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Short report

Evidence of HIV pre-exposure or post-exposure prophylaxis (PrEP/PEP) among blood donors: a pilot study, England June 2018 to July 2019

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ABSTRACT

Objective Due to increased use of pre-exposure prohylaxis (PrEP) and its potential to affect HIV screening of blood donors, we undertook antiretroviral residual testing among HIV-negative male donors in England.

Methods Residual plasma samples were obtainnd from 46 male donors confirmed positive for syphilis and 96 donors who were repeat reactive for HIV antibodies in screening but confirmed as HIV-negative by reference testing. These were tested for concentrations of tenofovir and emtricitabine by high-performance liquid chromatograhpy coupled with mass spectrometry.

Results We found evidence of pre-exposure or post-exposure prophylaxis (PrEP/PEP) use in three male blood donors confirmed positive for syphilis (3 out of 46 screened, 6.5%). Two were estimated to have taken PrEP/PEP within a day of donating, and the third within 2 days. Two were new donors, whereas one had donated previously but acquired syphilis infection after his last donation.

Conclusions Our findings indicate that a small proportion of blood donors have not been disclosing PrEP/PEP use and therefore donating in non-compliance to donor eligibility criteria.

STUDY

The use of pre-exposure prophylaxis (PrEP) for prevention of HIV transmission has expanded rapidly in high-income countries over the past 5 years.[1] PrEP consisting of oral tenofovir disoproxil fumarate and emtricitabine (FTC) taken daily or on-demand prior to potential sexual exposure has been shown to be highly effective in preventing HIV infection in men who have sex with men (MSM; 86%).[2–5] In England, it has been mainly supplied through the Impact Trial (2017–2020[6]), via genitourinary medicine clinics or on-line sources since 2015. However, PrEP was finally made available via the NHS on March 2020.[7] It has been estimated that by the end of 2019, 19 500 people, largely gay and bisexual men, were accessing PrEP in the UK.[8] Although PrEP has contributed to the declining numbers of new HIV diagnoses, it has alerted the international blood transfusion communities to consider its potential effects on blood safety.[9 10]

Blood transfusion is a more effective means of virus transmission than sexual behaviour; HIV transmission via blood transfusion is possible and has been described in cases of non-detectable viral load.[11 12] With a combination of donor deferral policies together with highly effective serological and molecular screening of blood donations, the risk of not detecting and releasing a potentially infectious HIV donation has been estimated around 0.04/million donations in the UK (95% CI 0.01 to 0.07) and no transfusion-transmitted HIV infection has been reported in the UK since 2002.[13 14] However, the effects of PrEP on assays used to screen blood donors for HIV are well recognised by international blood transfusion communities. Both suppression of viral load and delayed seroconversion have been observed, most often in 'on demand' PrEP users or with suboptimal adherence.[15 16] In particular, caution has been urged in the interpretation of negative and indeterminate serology results in those donors who are on PrEP. In England, a 3-month precautionary deferral of anybody taking PrEP was introduced into the donor questionnaire in March 2019 for the aforementioned reasons. Prior to that, PrEP use was expected to be captured through a general question asking donors about use of any prescribed medicines or over-the-counter drugs and treatments that they may have purchased themselves in the last 7 days.

A resurgence of syphilis during the last decade has also been documented in MSM population.[17] It is likely that the introduction of PrEP has led to increased sexual risk behaviours such as increasing number of partners and reduced condom use, and consequently to increased syphilis transmission.[18] Although syphilis is not a major blood transfusion risk in developed countries, it may be considered a marker of being in a high-risk socio-sexual network whether the donor knows this or not and hence many countries have continued to screen blood donations for syphilis.

Due to the increased use of PrEP, its potential to affect HIV screening and knowledge that pre-donation information may not reach all donors, we have undertaken testing for traces of antiretrovirals to get a better understanding of undeclared PrEP use among HIV-negative male blood donors in England. We focused on two defined groups of males: those HIV-reactive at screening but subsequently confirmed negative and those who were confirmed positive for treponemal antibodies denoting syphilis infection. This information will

Table 1 Characteristics of male blood donors with syphilis, July 2018 to June 2019 (n=46)

