Improving sexual health through partner notification: the LUSTRUM mixed-methods research Programme including RCT of accelerated partner therapy

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Disclaimer

This report contains transcripts of interviews conducted in the course of the research, or similar, and contains language which may offend some readers.

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Claudia S Estcourt

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Nicola Low

- World Health Organization (WHO) contracts to conduct work about the effectiveness of different strategies for partner notification for sexually transmitted infections (STI). She is a member of the WHO STI Guidelines Development Group, which assesses evidence and makes decisions and recommendations about partner notification strategies.
- Senior editor (unfunded) of a systematic review of partner notification strategies for the Cochrane STI Group.

Paul Flowers

- NIHR EPIToPe – Evaluating the Population Impact of Hepatitis C Direct Acting Antiviral Treatment as Prevention for People Who Inject Drugs.
- NIHR Shaping care home COVID- testing policy: A pragmatic cluster randomised controlled trial of asymptomatic testing compared to standard care in care home staff (VIVALDI-CT) (NIHR154310).
- Australian Research Council AMR Scapes: Building public trust in expert knowledge on the 'superbugs' crisis.
- UKRI A phase III prospective, interventional, cohort, superiority study to evaluate the benefit of rapid COVID-19 genomic sequencing (the COVID-19 GENOMICS UK project) on infection control in preventing the spread of the virus in United Kingdom NHS settings.
- CSO An implementation science evaluation of Scotland's first Heroin Assisted Treatment.
- CSO Optimising hepatitis C treatment for people who inject drugs: Developing a primary care-based patient pathway.
- CSO Optimising services for people at highest risk of HIV: developing best practice in delivering HIV Pre-Exposure Prophylaxis (PrEP) through evaluation of early implementation across Scotland.
- UK Gov Co-Chair of the UK Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI) sub-group 'Behavioural Interventions'.
- Scottish Government's COVID-19 Advisory Sub-Group on Education and Children's Issues.
- Scottish Government's COVID-19 Advisory Sub-Group on Universities and Colleges.

John Saunders

- NIHR, Co-Investigator, Programme Grant NIHR200856 Improving care for people with sexually transmitted infections (STIs) in a digital NHS.
- Scottish CSO, Co-Investigator, Scottish government health directorates research grant, Optimising services for people at highest risk of HIV: developing best practice in delivering HIV Pre-Exposure Prophylaxis (PrEP) through evaluation of early implementation across Scotland.
- NIHR, Co-Investigator, Health Protection Research Unit in Blood Borne and Sexually Transmitted Infections.

- British HIV Association/British Association for Sexual Health and HIV, Conference attendance registration 2019, 2020, 2021.
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- Scottish Government Chief Scientist's Officer (CSO) 'Optimising Services for People at Highest Risk of HIV: Developing Best Practice in Delivering HIV Pre-Exposure Prophylaxis (PrEP) Through Evaluation of Early Implementation Across Scotland', Grant reference number: HIPS/17/47, 24 months from December 2017 to December 2019.
- Public Health Scotland (established 1 April 2020), Non-Executive Director of Board.
- Glasgow Caledonian University – Unpaid Honorary Professor from April 2022.
- University of Glasgow – Unpaid Honorary Clinical Associate Professor to March 2022, Honorary Senior Research Fellow from April 2022.

Anne M Johnson

- President, Academy of Medical Sciences.
- UKRI, Advice on various funding advisory committees and scientific advisory groups.
- HM Government, Independent scientific advice on COVID-19 including SAGE sub-group
- Chair, Committee for Strategic Coordination of Health of Public Research.
- Member (ex-officio), Committee on Science and Technology.

Jackie A Cassell

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Scientific summary

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Scientific summary

Background

Sexually transmitted infection (STI) diagnoses have increased since 2010. Young people and men who have sex with men (MSM) are disproportionately affected. Chlamydia is the most commonly reported STI in Britain. Two-thirds of chlamydia infections are diagnosed in heterosexual people under 25 years, while gonorrhoea, syphilis and human immunodeficiency virus (HIV) infections are more common in MSM.

