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Commentary

Could low dead-space syringes really reduce HIV transmission to low levels?

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ABSTRACT

Studies published by Zule and colleagues have suggested that use of low dead-space syringes (LDSS) instead of high dead-space syringes (HDSS) by injecting drug users (IDUs) could dramatically reduce HIV transmission. However, evidence is limited because experiments have considered a small range of syringe types and have been unable to reliably estimate the efficacy of using LDSS for reducing HIV transmission. We critically appraise available evidence to determine whether using LDSS is likely to dramatically reduce HIV transmission.

We systematically review the literature on the dead-space volume of syringes and estimate the factor difference in blood volume transferred from sharing LDSS or HDSS. Existing data on the relationship between host viral load and HIV transmission risk is used to evaluate the likely efficacy of using LDSS instead of HDSS. An HIV transmission model is used to make conservative impact projections for switching to using LDSS, and explore the implications of heterogeneity in IDU transmission risk and syringe preferences.

Although highly variable, reviewed studies suggest that HDSS have on average 10 times the dead-space volume of LDSS and could result in 6/54/489 times more blood being transferred after 0/1/2 water rinses. Assuming a conservative 2-fold increase in HIV transmission risk per 10-fold increase in infected blood inoculum, HDSS use could be associated with a mean 1.7/3.6/6.5-fold increase in transmission risk compared to LDSS for 0/1/2 rinses. However, even for a low efficacy estimate, modelling suggests that partially transferring to LDSS use from using HDSS could dramatically reduce HIV prevalence (generally >33% if LDSS use is 50%), but impact will depend on IDU behavioural heterogeneity and syringe preference.

Indirect evidence suggests that encouraging HDSS users to use LDSS could be a powerful HIV prevention strategy. There is an urgent need to evaluate the real life effectiveness of this strategy.

Introduction

In this issue (Zule, Cross et al., 2012) and elsewhere, Zule et al. has presented evidence suggesting the use of low dead-space syringes (LDSS), instead of high dead-space syringes (HDSS), could be an important strategy for reducing the transmission of HIV and HCV amongst injecting drug users (IDUs). The evidence for this hypothesis comes from different sources, but is primarily based on experimental data suggesting LDSS may retain 40 times less fluid than HDSS (Zule, Ticknor-Stellato et al., 1997). This finding, with associated experimental data that found the volume of blood retained in LDSS after 2 rinses could be about 1000 times less than in HDSS (Zule et al., 1997), led Zule et al. to suggest, with support from modelling (Bobashev & Zule, 2010), that HIV epidemics may not be sustainable in settings where HDSS are infrequently used.

Epidemiological evidence linking the use of HDSS with increased HIV or HCV transmission risk is emerging, but is still limited (WHO, 2012). At the individual level, data from IDUs in Texas (Zule, Desmond et al., 2002) showed a borderline association between prevalent HIV infection and the use of HDSS, but were unable to sufficiently control for important confounders, whereas more recent data from South Carolina (Zule & Bobashev, 2009) showed a strong association with HIV and HCV prevalent infection and ever using HDSS, after controlling for numerous factors. A similar but weaker association (only significant when not controlling for confounders) between prevalent HCV infection and HDSS use was also found in Budapest (Gyarmathy, Neaigus et al., 2009). However, no analyses have shown an individual-level association between recent use of HDSS and risk of HIV or HCV incident infection, or a dose response association between different levels of HDSS use and the risk of HIV or HCV prevalent or incident infection.

Weak evidence is also provided at the ecological level, with a possible association between majority use of LDSS and lower HIV prevalence at the city level (Zule et al., 2012) compared to cities with majority use of HDSS. Although at face value this supports

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the hypothesis that using LDSS is protective, the association needs rigorous evaluation. For example, it is necessary to understand why certain settings seem to not fit with the relationship (Tallinn in Estonia and Ho Chi Minh City in Vietnam), and to determine whether other factors could have resulted in the observed association, as was potentially the case in a previous ecological analysis considering Hungary and Lithuania (Gyarmathy, Neaigus et al., 2010).

Although it seems biologically plausible that the use of LDSS instead of HDSS could provide some protection against the transmission of HIV and HCV, there is still considerable uncertainty over the level of this protection. Therefore, we review and re-evaluate the degree to which LDSS could transmit fewer infections than HDSS, and how this could translate into an effect of using LDSS on HIV prevalence within an IDU population. To this end, we consider the following questions:

1. How much less dead-space is there in LDSS compared to HDSS?
2. How much less blood is transferred by LDSS compared to HDSS?
3. How could the differences in blood transferred between LDSS and HDSS translate into differences in infectivity?
4. What impact could using LDSS have on a HIV epidemic where HDSS are currently used?

How much less dead-space is there in a LDSS compared to a HDSS?