Donation month	Donor type	Age group	Ethnicity§	Possible source of infection and likely timing	Male partners	Syphilis status	Evidence of PrEP use
07/2018	Repeat	31–40	White British	Two new female partners	No	Past	No
07/2018	First-time	51–60	Asian	None identified	No	Past	No
08/2018	Repeat	61–70	White British	New sexual female partner; 2 months ago	No	Acute	No
09/2018	First-time	21–30	White British	None identified	No	Past	No
09/2018	First-time	41–50	White Other	None identified	No	Past	No
09/2018	First-time	41–50	White British	New sexual male partner; 3–6 months ago	Yes	Acute	No
10/2018	First-time	31–40	White British	Known past syphilis	No	Past	No
10/2018	First-time	61–70	White British	None identified	No	Past	No
11/2018	Repeat	61–70	White British	None identified	No	Past	No
11/2018	First-time	31–40	White British	Known past syphilis	No	Past	No
11/2018	Repeat	31–40	White British	Wife diagnosed with syphilis	No	Acute	No
11/2018	First-time	31–40	White British	Known past syphilis	No	Past	No
11/2018	First-time	51–60	Black African	Known past syphilis	No	Past	Yes*
12/2018	First-time	21–30	Black African	None identified	No	Past	No
12/2018	Repeat	21–30	White British	Male partners	Yes	Past	No
01/2019	Repeat	51–60	White British	New sexual female partner; few months ago	No	Acute	No
01/2019	Repeat	51–60	White British	New sexual female partner; few weeks ago	No	Acute	No
01/2019	Repeat	31–40	White British	New sexual female partner; 5 months ago	No	Acute	No
01/2019	Repeat	51–60	White British	None identified	Yes	Past	No
02/2019	First-time	21–30	White British	None identified	Yes	Acute	No
02/2019	Repeat	41–50	White British	None identified	No	Acute	No
02/2019	First-time	41–50	White Other	Known past syphilis	No	Past	No
02/2019	Repeat	51–60	Unknown	New sexual female partner; few months ago	No	Acute	No
02/2019	First-time	21–30	White British	No response	No	Past	No
03/2019	Repeat	41–50	White British	Known past syphilis (year ago)	Yes	Past	Yes†
03/2019	Repeat	41–50	White British	New sexual female partner; 1 month ago	No	Acute	No
03/2019	First-time	31–40	White British	Known past syphilis	Yes	Past	No
03/2019	First-time	31–40	Other	Known past syphilis	No	Past	No
03/2019	First-time	41–50	Asian	None identified	No	Past	No
04/2019	First-time	31–40	White Other	No response	Yes	Past	Yes‡
04/2019	First-time	31–40	White Other	Known past syphilis	Yes	Past	No
04/2019	Repeat	41–50	Asian	None identified	No	Past	No
04/2019	First-time	31–40	Asian	Known past syphilis	No	Past	No
04/2019	First-time	31–40	White British	Known past syphilis	Yes	Past	No
05/2019	First-time	31–40	White Other	None identified	No	Past	No
05/2019	First-time	51–60	Asian	None identified	No	Past	No
05/2019	First-time	31–40	White British	None identified	No	Past	No
05/2019	First-time	41–50	White Other	Known past syphilis	Yes	Past	No
05/2019	Repeat	21–30	White British	Male partner	Yes	Acute	No
05/2019	Repeat	31–40	White British	Male partners	Yes	Past	No
05/2019	First-time	61–70	White British	Female partners	No	Past	No
06/2019	First-time	31–40	White Other	Female partners	No	Acute	No
06/2019	First-time	31–40	Asian	None identified	No	Past	No
06/2019	First-time	21–30	White British	Male partner years ago, now female partners	Yes	Acute	No
06/2019	First-time	41–50	Black African	Known past syphilis	No	Past	No
06/2019	First-time	51–60	Asian	None identified	No	Past	No

Known past syphilis infection is marked in red; past syphilis is a contra-indication for blood donation.
*TFV 73.58 ng/mL, FTC 748.46 ng/mL.
†TFV 210.52 ng/mL, FTC 412.78 ng/mL.
‡TFV 39.96 ng/mL, FTC not detected.
§Asians included individuals born India (n=4), Pakistan (n=2) and Bangladesh (n=1); White Other included those born in Romania (n=4) and one born in Turkey, Luxembourg and Spain; Black Africans were from Ghana (n=1) and Uganda (n=1); an indivual classed as Other was born in Brazil.
FTC, emtricitabine; PrEP, pre-exposure prophylaxis; TFV, tenofovir.

guide the further measures taken within the blood services in order to continue the provision of safe blood.

Residual plasma samples from 142 male blood donors were collected between July 2018 and June 2019. These included 46 donors confirmed positive for syphilis and 96 donors who were repeat reactive for HIV antibodies on screening but confirmed as HIV-negative by reference testing. This HIV testing pattern was considered as a potential marker of PrEP use because of antibody suppression. All confirmed positive donors are routinely contacted for a post-test discussion about follow-up required but also aiming to identify any risk factors. The male HIV-screen reactive donors were also contacted by phone as part of the pilot study to collect information about awareness of PrEP, PrEP use and any specific risk factors for HIV infection. These data were analysed after anonymisation together with basic donor characteristics including age,

ethnicity, previous donation history and laboratory testing data.

