Free HIV self-test for identification and linkage to care of previously undetected HIV infection in men who have sex with men in England and Wales (SELPHI): an open-label, internet-based, randomised controlled trial

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Summary

Background High levels of HIV testing in men who have sex with men remain key to reducing the incidence of HIV. We aimed to assess whether the offer of a single, free HIV self-testing kit led to increased HIV diagnoses with linkage to care.

Methods SELPHI was an internet-based, open-label, randomised controlled trial that recruited participants via sexual and social networking sites. Eligibility criteria included being a man or trans woman (although trans women are reported separately); being resident in England or Wales, UK; being aged 16 years or older; having had anal intercourse with a man; not having a positive HIV diagnosis; and being willing to provide name, email address, date of birth, and consent to link to national HIV databases. Participants were randomly allocated (3:2) by computer-generated number sequence to receive a free HIV self-test kit (BT group) or to not receive this free kit (nBT group). Online surveys collected data at baseline, 2 weeks after enrolment (BT group only), 3 months after enrolment, and at the end of the study. The primary outcome was confirmed (linked to care) new HIV diagnosis within 3 months of enrolment, analysed by intention to treat. Those assessing the primary outcome were masked to allocation. This study is registered with the ISRCTN Clinical Trials Register, number ISRCTN20312003.

Findings 10 111 participants (6049 in BT group and 4062 in nBT group) enrolled between Feb 16, 2017, and March 1, 2018. The median age of participants was 33 years (IQR 26–44 years); 9000 (89%) participants were White; 8118 (80%) participants were born in the UK; 81 (1%) participants were transgender men; 4706 (47%) participants were university educated; 1537 (15%) participants had never been tested for HIV; and 389 (4%) participants were taking pre-exposure prophylaxis. At enrolment, 7282 (72%) participants reported condomless anal sex with at least one male partner in the previous 3 months. In the BT group, of the 4511 participants for whom HIV testing information was available, 4263 (95%) reported having used the free HIV self-test kit within 3 months. Within 3 months of enrolment there were 19 confirmed new HIV diagnoses (0·31%) in 6049 participants in the BT group and 15 (0·37%) of 4062 in the nBT group (p=0·64).

Interpretation The offer of a single, free HIV self-test did not lead to increased rates of new HIV diagnoses, which could reflect decreasing HIV incidence rates in the UK. Nonetheless, the offer of a free HIV self-testing kit resulted in high HIV testing rates, indicating that self-testing is an attractive testing option for a large group of men who have sex with men.

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Introduction

In the UK, from 2015 onwards, HIV incidence in men who have sex with men (MSM) began a rapid decline.[1–4] Combination prevention was central to this decline,[1,4] through expansion of HIV testing, early initiation of antiretroviral therapy (ART) after HIV diagnosis, and increased use of pre-exposure prophylaxis (PrEP).[5,6]

Globally, knowledge of HIV status through testing remains key to attaining UNAIDS 95-95-95 goals[7] and progressing to global targets for elimination of HIV transmission. In the UK, despite the decline in incidence, MSM remain at highest risk of HIV, and although testing rates have increased over the past decade, the number of diagnoses that are late (CD4 count <350 cells per µL) remains too high. An estimated 4200 MSM are living with undiagnosed HIV in the UK.[2] Early diagnosis of HIV and initiation of ART also has population-level benefits because effective HIV viral suppression in

Research in context

Evidence before this study

Before this trial, almost a quarter of men who have sex with men (MSM) in the UK living with HIV were estimated to be unaware of their HIV infection and disproportionally contributing to onward transmission. Clearly, innovative HIV testing strategies were required. HIV self-testing had the potential to increase initial and repeat testing rates due to confidentiality and convenience, and they needed to be evaluated in a European setting. Formative qualitative research done to inform the trial indicated a role for HIV self-testing. We found that MSM preferred blood-based self-tests, delivered through the postal system and with clear links to further support included. Our 2020 meta-analysis comparing HIV self-testing to standard HIV testing approaches for key populations included ten randomised controlled trials, seven of which were done with MSM and small numbers of transgender people. We found that HIV self-testing increases HIV testing uptake and frequency, without adverse effects on condom use. HIV self-testing detected greater numbers of positive results than standard testing services, including mail and online delivery approaches, for MSM and transgender people. However, these data on positive HIV self-tests often relied on self-report, and often had low survey completion rates. In addition, HIV self-testing led to worse linkage to care for key populations overall, but these results were not statistically significant for MSM and transgender people.

Added value of this study

The SELPHI trial remains the largest HIV self-testing trial implemented in a high-income setting and one that was also fully internet-based. The SELPHI trial, and associated formative work, has generated a substantial body of evidence supporting the development, implementation, and evaluation of HIV self-testing among MSM and transgender people in high-income settings. The trial addressed key questions regarding the potential of HIV self-tests for increasing HIV testing uptake without reducing STI testing or linkage to HIV care. For high prevalence settings, this trial provides useful evidence on how self-testing offered through an internet-based platform could be used to increase HIV testing among MSM.