We undertook a review in pubmed to find articles that measured the quantity of dead-space fluid retained by different HDSS and LDSS. The search was undertaken on 5th September 2012 and used the following search terms: "syring* AND (residual OR "deadspace" OR "dead-space" OR "dead space")". The reference list for each article was also scanned for additional relevant articles. The search found 280 hits, of which 12 studies included 48 estimates of the dead-space of different LDSS and HDSS (Bhambhani, Beri et al., 2005; De Stefano, Abechain et al., 2011; Exchange supplies, 2012; Gaughwin, Gowans et al., 1991; Hall, Thompson et al., 1984; Hoffman, Larkin et al., 1989; Macfie, 1990; Nelson, Sutanto et al., 1999; Ribeiro, Messias et al., 2009; Strauss, van Zundert et al., 2006; Watanachai & Suprasongsin, 2003; Zonouzi, 2010; Zule et al., 1997). The studies covered a wide range of different syringe volumes (from 0.3 to 20 ml), needle lengths (8–25.4 mm), and needle gauges (23–30 gauge). Fig. 1 presents the estimates from these different studies, and in agreement with Zule et al. shows that HDSS retain greater fluid than LDSS. However, there is considerable variability in the estimates depending on syringe volume and needle type (detachable or integrated). On average, the difference is much smaller than Zule et al. previously estimated, with a mean of 6 μl [range 0.62–41 μl] being retained by integral LDSS and 60 μl [range 26–98 μl] by HDSS. This translates to roughly 10 times more fluid being retained by HDSS compared to integral LDSS, less than the 40 times estimated by Zule et al. (1997). Even smaller ratios between HDSS and LDSS have been found by single authors, for example a recent study (Strauss et al., 2006) examined the dead-space of different 1 and 2 ml LDSS and HDSS – finding only 2.3 to 5-fold greater dead-space with their detachable HDSS (estimated 15 μl dead-space for their 1 ml integral LDSS). These differences are likely due to the wide variety of syringes in production by different producers, and also to a smaller extent the different length and gauge of needle used.

A 2012 study conducted in 17 countries in Eastern Europe and Central Asia determined that injectors avoided using LDSS because most had integrated needles (which prevented replacement if clogged or blunted), and were supplied in small sizes (usually 1 ml syringes) (Ibragimov & Latypov, 2012). These preferences have important consequences for retained fluid volume. Data from the review suggested substantial differences in dead-space between LDSS with detachable and integrated needles. LDSS with detachable needles (plunger has displacement spike that reduces dead-space, Exchange supplies, 2012) still have considerable dead-space, with three times the dead-space of integral LDSS and only 66% less dead-space than HDSS. Lastly, as should be expected, larger volume syringes tend to have larger dead-space (De Stefano et al., 2011; Macfie, 1990; Zule et al., 2012) due to wider syringe diameters, but not to a great extent.

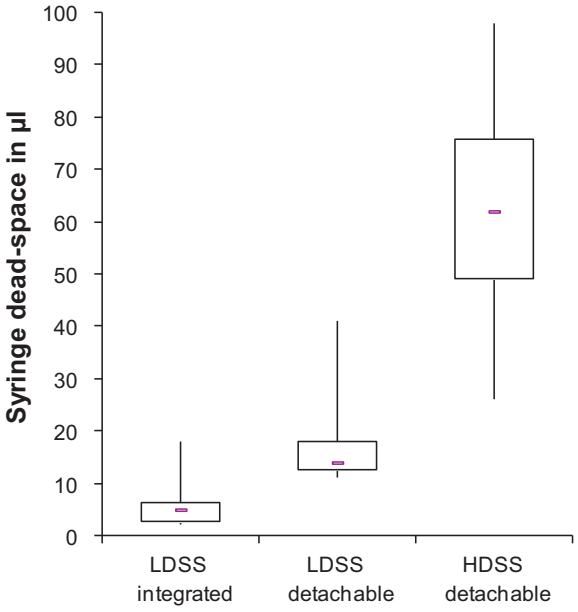

Fig. 1. Syringe dead-space volume by type of syringe, for data found in the review. The box plots signify the variability (middle line is median, limits of boxes are 25% and 75% percentiles and whiskers are minimum and maximum estimate) in the syringe dead-space of different syringe types. LDSS denotes low dead-space syringes and HDSS denotes high dead-space syringes.

How much less blood is transferred by LDSS compared to HDSS?

The amount of blood and viable HIV that is retained by a syringe and subsequently transferred to the next user increases with the volume of dead-space in the syringe (Abdala, Gleghorn et al., 2001; Gaughwin et al., 1991; Zule et al., 1997) and if the previous injector booted (Gaughwin et al., 1991), whereas it decreases with the number of rinses with water and the volume of water used to rinse (Abdala et al., 2001; Gaughwin et al., 1991).

Experimentally, Zule's study from 1997 (Zule et al., 1997) estimated that on average >842 times more blood would be transferred to the next user from re-using HDSS instead of LDSS after two rinses with water (Table 1). However, a similar experiment undertaken by Gaughwin et al. (1991) found much smaller differences than Zule, with HDSS transferring about 10–30 times more blood than LDSS following one rinse, or 2–20 times more blood after three rinses (no estimates reported for 2 rinses). Similarly, Abdala et al. examined the viability of HIV-1 recovered from LDSS and HDSS, finding viable HIV-1 in just over twice as many HDSS than LDSS after one rinse with water (Abdala et al., 2001).

In the absence of experimental data, theoretical estimates for the volume of blood transferred can also be calculated to explore the effect of different injection practises such as registering, booting, and rinsing with water (see Box 1 – similar calculations previously undertaken by Zule et al. (2002)). Model projections based on the mean dead-space volumes from our review suggest