Human immunodeficiency virus prevention and testing strategies among men who have sex with men in the UK: the PANTHEON research programme including the SELPHI RCT

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Scientific summary

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Scientific summary

Background

In 2014, the number of newly human immunodeficiency virus (HIV) diagnosed men who have sex with men (MSM) was at an all-time high and the 3000 new infections/year were a significant cost to the NHS, accruing £1 billion in future costs every year. Approximately 25% of all HIV-positive MSM were unaware of their infection and disproportionately contributed to onward transmission (between 60% and 80% of transmissions) and late presentations, with greatly increased risk of death. Uptake and frequency of HIV testing among MSM in 2014 was low. Innovative strategies, such as HIV self-testing (HIVST), which, due to associated confidentiality and convenience, could increase initial and repeat testing rates and diagnosis, had not been evaluated. It was also unclear whether other HIV prevention initiatives in addition to self-testing could offer value for money. In practice, assessing the cost-effectiveness of a range of prevention interventions required modelling.

Aims and objectives

Our aim was to assess the acceptability, effectiveness and cost-effectiveness of HIVST, and to examine the best economic value of a wider set of HIV prevention initiatives.

Main research questions

For MSM in the UK:

1. Does provision of free HIVST result in the earlier diagnosis of HIV infection?
2. Which HIV prevention initiatives are most cost-effective?

Specific objectives

Workstream 1: feasibility

- To identify the most up-to-date evidence of HIVST among MSM (systematic review and systematic mapping process).
- To increase understanding of accessibility and feasibility of HIVST among MSM and identify barriers and facilitators to HIVST in a range of models and contexts (focus groups and interviews).
- To explore how those utilising self-tests experience HIVST and the implications for further intervention development and scale-up.
- To explore how the HIV Self-testing Public Health Intervention (SELPHI) intervention might be experienced by and the pathways to impact on behaviour for different groups of randomised controlled trial (RCT) participants.
- To develop and undertake a process evaluation to assess what worked well about the RCT intervention and for whom.

Workstream 2: intervention

- To assess whether free self-testing for HIV with reminders to test results in earlier diagnosis of HIV infection compared with standard of care through an internet-based, randomised trial (SELPHI).

- To explore testing pathways, practices, effects and perspectives on self-testing through qualitative interviews, including in key groups (Asian, black and Latin American MSM and *trans* people).

Workstream 3: modelling and economic evaluation

- To estimate HIV incidence and predictors and describe risk behaviours in HIV-negative MSM at the time of HIV infection and after diagnosis through a web-based longitudinal cohort study to provide key parameters for the cost-effectiveness model.
- To identify efficacious existing HIV prevention strategies in MSM from high-income countries (systematic review).
- To estimate the cost of health care for people diagnosed with HIV living in England and Wales.
- To model the cost-effectiveness of HIV prevention strategies, including HIV testing interventions, using a simulation model to determine the cost-effectiveness (from an NHS perspective with outcomes as quality-adjusted life-years) of strategies for preventing HIV transmission, alone and in combination.

Methods

We divided the programme into three workstreams that were undertaken between 2015 and 2021.

Workstream 1: feasibility

Study 1A: we conducted a systematic mapping process from which the outputs were used to populate the HIV self-testing and research policy hub website HIVST.org. We collaborated with the World Health Organization (WHO) on four systematic reviews to provide the foundation for the updated WHO Global Guidelines on HIVST, which was launched in December 2019.

Study 1B: we undertook six focus-group discussions (FGDs) with MSM to increase understanding of accessibility and feasibility of HIV self-testing among MSM and identify barriers and facilitators in a range of models and contexts to inform development of the intervention.

Eighteen key informant interviews were conducted with service providers and commissioners to explore similar themes as the MSM FGD.

Study 1C: development of manual and materials to promote and support the interventions in the RCT and RCT study website design.

Study 1D: we undertook a process evaluation to examine the implementation of the planned intervention in the SELPHI RCT. The process evaluation explored the mechanisms of impact, and contextual factors that affect impact and potential normalisation of the intervention with the target population.

Workstream 2: intervention

Study 2A: building on the work from workstream (WS) 1 to inform the design of the trial and intervention, we undertook a RCT to assess whether offering free HIVST kits via the internet increased the rate of HIV diagnosis in MSM and *trans* people with linkage to clinical care. The trial aimed to enrol 10,000 HIV-negative participants, age > 16 years, resident in England or Wales, who were willing to provide name, date of birth and a valid e-mail address and who gave consent to linkage with surveillance and clinical databases. Online advertising was used to recruit men potentially interested in HIVST through the geo-location social-sexual networking applications (apps) (Grindr, Growlr, Scruff and Hornet) as well as targeted Facebook advertising.