Implications of all the available evidence

Because the HIV response in high-income countries is increasingly focused on the elimination of new transmissions, HIV self-testing plays a key role in expansion of HIV testing to facilitate timely HIV diagnosis and access to care. Questions remain as to how HIV self-testing is best situated alongside multiple testing opportunities before widespread implementation and, in particular, how to support HIV self-testing provision in a way that responds to existing inequities (related to ethnicity, migration status, geography, gender and sexual identity, health status, and digital literacy) while improving health.

people living with HIV eliminates sexual transmission to other individuals.[8] It is important that MSM are diagnosed as soon as possible after acquiring HIV infection because up to 80% of all HIV transmissions are estimated to derive from individuals who are undiagnosed.[9] National and international guidelines for recommended frequency of HIV testing in MSM are similar in the USA, Australia, and the UK, where annual HIV testing for sexually active MSM is recommended, and testing every 3–6 months is recommended for individuals who have frequent condomless anal sex, have multiple sexual partners, or partake in sexualised drug use.[10–12]

However, although the rates of HIV testing in MSM living in the UK are increasing, they remain suboptimal.[13,14] In particular, rates of testing are low in MSM at increased risk of HIV infection through condomless anal sex with multiple partners. Our published analysis of baseline characteristics in the SELPHI trial found that less than 60% of MSM who had two or more recent condomless anal sex partners had tested for HIV in the 6 months before enrolment.[15] Factors associated with lower than recommended rates of HIV testing were lower levels of formal education and living in Wales or the northeast of England, which indicates potential geographical barriers to testing.[15]

The motivations that influence testing behaviours of MSM, particularly those who engage in high-risk behaviours, are complex. However, one factor that affects HIV testing is the influence of structural barriers to obtaining a test, including time constraints or geographical distance to clinics. A further barrier to testing could be concerns about disclosure of sexual practices and sexual activity, and perceived stigma,[16–20] particularly in MSM who do not identify as gay. With HIV self-testing, the person not only takes the sample but also immediately processes it themselves, so only they are aware of the result. Increased ease of access to HIV testing is a key attribute of HIV self-testing, but there is little evidence about whether increasing access to this modality increases HIV diagnosis rates in MSM.

The aim of the first stage of randomisation in the SELPHI randomised controlled trial was to assess if the offer of a single free HIV self-testing kit to MSM led to increased diagnosis of HIV infections and linkage to care. Data for trans women were collected as part of this trial; however, their data are reported separately.

Methods

Study design

SELPHI was an open-label, internet-based randomised controlled trial with a two-stage randomisation (appendix p 8) that has been described in full previously.[21]

See Online for appendix

All trial processes, including recruitment, took place online, although participants had to be resident in England or Wales, UK, to receive delivery of the test kit. The main rationale for the first stage of randomisation was to evaluate the role of self-testing in detecting prevalent (possibly long-standing) HIV infections. In this Article, we report the procedures and results of the first stage of randomisation. Results from the second stage of randomisation will be published separately. The full study protocol is available online. Ethics approval was granted by the UCL Research Ethics Committee (REC Number 9233/001).

For the **full study protocol** see http://www.selphi.org/application/files/3516/4154/9192/SELPHI_Protocol_V4.0_17Dec19.pdf

Extensive formative work was conducted before the trial to explore the acceptability of HIV self-testing among MSM and assess preferences for types of HIV self-testing kits. The formative work informed the design of specific intervention components to boost engagement in care for individuals who received a reactive (ie, a positive) HIV self-test result, and to provide risk-reduction information and signposting to HIV testing services for those randomly assigned to not receive a baseline HIV test. This formative work also informed the design of supportive mechanisms within the intervention to reduce the risk of adverse emotional reactions or other types of harm following a reactive HIV self-test in the randomised controlled trial.[17,18]

Participants

Participants were recruited through sexual and social networking sites including Grindr, Hornet, Recon, Scruff, and community Facebook webpages, using tailored advertising targeted to a broad spectrum of MSM and transgender people.[22] Eligibility criteria for participants included age 16 years or older; residence in England or Wales; being a man (including transgender men) or transgender woman; having ever had anal intercourse with a man; not being known to be HIV positive; being willing to provide name, date of birth, and a valid email address; and providing consent to link to the UK national HIV surveillance databases held by Public Health England. Very few transgender women were recruited and their data have been described separately;[23,24] these data are not included in the analysis presented in this Article. Data on gender were collected through a self-reported survey at enrolment. Participants were asked the question "how do you describe yourself?", and the options for answers were: man, trans man, woman, trans woman, non-binary, or other.

Randomisation and masking

The first stage of randomisation took place at enrolment. Following online consent, eligible participants were randomly allocated (in a 3:2 ratio) to the offer of a single free baseline HIV self-test kit (baseline test [BT] group) or no offer of a baseline HIV self-test kit (no baseline test [nBT] group). The second stage of randomisation took place at month 3 and was open to participants allocated to the BT group and who met further eligibility criteria. Due to the large number of participants, a simple approach that randomly assigned participants using a completely automated random number generator was used. Given the nature of the intervention, participants were not masked to intervention allocation. Those assessing outcomes were masked to allocation, whereas those analysing the data knew the group assignment.

Procedures

Participants in the nBT group were offered additional information on how to undertake HIV testing through routine services including how to access a nearby clinic as part of standard of care. Participants randomly assigned to the BT group were offered a free HIV self-test kit (BioSURE, Waltham Abbey, UK) immediately after randomisation. This kit incorporates an antibody immunoassay detecting HIV 1/2 antibodies (from approximately 28 days after infection) and requires a whole blood sample from a finger prick. The HIV self-testing kits were posted directly to the participants by the manufacturer.

Participants who ordered a kit were contacted 2 weeks later asking whether they had received and used the kit, the result of the test, and, if reactive, if they had been to a clinic to have the result confirmed. Participants who reported not receiving a kit or receiving a faulty kit were sent a replacement. All participants (in both the BT and nBT groups) received an online survey 3 months after enrolment that asked questions about testing for HIV and other sexually transmitted infections (STIs) and about sexual behaviour since enrolment. Participants in the BT group were asked again about the use of the self-test kit. If participants did not complete the online survey that was sent at 3 months they were sent a reminder 2 weeks later. A final online survey was sent to all participants between April 25 and May 9, 2019. This final survey largely asked the same questions as the survey that was sent at 3 months, although with different timeframes. Additional questions about any potential harms from self-testing were also included but will be reported elsewhere. Participants who completed the final survey were offered a free BioSURE self-testing kit. Survey invitations and responses were securely managed by Demographix, an online research company.

