and non-B-subtype virus
 - More pediatric cases with non-B subtypes
 - More females with non-B subtypes (esp. C-subtype)
 - B-subtype sequences remain predominantly associated with males

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Conclusions



- HIV-1 phylogenetic clusters in Australia
 - Overall ~23% sequences classified within clusters
 - Similar proportions of B-subtype (23%) and non-B-subtype (25%) sequences within clusters
 - Higher proportion of male/female clusters in non-B
 - C-subtype (S Africa, India): 90%
 - AE-subtype (SE Asia): 50%
 - B-subtype: 12%
 - No obvious clustering according to state. Significant proportion of clusters involve sequences from more than 1 state (20% of pairs, 44% of larger clusters)

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Conclusions



- Highlights the national structure of HIV-1 in Australia
 - Common challenges to all states
 - Growing impact of travel and migration
 - Benefits of engagement with international partners
 - Provides a basis for creating and monitoring prevention strategies
- Valuable data: now and for future
 - Collaborative network: facilitated engagement with clinical, scientific and community organizations

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Acknowledgements



- Western Australia
 - George Guelfi
 - Mina John



- NSW
 - Tony Kelleher
 - Angie Pinto
 - Roger Garsia



- South Australia
 - IMVS
- VIDRL
 - Megan Gooley
 - Mike Catton



- Queensland
 - Helene Johanson
- STI/HIV conference (ISSTD scholarship)



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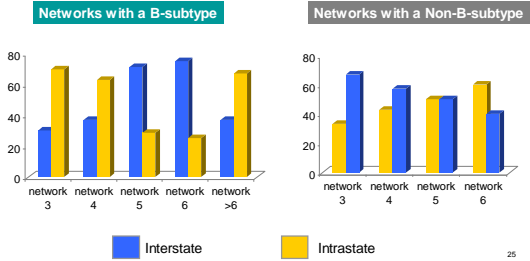
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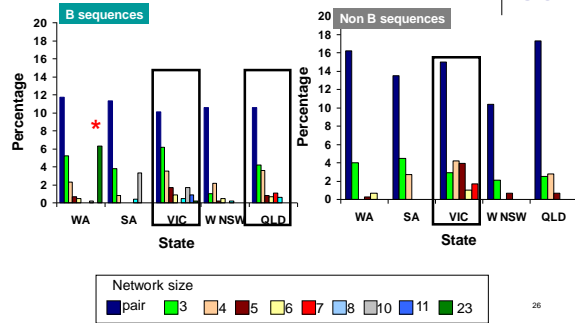
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Results: Proportion of sequences from interstate or intra-state networks according to size



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Results: network size in B and non-B subtypes for each state



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Results: Factors associated with a sequence being classified into a cluster (y,n:>18yo)



	Overall	WA	SA	VIC	WM NSW	QLD
AGE	-0.003 p<0.001	-0.005 p<0.001	-0.002 p=0.3	-0.001 p=0.34	-0.008 p<0.001	-0.003 p=0.003
SEQ ERA	0.05 p<0.001	0.05 p<0.001	0.07 p<0.001	0.03 p=0.002	0.02 p=0.13	0.04 p=0.001
Gender	-0.01 p=0.023	-0.06 p=0.17	0.02 p=0.69	-0.09 p=0.03	-0.02 p=0.59	-0.02 p=0.54
Non-B vs B	-0.05 p=0.021	-0.07 p=0.058	-0.08 p=0.11	0.05 p=0.08	-0.02 p=0.67	0.07 p=0.02
State	0.01 p=0.41	-	-	-	-	-

Coefficient and significance

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Variables associated with the classification of sequences into larger network size 2-3 or >3. (>18yo, not pairs)



	Overall	WA	SA	VIC	W NSW	QLD
AGE	0.002 p=0.2	-0.001 p=0.72	-0.001 p=0.8	0.001 p=0.77	-0.01 p=0.04	0.006 p=0.01
SEQ ERA	0.03 p=0.05	0.09 p=0.004	-0.003 p=0.96	0.003 p=0.88	0.02 p=0.7	0.03 p=0.4
Gender	-0.12 p=0.008	-0.02 p=0.86	0.03 p=0.8	-0.4 p<0.001	0.13 p=0.17	-0.04 p=0.6
Non-B Vs B	-0.03 p=0.34	-0.34 p<0.001	-0.07 p=0.6	0.09 p=0.12	-0.07 p=0.51	0.03 p=0.7
State	0.003 p=0.7	-	-	-	-	-

Coefficient and significance

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