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**Dried Blood Spot (DBS) and mini-tube (MT) blood sample collection kits for postal HIV testing services: A comparative review of successes in a real-world setting**

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**Abstract**

**Objectives:** This is a comparative review between using dried blood spot (DBS) and mini-tube (MT) HIV sampling kits as part of an online sexually transmitted infection (STI) postal testing service. England has recently seen increases in internet-based and postal (eHealth) STI services. Expanding accessibility and testing for patients, cost implications, and narrowing the HIV undiagnosed margin are drivers for this. **Methods:** In 2017, data were reviewed from an online postal STI kit requesting service at a time of transitioning from MT to DBS. We compared the STI postal kit and HIV blood sample return rates, and the successful processing/analysis rates of the DBS and MT kits. Descriptive statistics were applied to participant characteristics, with Pearson's Chi-squared or Fisher exact test used to demonstrate statistical differences. We also describe and calculate a 'request-to-result ratio'

(RRR) for both kit types. The RRR is defined as the number of online kit requests required to produce one successfully analysed result. **Results:** 550 STI postal kit requests from a North-West of England region were reviewed from 13/06/17 – 22/09/17 (275 MT, 275 DBS). Baseline characteristics between the two groups were comparable, (63% female, 90% white British, and 86% heterosexual with a median age of 26 years). The successful processing rate for the DBS was 98.8% c.f. 55.7% for the MT ( $p < 0.001$ ). The RRR for MT was 2.96, c.f. 1.70 for DBS. There was a 5.4% false positive HIV rate in the MT c.f. none in the DBS. **Conclusions:** This comparative analysis suggests that in this community setting, the use of postal HIV DBS kits resulted in a significantly improved RRR compared with MT. The biggest factor was the large number of MT samples not analysed due to inadequate blood volumes. The unexpected level of false positive results in the MT samples needs confirming in larger studies.

## **Introduction**

Postal sampling kits for HIV and sexually transmitted Infections (STIs) are being rapidly adopted as part of an expansion of eHealth.<sup>1</sup> In England there has been a drive towards increasing the uptake of STI testing without increasing staffing pressures,<sup>2,3</sup> and diagnosing those infected with HIV who are unaware of their HIV status, which in turn will meet international HIV testing targets.<sup>4,5</sup>

The effectiveness of postal testing kits has not been robustly tested and relies on many assumptions around the utility of the postal sampling/testing process as a whole.

Ideally, each kit is requested online (internet-based), dispatched, received by the laboratory and processed. The generated results are then conveyed to the client either electronically or via a telephone call from the service to the client in the instance of non-negative results.

This system is a multi-stepped process which requires evaluation. The importance of research into sample collection methodology and clinical laboratory techniques and diagnostics is clear, yet lacking.

In England, HIV testing on finger-prick capillary blood sampling (CBS) into mini-tubes (MT) is the commonest form of sampling employed. Blood is collected into a 500µL MT, processed in the laboratory and tested for HIV antibody/antigen. Other systems use finger-prick CBS applied onto specialised filter paper [dried blood spot (DBS)]. The sample volumes required for DBS are smaller and can remain stable for months until they are processed.<sup>6</sup> The processing of DBS samples requires an additional sample extraction step prior to analysis<sup>7</sup> making them more costly, with fewer laboratories accredited to analyse them.

We worked with the HIV and Sexual Health awareness charity Saving Lives (SL), who developed a postal STI and HIV testing service in collaboration with their partners and Public Health England Birmingham laboratories.

We aimed to ascertain how DBS HIV kits compared to MT kits in this postal testing service. The primary objectives were to record the STI kit request and subsequent return rates and determine the proportion of blood samples successfully processed and analysed for both kit types.

All kits contained identical capillary lancets with instructions, were requested and dispatched from the same provider, and analysed in the same accredited laboratory for both HIV and syphilis.

Additionally the kits contained sample collection systems for chlamydia and gonorrhoea. Our secondary aim was to describe a request-to-result ratio (RRR); the required number of kit requests to obtain one successfully processed result. We also calculated the false positivity rates of DBS and MT.

## **METHODS**

### Design

This pragmatic review consecutively compared MT followed by DBS regarding their performance as part of an STI postal sampling kit.

We determined the online request, return, processing and analysis rates of the HIV blood sampling component of the STI kits for a single service, whose consumers were requesting STI self-sampling kits from an online platform.

The study was conducted when a North-West of England sexual health clinic (local HIV prevalence 1.09/1,000 people)<sup>8</sup> that SL provided a service for, was motivated to move away from MT blood collection systems, towards DBS, primarily due to high sample rejection rates.

This service evaluation used retrospective anonymised data collected for the purposes of routine clinical care from the SL database. Participants had consented for their anonymised data to be shared by a third-party organisation (SL). We used the MRC “Is my study research?” toolkit on

<http://www.hra-decisiontools.org.uk/research/> which considered the study as research. We subsequently used the MRC “Do I need NHS REC approval?” decision toolkit on <http://www.hra-decisiontools.org.uk/ethics/>, which stated that research ethics committee (REC) approval was not required.

For details on information governance for the online IT systems please see *appendix 1*.

The primary analysis compared rate outcomes among those who used the MT for HIV sampling with those who used DBS.