Outcomes

The primary outcome was a confirmed HIV diagnosis within 3 months of enrolment, with date of diagnosis defined as the date of the first confirmatory test at a clinic. Data on HIV diagnoses were primarily obtained from linkage to national HIV surveillance databases (appendix p 2), which are maintained by Public Health England. From Oct 1, 2021, Public Health England was replaced by the UK Health Security Agency (UKHSA). Linkage was performed by UKHSA staff masked to the randomised allocation using a deterministic, hierarchical

algorithm followed by a manual review of putative matches. Matches were classified as definite (exact matching on several fields, including date of birth, and no conflicting criteria) or partial (matching on some fields, but not all). Consistency between HIV diagnoses reported in follow-up surveys and those recorded in UKHSA databases was cross-checked. Participants who reported a positive self-test in the survey that was sent out 2 weeks or 3 months after enrolment or in the final survey who did not link with the UKHSA databases were contacted by a study clinician to verify that they had linked to care. Participants who withdrew from the trial but did not ask for their data to be removed were included in the UKHSA linkage. The primary analyses included all UKHSA diagnoses (ie, definite or partial) and verified self-reports.

Secondary outcomes, which were primarily assessed using the survey sent 3 months after enrolment, were overall frequency of HIV testing irrespective of testing modality, frequency of STI screening, and frequency of condomless sex. Additional information on the use of kits and HIV testing in the BT group was obtained from the survey sent 2 weeks after enrolment and from the data provided by UKHSA. Other secondary outcomes were markers of recent of infection at the time of HIV diagnosis (eg, CD4 count or antibody avidity assays) in participants for whom data were available, and diagnosis of a new STI. These other secondary outcomes are not discussed in this paper because there were too few primary outcomes for these secondary analyses to be of interest, Furthermore, there was no difference in STI testing between groups, which lessened interest in findings on STI diagnoses.

Statistical analysis

The target sample size of 10 000 was determined by the number of self-test kits that could be acquired within the study budget. To assess whether this sample size provided adequate statistical power we considered plausible HIV seroprevalence values between 1·5% and 2·5% and various diagnosis rates in the BT and nBT groups.[21] Statistical power was acceptably high (>90%) when the absolute difference in diagnosis rates between the two groups was at least 30%.

Analyses of the primary outcome were performed using the intention-to-treat principle, including participants in the BT group who did not order a kit when offered and those randomly assigned to the nBT group who accidentally received a kit due to a duplicate enrolment. Participants were only excluded if they were determined to be ineligible after randomisation (figure 1) or asked for all their data to be removed. Sensitivity analyses of the primary outcome involving looser and stricter criteria for an HIV diagnosis were also performed. Comparisons of outcomes between randomised groups used χ^2 tests for categorical data and Mann-Whitney U tests for ordinal data. Because of the very large sample size, many statistically significant associations were found, even when the size of the effect was modest. It is therefore more informative to focus on estimates and confidence intervals than on p values. The time to HIV diagnosis was examined using a Kaplan-Meier plot. In this analysis, participants randomly assigned to the offer of reminders to complete HIV self-tests every 3 months and free HIV self-test kits in the second stage of randomisation were censored on the date of this randomisation, because this group were offered regular self-testing kits. Other participants were censored on March 31, 2019, by which time almost all HIV diagnoses in the UK should have been reported to UKHSA. Analyses were done with Stata (version 16.0). The SELPHI trial is registered with the ISRCTN Clinical Trials Register (ISRCTN20312003).

Role of the finding source

The funders had no role in study design, data collection, data management, data analysis, data interpretation, or conduct of the study. The funders had no role in preparation, review, or approval of the manuscript, or in the decision to submit the manuscript for publication.

Results

10 719 participants were randomly assigned to the BT or nBT group between Feb 16, 2017, and March 1, 2018 (figure 1). Of those, 648 were later deemed ineligible (figure 1), nine asked for all of their data to be withdrawn, and 24 were transgender women whose data are reported elsewhere.[23,24] These exclusions left 10 111 participants in the analysis dataset. Of these participants, 6049 (60%) were allocated to BT and 4062 (40%) to nBT. 262 (3%) participants subsequently withdrew or unsubscribed from further contact but were assessed for the primary outcome.

The baseline characteristics and associations with previous HIV testing behaviour in all participants (randomised groups combined) have been described.[16] Median age was 33 years (IQR 26–44), 89% participants were White, 80% born in the UK, and 47% university educated (table 1). Only 1% participants were transgender men. 17% participants had completed HIV tests in the 3 months before enrolment, but 15% had never tested. The most recent HIV test was at a sexual health clinic for 60% of participants, with a self-sample test for 17% of participants, a self-test for 7%, and other methods for 16%. In terms of numbers of condomless anal sex partners in the 3 months before enrolment, 3330 (33%) participants reported only one partner, 2943 (29%) participants reported two to four partners, and 1009 (10%) participants reported five or more partners. At the time of enrolment, 389 (4%) participants were taking PrEP. Baseline characteristics were reasonably balanced over the two groups.

3895 (64%) of 6049 participants in the BT group completed the survey sent 2 weeks after enrolment. The

survey 3 months after enrolment was completed by 4041 (67%) participants in the BT group and 1566 (39%) of the 4062 participants in the nBT group. Higher rates of completion were identified for several baseline characteristics: participants who were older, those who were better educated, and those who had tested for HIV more recently (appendix pp 3–4). Additionally, race and ethnicity and the number of condomless anal sex partners were associated with completion of this survey in the nBT group. The final survey was sent a median of 19 months (IQR 17–22) after enrolment, and was completed by 1695 (28%) participants in the BT group and 1069 (26%) participants in the nBT group.

