Background
It is important to distinguish recent from established HIV-1 infection quickly and efficiently to assess seroconversion and to inform initiation of antiretroviral treatment (ART) early in infection. ART will rapidly reduce the viral load and thus limit the size of the cellular viral reservoir, improve immune function and reduce the forward transmission of HIV-1 infection.

“Recent HIV-1 infection” refers to an approximate three-month time interval following HIV-1 acquisition and represents an part of a spectrum of infections described by the Fiebig staging schema.1 This staging relies on the detection of HIV-1 RNA, p24 antigen and sequential immunoassay reactivity to specific viral antigens.

Objectives
The broad dynamic range of the sample to cutoff (S/CO) ratio for the fourth generation ARCHITECT HIV Ag/Ab Combo chemiluminescent magnetic microparticle-based immunoassay (CMA) (ARCHITECT, Abbott, Chicago, IL), correlates with the level of HIV-1 p24-antigen and antibody.2

Although the high viremia levels associated with acute HIV-1 infection (AHI) contribute to S/CO values of ≤15, it is common to see S/CO values >15 when the Western blot (WB) is negative during recent infection because the ARCHITECT will detect low-level HIV-1 specific antibody below the WB sensitivity.3

We sought to characterize the association between the ARCHITECT S/CO ratio, Fiebig stage and recency of HIV-1 infection in clinical specimens.

Materials & Methods
Specimens were obtained from an academic hospital referral laboratory and re-search HIV vaccine trials. A retrospective analysis of specimens obtained be-tween May 2011 to September 2015 used a 4th generation HIV-1/2 diagnostic al-gorithm comprised of the ARCHITECT, Multispot (Bio-Rad), Western blot (Bio-Rad) and HIV-1/2 plasma RNA (Abbott m2004).4

The ARCHITECT sample to cutoff ratio algorithm for the S/CO and Fiebig stage (FS) was as follows:

- **Negative infection:** S/CO <1.0
- **Acute infection (AHI) or FS I-II:** S/CO ≥1, Bio-Rad Multispot HIV-1/2 rapid test (MS) non-reactive and a positive plasma HIV-1 RNA.
- **Recent early infection or FS III-IV:** S/CO ≥1, MS reactive with negative or indeterminate WB.
- **Recent infection or FS V:** S/CO ≥1, positive HIV-1 WB without a p31 band.
- **Established infection or FS VI:** S/CO ≥1, positive HIV-1 WB with a p31 band present.

**Results**

**Updated values are in bold.** From 43,264 specimens tested, 42,543 were considered negative with a S/CO median and interquartile range [IQR] of 0.13 [0.01-0.16]. A total of 721 (1.7%) specimens were ARCHITECT reactive; however, only 43 (6.0%) were MS non-reactive and confirmed as AHI by HIV-1 RNA with a S/CO median [IQR] of 12.5 [4.2-65] and a viral load median [IQR] of 1.45×106 RNA copies/mL [4.48×10^5 – 10.0×10^6].

Of the 678 MS-reactives, 19 were WB indeterminate with a S/CO median [IQR] of 55 [38-110] and were considered to be recent early infections. The rest were divided in two groups; 111 were WB-positive without p31 (recent HIV infection) and 548 were p31-positive (established HIV infection) with a median S/CO of 139 [51-603] and 826 [584-1023], respectively.

**Conclusions**

The broad range of ARCHITECT S/CO values can be used to presumptively differentiate between AHI, recent and established HIV infection while awaiting confirmation by other methods. In conjunction with a rapid orthogonal confirmatory test, the S/CO information may be helpful to accurately assign HIV-1 infection recency and emphasize to the clinician the urgency for considering the use of early antiretroviral therapy during the acute and recent HIV-1 infection periods. The use of the S/CO ratio for this purpose requires further validation in the clinical laboratory setting.

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**References**