Preventing onward transmission is essential to STI and HIV control. Partner notification (PN), also known as contact tracing and management, is a key intervention in which sex partners (SPs) of people with diagnosed infections are identified, tested and treated. PN also provides opportunities to engage people at high risk of infection who might not present for care. Better PN for MSM with infections such as gonorrhoea could enable earlier HIV diagnosis in partners because co-infection is common in this group. However, PN is challenging, and monitoring of performance is limited by the lack of standardised outcome measures and blunt classifications of sex partnership types. Accelerated partner therapy (APT) is a promising new PN method, but its role in preventing transmission is unknown.

Aims and objectives

The Limiting Undetected Sexually Transmitted infections to RedUce Morbidity (LUSTRUM) Programme aimed to improve the sexual health of people at high risk of STIs and HIV by improving PN outcomes. The Programme had three interconnecting streams:

STREAM A: Accelerated partner therapy trial preparation and implementation

Specific objectives:

- Develop a clinically useful SP classification.
- Optimise the acceptability of the APT intervention.
- Determine the effectiveness and costs of APT and understand how APT worked in practice.

STREAM B: Mathematical modelling and health economic analysis

Specific objectives:

- Quantify the effects of APT on chlamydia transmission and re-infection.
- Estimate the cost effectiveness of APT, compared with standard PN.

STREAM C: Development of partner notification interventions for men who have sex with men

Specific objectives:

- Explore costs and outcomes of PN and testing for HIV.
- Investigate PN for gonorrhoea in MSM to identify undiagnosed HIV infection using mathematical modelling.
- Explore barriers and facilitators to PN for bacterial STIs and develop a PN intervention.

Methods

A1. Development of a clinically usable sex partner classification

We synthesised evidence about partnership types from: the third British National Survey of Sexual Attitudes and Lifestyles, 259 dating applications and published literature. Then, we conducted qualitative interviews with members of the public and patients (*n* = 57), and health professionals (*n* = 27). We developed definitions for partnership types through external multidisciplinary expert consultation.

A2. Optimisation of the accelerated partner therapy intervention

We analysed videos of APT role-play consultations and synthesised published evidence about relevant behaviours; explored barriers and facilitators to receiving or delivering APT, including focused work with 25 people with mild learning disabilities, 56 members of the public and patients and 30 healthcare professionals (HCPs); modified and specified key components of APT, wrote a manual and training package, and created online videos.

A3. Randomised controlled trial of accelerated partner therapy

We conducted a cluster crossover randomised controlled trial with a process and cost-consequence evaluation. Dynamic modelling is described in Stream B.

Clusters were 17 sexual health clinics in diverse areas of England and Scotland.

Participants [index patients (IPs)] were heterosexual women and men, aged ≥ 16 years with a positive test for *Chlamydia trachomatis* and/or a clinical diagnosis of pelvic inflammatory disease or cervicitis (women) or non-gonococcal urethritis or epididymo-orchitis (men) and reporting at least one contactable sexual partner in the past 6 months.

Intervention: APT was offered *as an additional partner notification method* for IPs. A HCP assessed their SP(s) by telephone, then sent or gave the IP antibiotics and STI and HIV self-sampling kits for their partner(s). The control arm received standard PN alone. The intervention was implemented at the level of the sexual health clinic, with clinics randomised to intervention or control arm in the first phase by random permutation.

The primary outcome was the proportion of IPs testing positive for *C. trachomatis* 12–24 weeks after the PN consultation. Secondary outcomes included: the proportion of SPs treated; the proportion of partners notified; costs; cost effectiveness; model-predicted chlamydia prevalence.

The primary outcome analysis was by intention to treat, fitting random-effects logistic regression models that account for clustering of IPs within clinics and trial periods.

Process evaluation: We collected qualitative data through six focus groups and individual interviews (*n* = 10) with purposively sampled HCPs (*n* = 34 from 14 sites), IPs (*n* = 15) and SPs who received APT (*n* = 17). Quantitative data were collected within a clinical management and PN data collection system (RELAY).

Cost-consequence analysis (CCA): We collected data on costs and resource use during the trial and used unit costs from the trial and the Personal Social Services Research Unit.