5996 (99%) of 6049 participants in the BT group accepted the offer of a free HIV self-test kit, but of these, 224 (4%) participants reported not having received the kit. Information on HIV testing within 3 months of enrolment was available for 4511 participants in the BT group and 1574 participants in the nBT group, based on those who either completed the survey sent 2 weeks after enrolment (BT group only) or completed the survey sent 3 months after enrolment, or who had a confirmed HIV diagnosis in this time period. 4263 (95%) participants in the BT group reported having used the SELPHI self-test kit. Another 105 participants reported accessing another HIV test (including three who used a non-SELPHI self-test kit), giving a total of 4368 (97%) in the BT group who had received any HIV test within 3 months of enrolment. This proportion is much higher than that observed in the nBT group (670 participants [43%]; table 2). Of the 3722 participants in the BT group had used the SELPHI HIV self-test kit and responded to further questions, 892 (24%) reported having had an additional HIV test within 3 months of enrolment. Among the 1566 participants in the nBT group who completed the 3-month survey, the proportion with an HIV test between enrolment and 3 months (670 participants [43%]) was twice as high as the

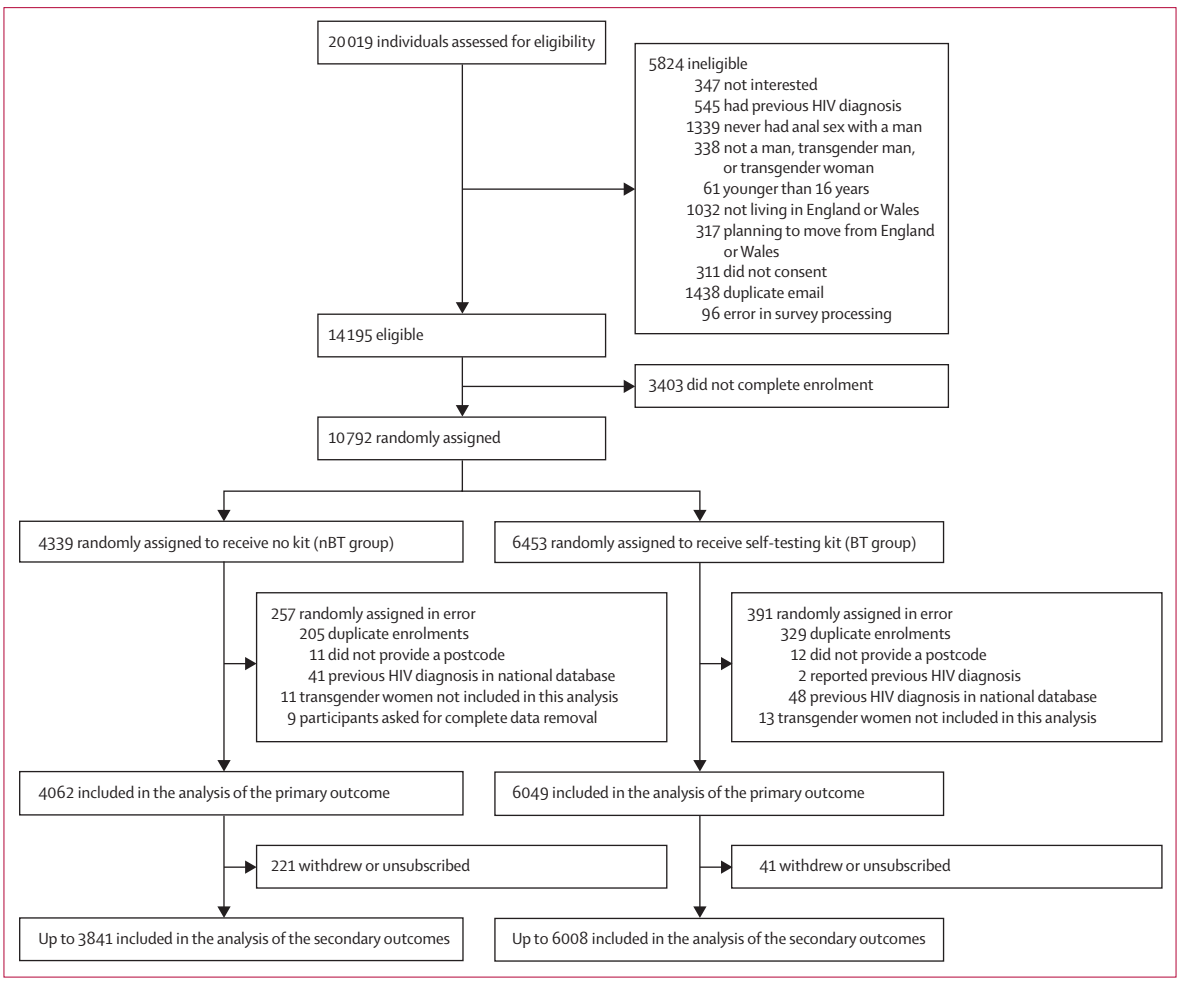

Figure 1: **Trial flow diagram for the first stage of randomisation**
Excluded participants could only be included in one ineligibility category or be categorised as having been randomly assigned in error. Due to the nature of the ascertainment of the primary outcome (linkage with national databases), all randomly assigned participants are included in the analysis of the primary outcome. Participants who had been randomised in error, who were transgender women, or who asked for complete data removal were excluded from this analysis.

proportion who had an HIV test in the 3 months before enrolment (324 participants [21%]; p<0·0001).