#### Laboratory methodology

Please see *appendix 2* for details of laboratory sample processing and analysis.

#### Statistical analysis

Anonymised data was extracted from the SL charity database. These data are routinely collected, as quality control information is required as part of the standard clinical service provided to local sexual health services. This information was transferred into Microsoft Excel (2016) where data management was conducted.

User baseline characteristics, STI kit return rates, HIV sample return rates, completed processing and analysis rates of the MT and DBS, were compared using Pearson’s Chi-squared test, or Fisher exact test where values were  $\leq 5$ .

The RRR was calculated by dividing the kit request number by the number of successfully processed and resulted samples. Analyses were performed using Microsoft Excel (2016).

## **RESULTS**

### Baseline characteristics

550 postal STI kits (275 MT, and 275 DBS) were requested online between dates 13/06/17 – 22/09/17. From 13/06/17 – 04/08/17 the kits contained MT for HIV sampling, and from 04/08/17 – 22/09/17, contained DBS. The overall baseline characteristics of those requesting were comparable between the MT and DBS groups (63% female, 90% white British and 86% heterosexual, with a median age of 26 years) (see Appendix 3: Baseline characteristics).

#### Kit return and processing rates

There was no statistical difference in either kit or HIV sample return rates between the MT and DBS. The DBS samples demonstrated a significantly higher successful HIV sample processing rate than the MT, with 98.8% of DBS samples being successfully processed c.f. 55.7% of MTs.

*Table 1. Summary of comparisons of MT and DBS for HIV sampling*

<b>Test type</b>	<b>STI Kit Return/Request n (%)</b>	<b>HIV Sample Return/STI kit return n (%)</b>	<b>Successful HIV sample processing &amp; analysis/HIV sample return n (%)</b>	<b>Overall HIV result obtained/STI kits requested n (%)</b>	<b>Request-to-result Ratio (RRR) n (ratio)</b>
<b>Mini-tube</b>	189/275 (68.7)	167/189 (88.4)	93/167 (55.7)	93/275 (33.8)	275/93 (2.96)
<b>Dried Blood Spot</b>	183/275 (66.5)	164/183 (89.6)	162/164 (98.8)	162/275 (58.9)	275/162 (1.70)
<b>p-value</b>	0.58	0.70	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>

#### Sample processing failures

We considered reasons why blood samples were not processed for analysis. A significantly higher number of MT (62/96) was not processed due to an insufficient sample being provided compared with the DBS (2/21) (see Appendix 4: Reasons for samples not being analysed).

#### False positivity

Of the successfully analysed samples, the MT produced a 5.4% false positive rate compared with none for those testing by DBS.

## **DISCUSSION**

In this comparative review, we found DBS sampling for HIV had significantly better processing and analysis rates than MT. A large proportion of MT samples had insufficient blood volumes which appear to be the leading cause for discrepancy in performance.

STI kit and HIV sample return rates were similar in both groups (just below 70%) which are high for a free postal testing service. We were surprised that the MT return rate was as high as the DBS kits as this has not been the case at SL other testing sites (data not shown, personal communication, D Hartland).

This small analysis yielded an unexpected high false positive HIV rate among MT users. This could be due to the reduced stability of MT samples over time. This has major clinical implications if this were replicated in a larger dataset.

### Limitations

We acknowledge several limitations to this comparative review. It was conducted consecutively for pragmatic reasons, but ideally we would have preferred a parallel comparison. Selection bias is diminished by similarities of the baseline characteristics. All kits were processed in the same laboratory, with staff receiving the same standardised training.

Due to the methodology, we were unable to produce sensitivity or specificity data for this sample, which would have provided measures of test accuracy in a real-world setting.

The duration of the review was short and participant numbers relatively small. This may explain the lack of HIV positive diagnoses in this low prevalence area. This review may not be generalizable as it

was conducted at a single centre. An observation of a larger number of kits over several regions may improve the robustness of this comparative review.

A patient satisfaction questionnaire, would have provided a richer source of information around acceptability, and may provide insight on other aspects of the sampling process.

### Conclusion

Based on this small data set, we highlight the superior efficacy of DBS postal HIV kits compared with MT, as defined by its significantly better RRR. The RRR provides us with a different unit of measure for postal HIV and STI kit services. It can be objectively used to compare how system changes and service delivery models can affect overall kit performance.

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### Declaration of Interests

- *Dr S Taylor is the unpaid Medical Director of the Saving Lives charity which provides the postal testing systems described in this manuscript.*
- *Mr Daniel Hartland is the Director of operations for the Saving Lives charity which provides the postal testing systems described in this manuscript.*
- *Mr Mark Simpson is the head developer of the Saving Lives IT digital systems used in the postal testing systems described in this manuscript.*
- *SA, ES, SW and CA are employees of Public Health England Laboratories Birmingham.*

### Contributions

- *MP, ST and DH, SW drafted the manuscript.*
- *MS, DH and ST co-developed the Saving Lives postal testing system, extracted the data and ensured good clinical governance throughout the data extraction process.*
- *MP, ST and MW performed the statistical analysis.*
- *SA, ES, SW and CA developed and validated the HIV DBS testing system for PHE Birmingham described in this manuscript.*
- *All authors contributed to intellectual discussions and amendments to the final manuscript.*

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