In a two-stage randomisation process, participants were first randomised (3 : 2) to receive a free baseline HIVST or no free baseline HIVST (randomisation A). At 3 months, participants allocated to

receive a baseline HIVST were subsequently randomised (1 : 1) to receive the offer of regular (every 3 months) free HIVST, with testing reminders, versus no such offer (randomisation B) if they met further eligibility criteria. The primary outcome for randomisation A was a confirmed new HIV diagnosis within 3 months of randomisation (detection of prevalent infections, binary outcome). The primary outcome for randomisation B was the time from randomisation to a confirmed new HIV diagnosis (detection of incident infections, time-to-event outcome). The primary analyses compared the randomised groups as allocated (intention to treat). New HIV diagnoses were principally identified through linkage to national HIV surveillance databases maintained by the UK Health Security Agency (UKHSA). During the pilot phase, we conducted a mixed-methods study to assess trial feasibility and intervention acceptability using quantitative data from advertising sources and RCT surveys alongside qualitative data from a nested substudy.

Study 2B: as part of the extensive qualitative work in WS2, we conducted a series of face-to-face and remote interviews with MSM and *trans* people participating in SELPHI (from both intervention arms) to examine experiences of those utilising HIVST and the implications for further intervention development and scale-up. We focused on interviewing specific groups of participants who may have unique experiences with HIVST, including *trans* people, and MSM from Asian, black and Latin American backgrounds and a small group of MSM who reported harm from the study.

Workstream 3: modelling and economic evaluation

Study 3A: we conducted a 3-year web-based longitudinal prospective cohort study in MSM, the Attitudes to and UnderstandingRisk of Acquisition of HIV (AURAH2) study, which used 4-monthly online questionnaires to collect information on HIV status, HIV testing history, recent sexual behaviour, health and lifestyle factors and sexually transmitted infection (STI) diagnoses from 2015 to 2018. We linked all AURAH2 study participants data to the national HIV surveillance database managed by UKHSA (previously called Public Health England till October 2021).

Study 3B: to inform the cost-effectiveness modelling, we undertook a systematic review of HIV prevention strategies for MSM among high-income settings using published studies from 2012 up until 2021. The systematic review identified and described studies evaluating the efficacy or effectiveness of behavioural HIV-prevention interventions for reducing HIV incidence among MSM in high-income countries.

Study 3C: to better understand the cost-effectiveness of preventing HIV infection, we estimated the healthcare costs of people diagnosed with HIV living in England and Wales using data from a large English HIV treatment centre's electronic patient record system which was combined with National Reference Costs for England to estimate the frequency of hospital attendances (including inpatient episodes, day-case visits and outpatient visits) and costs.

Study 3D: finally we developed an existing individual-based stochastic model that simulates the UK population of MSM from the start of the epidemic, tracking detailed levels of condom-less anal sex with long-term and casual partners and hence risk of HIV acquisition. The Synthesis model was calibrated using longitudinal patterns of condom-less sex, particularly around the time of HIV infection, changes in risk behaviour as a result of receiving a diagnosis of HIV in MSM, and the proportion of men likely to have been infected by a long-term partner, so that the cost-effectiveness of all relevant prevention activities could be estimated.

Results

Workstream 1: feasibility

The systematic map consolidated all emerging evidence related to HIVST and populated HIVST.org by systematically searching databases and the abstracts of five conferences from 2006, with monthly

automated database searches until June 2019. We conducted four systematic reviews using the results from the systematic map to identify eligible studies for each review. The main review was a meta-analysis of RCT data relating to key populations that compared the effects of HIVST with standard HIV testing. It demonstrated that HIVST was safe and increased testing uptake, frequency and yield of positive results for MSM and *trans* people without negative effects on linkage to HIV care, STI testing, condom use or social harm for MSM and *trans* people.

The FGDs showed that HIVST was a widely acceptable intervention. MSM reported that HIVST reduced barriers related to convenience, stigma and privacy concerns and that HIVST facilitated more frequent testing, with the potential to reduce STI screening frequency. Interviews with key informants demonstrated the value of the increased choice that HIVST provides but highlighted the need to provide direct pathways into standard testing services and HIV care.

Workstream 2: intervention

An internet-based, open-label, randomised trial was developed informed by the feasibility work in WS1. The mixed-methods study evaluating the pilot phase of the RCT demonstrated that recruiting to the RCT was feasible, that the intervention was acceptable to participants and the kit had high reported usability.