For participants who reported taking a non-SELPHI HIV test in the 3 months after enrolment, sexual health clinics were the most common location or type of testing in both the BT and nBT groups, although self-sampling (ie, when a person collects their own test and then sends it to a laboratory for analysis) was also popular (table 3). 13% of participants in the nBT group and 7% of participants in the BT group who took a non-SELPHI test in the 3 months after enrolment reported that their last HIV test was a non-SELPHI self-test.

Of the 4449 participants who reported having used the self-test kit in surveys sent 2 weeks, 3 months, or approximately 19 months after enrolment (final survey), 4378 (98%) participants obtained a non-reactive result, 14 (<1%) participants obtained a reactive result, and 55 (1%) participants obtained no result (ie, no lines appeared or there was another problem with the test). Of the 14 participants with a reactive result, ten participants either reported a positive confirmatory clinic result or linked to the UKHSA database (implying a positive confirmatory result), and one participant reported a negative confirmatory clinic result. There were no reported false negatives, although false negatives would have been difficult to ascertain through the surveys. A study clinician attempted to contact the remaining three participants, but was not successful. Median time between enrolment and linkage to care for participants reporting using the SELPHI self-test kit was 9 days (IQR 6–12). One participant who reported a reactive self-test result did not link to care until 333 days after enrolment, and therefore did not meet the criteria for the primary outcome.

A total of 34 (0·3%) of all 10 111 participants had a confirmed HIV diagnosis within 3 months of enrolment (table 2). There was no evidence of a difference between the two groups (p=0·64), with 19 (0·31%) of 6049 participants in the BT group versus 15 (0·37%) of 4062 participants in the nBT group diagnosed with HIV (risk difference –0·1%, 95% CI –0·3 to 0·2). This finding was unchanged in sensitivity analyses (appendix p 5). An additional 51 participants had an HIV diagnosis after the 3-month time period (figure 2), again with no difference between the randomised groups. No clear differences in baseline characteristics were evident for participants with and without a confirmed HIV diagnosis (appendix p 6), including previous HIV testing history, although the number of events was too small for statistical comparison.

The proportion of participants who had an STI test between enrolment and 3 months was slightly lower in the BT group than in the nBT group (table 2). In an exploratory analysis, we observed that in participants who did not have any HIV test within 3 months of enrolment, STI testing was uncommon in both the BT group and the nBT group (table 4). In contrast, among

	BT group (n=6049)	nBT group (n=4062)	Total (n=10 111)
Median age, years (IQR)	33 (26–44)	33 (26–44)	33 (26–44)
Gender			
Cisgender men	6002 (99%)	4028 (99%)	10 030 (99%)
Transgender men	47 (1%)	34 (1%)	81 (1%)
Country of birth			
UK	4849 (80%)	3269 (80%)	8118 (80%)
Other	1200 (80%)	793 (20%)	1993 (20%)
Highest educational qualification			
University	2854 (48%)	1852 (46%)	4706 (47%)
Higher education	645 (11%)	474 (12%)	1119 (11%)
School	2264 (37%)	1536 (38%)	3800 (38%)
None	136 (2%)	104 (3%)	240 (2%)
Data missing	150 (2%)	96 (2%)	246 (2%)
Race or ethnicity			
White	5347 (88%)	3653 (90%)	9000 (89%)
Asian	181 (3%)	126 (3%)	307 (3%)
Black	100 (2%)	61 (2%)	161 (2%)
Mixed	214 (4%)	99 (2%)	313 (3%)
Other, unknown, or undisclosed	207 (3%)	123 (3%)	330 (3%)
Time since last HIV test			
<3 months	989 (16%)	706 (17%)	1695 (17%)
3–12 months	2250 (37%)	1471 (36%)	3721 (37%)
>1 year	1813 (30%)	1248 (31%)	3061 (30%)
Never	929 (15%)	608 (15%)	1537 (15%)
Data missing	68 (1%)	29 (1%)	97 (1%)
Location of last HIV test*			
Sexual health clinic	3030/5052 (60%)	2059/3425 (60%)	5089/8477 (60%)
Other NHS or clinical setting	430/5052 (9%)	279/3425 (8%)	709/8477 (8%)
Self-sample	826/5052 (16%)	554/3425 (16%)	1380/8477 (16%)
Self-test	336/5052 (7%)	220/3425 (6%)	556/8477 (7%)
Elsewhere	340/5052 (7%)	242/3425 (7%)	582/8477 (7%)
Data missing	90/5052 (2%)	71/3425 (2%)	161/8477(2%)
Last STI test			
<3 months	896 (15%)	631 (16%)	1527 (15%)
3–12 months	1814 (30%)	1225 (30%)	3039 (30%)
>1 year	2090 (35%)	1386 (34%)	3476 (34%)
Never tested	1223 (20%)	797 (20%)	2020 (20%)
Data missing	26 (<1%)	23 (1%)	49 (<1%)
Number of CAI partners in previous 3 months			
None	1716 (28%)	1112 (28%)	2828 (28%)
One	2000 (33%)	1330 (33%)	3330 (33%)
Two to four	1745 (29%)	1198 (29%)	2943 (29%)
Five or more	587 (10%)	422 (10%)	1009 (10%)
Data missing	1 (<1%)	0 (0%)	1 (<1%)
PrEP use			
Currently taking PrEP	241 (4%)	148 (4%)	389 (4%)
Not taking PrEP	5802 (96%)	3913 (96%)	9715 (96%)
Data missing	6 (<1%)	1 (<1%)	7 (<1%)

Data are n (%) unless otherwise specified. CAI=condomless anal intercourse. NHS=National Health Service. PrEP=pre-exposure prophylaxis. STI=sexually transmitted infection. *Denominator is the number of participants who had previously tested for HIV for whom data were available.

