An Abbott Architect Combo Signal to Cut-off Ratio with Adequate PPV to Confirm HIV-1

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BACKGROUND

An HIV testing algorithm that minimises the time to confirmation without losing sensitivity and specificity has clear advantages to both patients and clinicians. We hypothesised that:

- The PPV of the Abbott Architect HIV Ag/Ab Combo Assay increases with the signal to cut-off (S/CO) ratio
- A threshold S/CO ratio could be identified that has an adequate PPV to confirm the diagnosis of HIV-1 infection

METHODS AND RESULTS

Samples and Subjects

- HIV tests from reference laboratory in Sydney (Mar 2006-14)
- 138,991 testing episodes with 3,705 reactive results
- From metropolitan hospitals (inpatients and outpatients), infectious diseases clinics, sexual health clinics, a women's hospital, general practitioners and prison health services

Assessment of synchronous and subsequent supplemental tests

- Western Blot (WB)
- HIV p24 Ag assay (confirmed by neutralization)
- HIV-1 Ab particle agglutination assay
- HIV-1 viral load

Classification as "true" and "non-true" positive results (Tables 1 and 2)

- Criteria for classification of a true positive outlined in Table 1
- All other results were classified as non-true positive results

Random allocation to train and test samples

Train sample (N=1,845):
Used to identify the S/CO ratio above which all results were true positive
Threshold S/CO = 151.17

Test sample (N=1,860):
Used to calculate the PPV and sensitivity of the S/CO identified in train sample for a result being a true positive
See Table 3 and Figure 1

Table 1. Characteristics of testing episodes defined as true positives

Group	N	Western Blot (WB)	p24 Ag	HIV-1 Ab	WB repeated within 6 months	HIV-1 Viral Load within 2 weeks (copies/mL)
1: WB positive (N=1,989)	1,989	POS	POS or NEG	POS or NEG	U/A	ANY
2: Negative or indeterminate WB followed by a positive WB within 6 months (N=83)	63	IND	POS or NEG	POS	POS	ANY
	20	NEG	POS or NEG	POS or NEG	POS	> LLD or U/A
3: Negative or indeterminate WB and at least two positive results of the p24 Ag assay, the HIV Ab assay or the HIV viral load (N=338)	168	IND	At least one POS		IND (N=46) or U/A	≥ 10,000
	64	IND	At least one POS		IND (N=47) or U/A	LLD - 9,999
	48	IND	POS	POS	IND (N=8) or U/A	U/A[a]
	27	NEG	POS	POS or NEG	IND (N=16) or U/A	≥ 10,000
	5	NEG	POS	NEG	NEG	≥ 100,000
	2	NEG	At least one POS		IND (N=1) or U/A	LLD - 9,999
	6	NEG	POS	POS	IND (N=1) or U/A	U/A[a]
4: Negative or indeterminate WB, positive p24 Ag or HIV Ab and no HIV viral load available (N=150)	2	IND	POS	NEG	IND (N=1) or U/A	U/A[a]
	110	IND	NEG	POS	IND (N=23) or U/A	U/A[a]
	38	NEG	POS	NEG	IND (N=17) or U/A	U/A[a]

Abbreviations: IND, indeterminate; LLD, lower limit of detection; NEG, negative; POS, positive; U/A, unavailable.
[a]39 (19.1%) testing episodes in these subjects had VL measurement performed more than two weeks after the Abbott Combo and all had detectable HIV-1 RNA. 30 of these were done within three months and nine were tested more than three months after the index test episode.

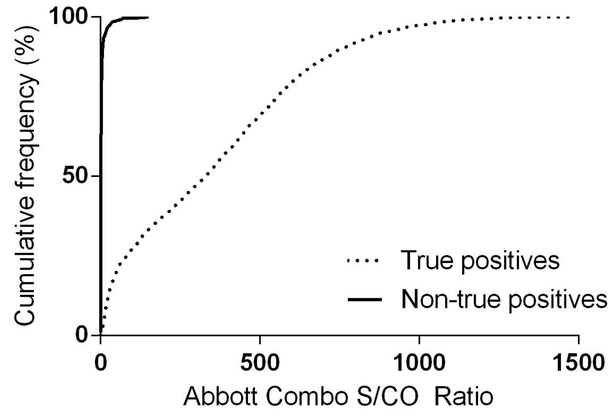
Table 2. Characteristics of study subjects at the time of testing stratified by true or non-true positive classification

	Total (N=3,705)	True positives (N=2,542)	Non-true positives (N=1,163)	P
Age in years, mean (SD)	36.9 (12.0)	37.3 (11.0)	36.0 (14.0)	0.003
Number of males (%)	2,840 (77)	2,286 (90)	554 (48)	<0.001
Median S/CO ratio (range)	101.4 (1.0-1,493.6)	328.3 (1.1-1,493.6)	1.9 (1.0-151.17)	<0.001

Table 3. Performance of selected S/CO ratios in the test sample

	Positive Predictive Value for a true positive result	Sensitivity for a true positive result
S/CO ratio > 151.17	100%	67.4%
S/CO ratio > 100	99.7%	73.8%
S/CO ratio > 50	99.0%	80.6%

Figure 1. Cumulative frequency distribution of the S/CO ratios of true and non-true positive Abbott Combo testing episodes



CONCLUSION

- The S/CO ratio of the Abbott Combo assay can be used in clinical decision making
- Given a sufficiently high S/CO ratio, the clinician will be able to deliver a test result to the patient without waiting for further confirmatory testing
- A S/CO ratio above 151.17 was highly predictive of HIV-1 infection in a low prevalence (0.15%) Australian population

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