In total 10,111 men were randomized, 6049 to a free HIV self-test at baseline (BT), and 4062 to no baseline test (nBT). Results from randomisation A demonstrated that of those randomised to a free HIV self-test at baseline, 73.5% reported using the HIVST kit. There were 34 new HIV diagnoses across both arms of the study (19 in BT and 15 in nBT) and, of those newly diagnosed, a large proportion had not tested for HIV in the previous 12 months. There was no significant difference between arms at 3 months in confirmed new HIV diagnoses that had linked to care (the primary outcome of the trial). Participants randomised to BT were more likely to self-report testing for HIV in the 3 months after enrolment than nBT [BT 4368/4511 (97%) vs. nBT 670/1574 (43%)].

In randomisation B, 2308 men were randomised, 1161 to the offer of regular (3-monthly) HIVST [regular test (RT)] and 1147 to no regular HIVST offer (nRT). Men in RT were much more likely to HIV test in each 3-month period compared with men in nRT. As expected, survey completion rates decreased over time and ranged from 47% to 4%. However, there was no significant difference in confirmed HIV diagnoses between arms [RT 10/1161 (0.9%) vs. nRT 8/1147 (0.7%)]. There were also no statistical differences in STI testing, STI diagnoses, or reported CAI between the groups.

HIVST facilitated more frequent testing, with the potential to reduce STI screening frequency.

Our mixed-methods substudy which interviewed *trans* people, and also used trial data, demonstrated that HIVST increased testing uptake and frequency by three times compared with standard care. *Trans* people reported HIVST benefits included increased autonomy, privacy, convenience and the avoidance of healthcare providers perceived to be discriminatory and services that increased gender dysphoria. The study of Asian, black and Latin American MSM showed that these groups were often excluded from lesbian gay bisexual trans queer + social environments because of their ethnicity. This had a potential downstream impact constraining the development of testing norms drawn from community and society. In addition, MSM from ethnic minority backgrounds sometimes had difficulty accessing bricks-and-mortar sexual health services, which HIVST mitigated.

The study of harms arising in the RCT found that these were very uncommon (reported by 1–2%). Harms were transient and most resolved without requiring intervention.

Workstream 3: modelling and economic evaluation

The AURAH2 study recruited 1167 MSM into the baseline study, of whom 622 joined the online component and were followed up over 3 years. In line with national data, the study demonstrated that

there had been a substantial decline in HIV incidence among MSM over the study period and that factors associated with incident HIV were injecting drug use, chemsex and high-risk sexual behaviour. Results from the study also showed that pre-exposure prophylaxis (PrEP) awareness and use increased substantially over the study period.

The systematic review of HIV prevention strategies among MSM in high-income countries identified 36 original papers, which were included in the review. Overall, PrEP was identified as the most effective intervention for reducing HIV incidence.

The cost of caring for people with diagnosed HIV infection using routinely collected data in combination with information on national unit costs was estimated to be £522 per quarter, excluding the costs of antiretroviral treatment. Outpatient visits accounted for most of the hospital activity, and for total costs. A higher quarterly cost was associated with being a new patient and having a low cluster of differentiation 4 count category, followed by current viral non-suppression or previous virological failure.

Results from the model-based economic evaluation showed that combination prevention, including a PrEP strategy, played a major role in the reduction in HIV incidence observed so far in the UK among MSM. Continuation of current activities may allow achievement of virtual HIV elimination among MSM in the UK and our modelling suggests they are likely to be cost-effective activities according to standard UK norms.

Future steps

Further work should aim to support the roll-out of HIVST at a national level to help address inequalities in access to HIV testing services that are experienced in particular by marginalised groups of MSM.

Conclusion

Human immunodeficiency virus self-testing is an acceptable and feasible HIV prevention tool for MSM and *trans* people. Although HIVST broadens the options for testing, and increases testing regularity, the trial results did not demonstrate that HIVST increased rates of HIV diagnosis. This likely reflects major national declines in HIV infections in MSM in the UK, which occurred after the study was planned and meant the study was not sufficiently powered to detect a difference. There were also no statistical differences in STI testing, STI diagnoses, or reported CAI between the groups. The cost-effectiveness evaluation found that strategies to increase the demand for HIV testing and condom and PrEP use are likely to substantially improve health outcomes. A reduction in the cost of delivery of HIV testing and PrEP is necessary in order to provide value for money.

Trial registration

This study is registered as ISRCTN20312003.

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