Table 1: **Baseline characteristics of participants randomly assigned (in a 3:2 ratio) to the offer of a single, free HIV test at enrolment (BT group) or to no offer of a test at enrolment (nBT group)**

participants who did have an HIV test, STI testing was more frequent in the nBT group than in the BT group. Among participants who had had HIV tests but not STI tests, most had used a self-sampling or a self-testing kit, including non-SELPHI tests (appendix p 7).

Participants in the BT group were slightly more likely to report one or more condomless anal sex partners in the 3 months after enrolment than those in the nBT group (table 2). Of those reporting one or more condomless anal sex partners, the proportion reporting an STI test seemed higher than in participants overall and was slightly higher in the nBT group than in the BT group (table 2).

	BT group (n=6049)	nBT group (n=4062)	Risk difference (95% CI)	p value
Primary outcome				
Confirmed HIV diagnosis*	19/6049 (0·31%)	15/4062 (0·37%)	–0·1 % (–0·3 to 0·2)	0·64
Secondary outcomes†				
Reported any HIV test	4368/4511 (97%)	670/1574 (43%)	54% (52 to 57)	<0·0001
Reported >1 HIV test	940/4368 (22%)	125/670 (19%)	3% (0 to 6)	0·10
Reported use of SELPHI or non-SELPHI self-test kit	4266/4511 (95%)	89/1574 (6%)	89% (88 to 90)	<0·0001
Reported any HIV test in participants who tested <3 months before enrolment	742/756 (98%)	222/325 (68%)	30% (25 to 35)	<0·0001
Reported an STI test	903/4028 (22%)	397/1563 (25%)	–3% (–5 to 0)	0·018
Reported an STI test and one or more CAI partners	663/2542 (26%)	281/927 (30%)	–4% (–8 to –1)	0·013
Number of CAI partners	..	..	..	0·010‡
None	1497/4039 (37%)	639/1566 (41%)	–4% (–7 to –1)	
One	1292/4039 (32%)	451/1566 (29%)	3% (1 to 6)	..
Two to four	931/4039 (23%)	328/1566 (21%)	2% (0 to 5)	..
Five or more	319/4039 (8%)	148/1566 (9%)	–2% (–3 to 0)	..

Data are n/N (%) unless otherwise specified. In view of the unequal allocation to single, free HIV test at enrolment (BT group) or to no offer of a test (nBT group), comparison of percentages is more interpretable than absolute numbers. p values were calculated using χ^2 tests. The denominators for each of the secondary endpoints differ because of missing data or because only a subset of participants were analysed. CAI=condomless anal intercourse. STI=sexually transmitted infection. UKHSA=UK Health Security Agency. *Data on HIV diagnoses were obtained from linkage to national UKHSA surveillance databases: 29 participants (18 in BT group, 11 in nBT group) were a definite match, four participants (one in BT group, three in nBT group) were a partial match, and one participant (none in BT group, one in nBT group) had a verified self-report only. †Outcomes are for tests taken or partners reported by participants who completed the 3-month survey; denominators are those who answered the relevant question in that survey. The 2-week survey was only used for use of SELPHI test kit. UKHSA linkage used for primary outcome and HIV testing (confirmed cases only). ‡p value refers to comparison of no *vs* one or more CAI partners.

Table 2: **Outcomes at 3 months after enrolment**

	BT group		nBT group	Total
	Used SELPHI kit	Did not use SELPHI kit		
Took a non-SELPHI test within 3 months of enrolment	892	124	661	1677
Location or type of non-SELPHI test				
Sexual health clinic	486 (54%)	88 (71%)	287 (43%)	861 (51%)
Other clinical setting	53 (6%)	4 (3%)	38 (6%)	95 (6%)
Self-sample	169 (19%)	13 (10%)	201 (30%)	383 (23%)
Self-test	66 (7%)	9 (7%)	89 (13%)	164 (10%)
Community service or setting	33 (4%)	4 (3%)	20 (3%)	57 (3%)
Elsewhere or unknown	85 (10%)	6 (5%)	26 (4%)	117 (7%)

Data are n or n (%). Participants in the BT group were offered of a single, free SELPHI HIV self-test at enrolment. Participants in the nBT group were not offered a test at enrolment.

Table 3: **Location or type of last non-SELPHI HIV test within 3 months of enrolment**

Discussion

In over 10 000 MSM enrolled in the SELPHI HIV self-testing trial, we observed no significant difference in HIV diagnoses between the men randomly assigned to received self-testing kits and those who were not. The low prevalence of new diagnoses probably reflects the major national declines in HIV infections in MSM in the UK, which occurred after the study was planned.[2]

Rates of HIV testing were very high in participants assigned to receive an HIV self-test and who completed a survey at 2 weeks or 3 months, with 97% reporting that they had done any HIV test within 3 months of enrolment (an HIV self-test in 95%). Of participants in the BT group who had used the SELPHI self-test kit and responded to further questions, a quarter reported having had an additional HIV test after the self-test, which could indicate that they wanted further reassurance of their negative HIV status. A further explanation for additional testing could also be that the SELPHI trial itself had raised awareness of HIV testing, prompting some participants to screen after a subsequent potential exposure within the follow-up period. The proportion of participants who had tested for HIV (by any test) within 3 months of enrolment was significantly higher in the BT group (97%) than in the nBT group (43%). However, among the 1566 participants in the nBT group who completed the survey that was sent 3 months after enrolment, the proportion who had an HIV test between baseline and 3 months (43%) was twice as high as the proportion of participants who had an HIV test in the 3 months before enrolment (21%). This finding suggests that participation in the SELPHI trial, even without an offer of a free HIVST kit, might have led to increased participant testing rates. As we found that HIV testing in participants in the BT group who completed a follow-up survey was close to 100%, the HIV diagnosis rate in all participants randomised to the BT group (0·31%) is probably close to the true proportion of individuals with undiagnosed HIV.[2] Applying this infection rate to the nBT group would result in approximately 13 expected infections, which is lower than the 15 infections diagnosed in this group, suggesting that all, or almost all, HIV infections in the nBT group were also diagnosed. One possible reason for the high rate of HIV diagnosis in the nBT group is that participants might have enrolled in SELPHI because they were considering testing for HIV, and when they were not randomly assigned to receive an HIV self-test kit within the trial (ie, they were assigned to the nBT group), these individuals decided to test elsewhere. All participants randomly assigned to the nBT group were offered information on accessing HIV testing through the trial