Concentrations of tenofovir (TFV) and FTC were measured in stored plasma samples by high-performance liquid chromatography coupled with mass spectrometry.[18 19] The lower limit of quantification was 5 ng/mL for both analytes, and the lack of detection of TFV/FTC analytes indicates that no PrEP had been taken within the last 5 days before donation. Plasma TFV concentrations of 10 ng/mL and higher are consistent with a PrEP dose within the previous 2 to 3 days, whereas plasma TFV concentrations around 100 ng/mL have been demonstrated in PrEP users 16 hours post dose. It is important to note that post-exposure prophylaxis (PEP) contains also TFV/FTC and hence with this study we cannot differentiate between PrEP and PEP use. However, PrEP use is generally more common and hence more likely here.

Signed consent was obtained from each donor at the time of donation. Donor consent to NHS Blood and Transplant (NHSBT) includes holding information about their health, attendances and donations. It also covers research which improves our knowledge of the donor population.

We found evidence of PrEP/PEP use in donation samples obtained from male donors confirmed positive for syphilis (table 1), but not in samples obtained from donors who were found HIV-reactive in screening. Of 46 samples from syphilis-positive donors, two had detectable levels of both TFV and FTC and one only TFV (6.5%). Two of them were estimated to have last taken PrEP/PEP medication within a day of donating, and the third one likely within 2 days. Blood donors in England were not specifically asked about PrEP usage at the time of this study, although they would have been expected to declare this under 'use of any medication', including over-the-counter medication.

Two of the syphilis-positive donors with evidence of PrEP/PEP use were new donors, whereas one had donated previously but acquired syphilis infection after his last donation. Interestingly, a third of the syphilis-positive donors should not have donated as they either had a history of syphilis or had injected non-prescribed drugs (14/46; 30%). These included the two donors with PrEP/PEP use, whereas no response was obtained from the third donor. The median age of syphilis-positive donors was 42 years (range 22 to 70 years); the donors with evidence of PrEP/PEP were aged between 31 and 60 years. Furthermore, most male syphilis-positive donors were White British born in the UK (27/46, 59%), including one donor with evidence of PrEP/PEP use. A total of 13 donors had likely recently acquired syphilis based on their positive IgM result, but all three PrEP/PEP donors had markers in keeping with past syphilis. One was a regular donor who had been diagnosed with syphilis over 1 year before this donation, and as he has already lost his IgM antibodies, his infection was classed as past. Another 13 donors had previous or current male partners, including two with evidence of PrEP/PEP use. One of them complied with the current MSM deferral rules whereas the other donor did not participate to post-donation discussion.

This is the first study in Europe to provide data on PrEP/PEP usage among blood donors, including those diagnosed with syphilis. The urgent need to investigate the extent of PrEP use among blood donors was highlighted by the recent study demonstrating PrEP use first by detecting analytes in 0.6% of first-time male donors in the USA (9/1494) and second by a survey where 5% of blood donors identifying as MSM reported taking PrEP.[11]

Our pilot findings indicate that a measurable proportion of blood donors were non-compliant due to their undisclosed PrEP use. Although a question on PrEP use has since been added to the blood donor questionnaire, we believe there is still a risk of non-compliance. The donors who had been non-compliant with the other high-risk behaviour–related questions were perhaps also unlikely to comply with a PrEP question; two out of three donors with evidence of PrEP use identified in this study did not disclose their previous treated syphilis infection. While the public health message 'undetectable equals untransmittable' (U=U) has been successfully communicated, it is not perhaps always remembered that this applies to sexual transmission only and not to risk of transmission via blood. We need to better communicate this particular message to blood donors and medical communities providing care to individuals on PrEP. Hence, different means of communications will need to be applied in parallel with clear and defined messages including donor selection criteria and explanations for a 3-month precautionary deferral of anybody taking PrEP. In order to understand the extent of PrEP use among blood donors in England, we need to consider larger studies. Furthermore, in future, all samples obtained from individuals with evidence of PrEP use should also be subjected for other HIV assays including proviral DNA testing. In countries where use of PrEP is increasing, it is important to consider clear donor messaging, further screening for PrEP and review whether the current HIV testing strategy is optimal in the PrEP era.

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Contributors HH conceptualised and planned the study, with input received from SI, SB and SK. VM and CR helped to organise the samples for testing; testing was performed by SDP, AA and LE in the laboratory of SK. HH also analysed the data and drafted the manuscript. All authors contributed to the manuscript and have confirmed the submitted version.

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