materials, which could have facilitated HIV testing elsewhere.

However, with an estimated total population of 700 000 MSM in the UK,[25] UKHSA estimates that there are 1760 MSM with undiagnosed HIV, giving a diagnosis rate of 0·25%.[2] With an overall diagnosis rate in this SELPHI trial of 0·34%, this difference would imply that we were not particularly effective in enrolling individuals who were most likely to have an undiagnosed HIV infection. It is well recognised that people who consent to take part in a clinical trial are not necessarily representative of the background population, with particular under-representation of minority ethnic groups.[2,26] Additionally, because stigma is associated with both HIV and being gay or bisexual in some populations, under-representation in this trial might have been an even greater issue. One of the main reported benefits of HIV self-testing is its capacity for complete privacy compared with all other modes of testing.[16,18] Taking part in a trial that required providing their name, address, and permission for linkage to the UK surveillance database and contact from the study team probably deterred some individuals from taking part. Roll-out of HIV self-testing would have to take in to account the effect of including notification of linkage to care through the national surveillance database against the need for individuals testing to have absolute privacy, confidentiality, and autonomy.

As we have reported previously,[15] MSM entering the trial had a low rate of HIV testing in the 3 months before enrolment. This rate was particularly low among men with at least two condomless anal sex partners in the previous 3 months,[15] who would be viewed as being at higher risk of HIV infections and who should, according to current UK testing recommendations for MSM, be testing at least every 3 months. Despite this low rate of testing, only 0·31% in the BT group and 0·37% in nBT group tested positive for HIV in the 3 months after enrolment. It is not clear why men entering the trial had such a low undiagnosed prevalence of HIV. In the formative work it was clear that MSM viewed HIV self-tests as having limited utility when testing in response to specific risk events (due to concerns about the window period and absence of immediate clinical support in the event of a reactive result), except in the case of substantial structural barriers to other testing opportunities. HIV self-tests were considered to have use when seeking reassurance of ongoing HIV negative status and thought to be useful if testing to satisfy norms and expectations of others (eg, peers, friends, or clinical staff) around regular testing.[17,18] Therefore, men who took part in the SELPHI trial could have accurately judged themselves to have been at low risk of HIV despite ongoing risk behaviours and might have enrolled in the trial to access HIV self-tests to confirm their low risk and to meet the normative expectations of their peer group. This outcome also indicates a further key benefit of HIV self-testing, which is that it has the potential to support health systems by removing the need to attend the clinical facilities to test for HIV, thereby saving both time and costs for patients and health-care providers. Another potential use for HIV self-testing is that it allows for regular testing, which is necessary for men on PrEP. However, the HIV self-tests that are currently available have lower levels of sensitivity and specificity than are required for this purpose.[27] However, we also found that participants in the BT group who did not use the SELPHI HIV self-test kit had higher rates of attendance at sexual health clinics and were less likely to use self-sampling than participants in the BT group who did use the SELPHI HIV self-test kit. This outcome implies that the participants in the BT group who did not use the kit did not like the self-managed processes, which reinforces the need for provision of a range of services, including clinical face-to-face services, to

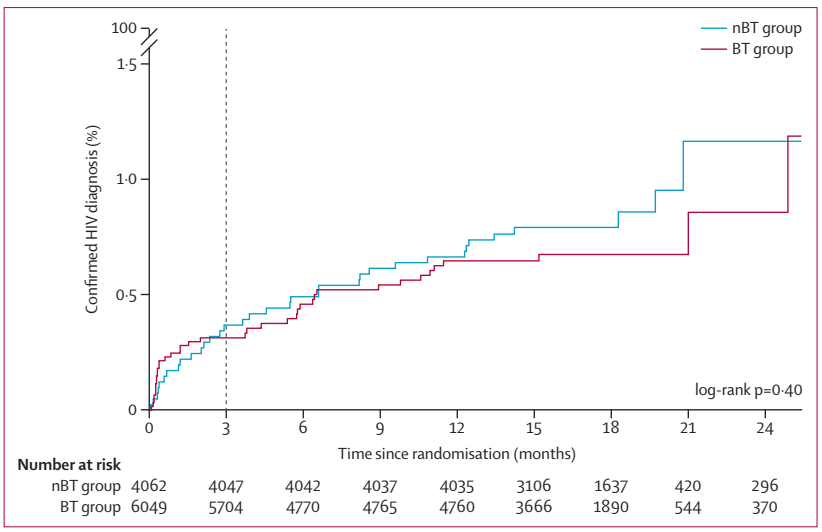

Figure 2: **Kaplan-Meier plot of time, in months, until confirmed diagnosis of HIV for participants in the BT group and those in the nBT group**
The vertical dashed line at 3 months shows when the primary endpoint was analysed.

	Completed any HIV test	Did not complete any HIV test	Total
BT group	n=3845	n=179	n=4024
Completed an STI test	894 (23%)	9 (5%)	903 (22%)
Did not complete an STI test	2951 (77%)	170 (95%)	3121 (78%)
nBT group	n=659	n=903	n=1562
Completed an STI test	369 (56%)	27 (3%)	396 (25%)
Did not complete an STI test	290 (44%)	876 (97%)	1166 (75%)

Data are n (%). Participants in the BT group were offered of a single, free HIV self-test at enrolment. Participants in the nBT group were not offered a test at enrolment. STI=sexually transmitted infection.

Table 4: **Joint analysis of HIV and STI testing between enrolment and 3 months for all participants**

enable patient choice. In addition, although there is a benefit in being able to test outside sexual health services, the key loss with HIV self-testing is testing data, which has been effective in the UK context in helping to understand shifts in patterns of infection.

It is clear from this trial and from other studies[25] that most individuals who HIV self-test (even in high incidence populations) will test negative. Therefore, delivery of HIV self-testing interventions must be designed to also facilitate uptake of HIV prevention interventions, such as condom distribution and access to PrEP, by individuals who test negative. Only 4% of participants were using PrEP at enrolment in this trial, which might have partly reflected the perceived limitations of self-tests for PrEP users; however, the number of people using PrEP is likely to increase and any HIV self-testing implementation programme will need to build in access to such HIV prevention initiatives as part of the intervention.

Consideration must also be given to encouraging uptake of STI testing in people who opt for HIV self-testing because a frequently raised concern about the provision of HIV self-testing is that it could lead to fewer visits to sexual health clinics and reduced testing for STIs. However, in our trial, participants in both BT and nBT groups who completed a follow-up survey had similar rates of STI testing in the 3 months after enrolment: in the BT group, the rate of STI testing was 22% and in the nBT group, the rate of STI testing was 25%. Future interventions must address both risks of HIV and other STIs and it is likely that the future of HIV self-testing will be linked to self-testing for other STIs.

HIV self-testing has further inherent challenges including linkage to care.[28] However, in our trial, the median time between enrolment and linkage to care for participants reporting positive results with the self-test kit was only 9 days (IQR 6–12). The SELPHI intervention had been structured to ensure that very clear information (developed through the formative work and more extensive than available commercial kits) was provided to participants with the HIV self-test kit about the necessary next steps, including confirmatory testing if participants tested positive on the HIV self-test.[22,29] This emphasis on clear information might have facilitated the rapid access to linkage to care.

There were several limitations to our study. The trial participants were, by the fact they chose to enrol in the trial, interested in HIV self-testing. However, we recruited a substantial proportion of men who, based on self-reported risk behaviours, were at a high risk of HIV infection. Another limitation of the study is the low, but typical, completion rates of surveys. Survey completion rates were especially low in the nBT group, in which only 39% completed the survey that was sent 3 months after enrolment. The low rate of survey completion is likely to have introduced bias into the analysis of the secondary endpoints, although not the primary endpoint, and caution in interpretation is needed. The direction of potential biases is difficult to predict, although there is probably a link between the likelihood of survey completion and positive health behaviours, such as seeking out testing for HIV and STIs. In addition, the requirement to provide personal details and agree to data linkage could have deterred some who might have valued the complete anonymity of HIV self-testing. A further potential area of concern is that the SELPHI intervention was an online intervention, which meant that participants needed to be sufficiently digitally literate, health literate, and aware of HIV to want to participate. Some people who are part of groups that are disproportionately affected by HIV are likely to be excluded from this kind of intervention. For example, another study showed that, even with optimised self-sampling packs and processes, people with mild learning difficulties or low health literacy, or both, found taking blood samples and using kits correctly to be challenging.[30] Furthermore, we did not recruit many Black men or many transgender men, who are both at increased risk of HIV, which could make our results less generalisable.

There are also several key strengths of our study, including the large sample size, the high degree of acceptability of the intervention, and the linkage with the national HIV database, which ensured that the primary endpoint was a hard public health endpoint of linkage to care and not self-reported testing.

In summary, we found that the offer of a single, free HIV self-test at enrolment to MSM who enrolled in a large online self-testing randomised controlled trial did not lead to increased rates of confirmed diagnosis of prevalent HIV infections in a 3-month time period. The absence of an increase in confirmed diagnoses of HIV could, however, largely reflect relatively low rates of undiagnosed infections because of a decreasing incidence rate of HIV in the UK.[1,2] Nonetheless, the offer of a free test did result in a much higher rate of HIV testing within the 3-month time period, without a reduction in STI testing, indicating that HIV self-testing is an appealing HIV testing option for a large group of men.

Contributors

AJR, ANP, FCL, SM and DD conceived the study and obtained funding. AJR drafted the manuscript and wrote the final version of the paper. LM and DD analysed the data. VD, JK, and PK undertook the linkage of study data to national HIV surveillance databases maintained by UKHSA. PW, TCW, KF, RP, MG, JK, MB, RT, YC-M, FB, DW, PK, and VD contributed to the study design, interpretation of the data, or writing of the paper, or a combination of all three. LM and DD take responsibility for the integrity of the data and for the accuracy of the data analysis. All authors reviewed and approved the final manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

MB has received speaker's fees from Gilead and Bristol Myers Squibb. FB and TCW have received consultancy fees from Gilead. All other authors declare no competing interests.

Data sharing

The policy of the SELPHI Core Management Group is to make deidentified participant data available to any researcher who submits a scientifically robust proposal, provided data exchange complies with information, governance, and data security policies in all the relevant countries. Our policy includes the replication of findings from published studies, although the researcher would be encouraged to work with the main author of the published paper to understand the nuances of the data. Enquiries should be addressed to DW (denise.ward@ucl.ac.uk) in the first instance.

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