B1 and B2. Modelling the effects of accelerated partner therapy on Chlamydia trachomatis *transmission*

We developed a new deterministic transmission model with a dedicated PN module, which allowed us to identify the effects of different index-partner combinations on chlamydia prevalence. We considered a population aged 16–34 years and calibrated the model to data from the third British National Survey

of Sexual Attitudes and Lifestyles. We then extended a previous modelling framework, informed by data from the *C. trachomatis* transmission model and the trial, to quantify expected rates of chlamydia reinfection (Estcourt CS, Stirrup O, Copas A, Low N, Mapp F, Saunders J, *et al*. Accelerated partner therapy contact tracing for people with chlamydia (LUSTRUM): a crossover cluster-randomised controlled trial. *Lancet Public Health* 2022;**7**(10):e853–65. https://doi.org/10.1016/S2468-2667(22)00204-3).

B3. Cost-effectiveness analysis of accelerated partner therapy compared with standard partner notification

We developed a spreadsheet-based model using output from the *C. trachomatis* transmission model to estimate the impact of APT on healthcare costs, major outcomes averted (MOA) and quality-adjusted life-years (QALYs) in a simulated population of 100,000 adults aged 16–34 years.

We calculated incremental cost-effectiveness ratios (ICERs) for APT, compared with standard PN and undertook sensitivity and scenario analyses.

C1. Systematic review of economic studies of interventions related to partner notification for sexually transmitted infections in men who have sex with men

We searched six electronic databases up to June 2020. We included economic evaluation and cost analysis studies if participants were MSM with any STI and/or HIV and the intervention was related to PN, testing or treatment and summarised evidence using a narrative synthesis.

C2. Partner notification for bacterial sexually transmitted infections in men who have sex with men as a way to detect undiagnosed human immunodeficiency virus infection in partners

We reviewed modelling studies of PN and pre-exposure prophylaxis interventions in MSM and attempted to model PN with co-infections with gonorrhoea HIV.

C3. Barriers and facilitators of accelerated partner therapy and development of a novel partner notification intervention for men who have sex with men

First, we conducted a stakeholder event with 45 participants from across Britain [MSM, public health experts, service commissioners, multidisciplinary sexual HCPs, non-governmental organisations (NGOs), academics and dating app providers]. We explored the diverse and multilevelled social, cultural and healthcare system-level context shaping poor PN outcomes for one-off partners.

We conducted qualitative in-depth interview studies with men who had experienced PN (n = 14, Stream A) and focus groups with MSM (n = 28), clinical and other stakeholders (n = 11) to explore barriers and facilitators to PN. We used the behaviour change wheel within co-design of a potential new PN intervention.

Results

A1. We created usable definitions for five SP types (committed/established, new, occasional, one-off, sex work), broadly predicated on duration of the relationship, likelihood of future sex and degree of emotional connection.

A2. Modifications to the APT intervention included simplification of the patient packs, creation of 'how to' training films for participants and HCPs. People with mild learning disabilities found APT acceptable but described feeling overwhelmed by the packs. They recommended using photographs instead of diagrams of anatomical sites for self-sampling, and an 'easy read' format. The new partner types and APT processes were built into a new clinical management and PN data collection system called RELAY.

A3. In the trial, all 17 clinics completed both periods. One thousand five hundred and thirty-six and 1724 IPs provided data in intervention and control phases. In intervention and control phases, 666 (43.4%) and 800 (46.4%) IPs were tested for *C. trachomatis*; 31 (4.7%) and 53 (6.6%) were positive, adjusted odds ratio (aOR) 0.66 [95% confidence interval (CI) 0.41 to 1.04; $p = 0.07$]. The proportion with ≥ 1 SP treated was 775/881 (88.0%) in intervention and 760/898 (84.6%) in the control phase, aOR 1.27 (95% CI 0.96 to 1.68; $p = 0.10$) (Estcourt C, Mapp F, Stirrup O, Copas A, Howarth A, Owusu M, *et al.* O18.2 Does Accelerated partner therapy improve partner notification outcomes for people with chlamydia? The LUSTRUM cluster cross-over randomised control trial. *Sex Transm Infect* 2021;**97**:A57–8. http://doi.org/10.1136/sextrans-2021-sti.153).

In total, 4807 SPs were reported, of whom 1636 (34%) were committed/established partners. Overall, 293/1536 (19.1%) of IPs in intervention phase chose APT for a total of 305 partners, of whom 248 accepted. Partner types were committed/established, 166/305 (54.4%); new, 85/305 (27.9%); occasional, 45/305 (14.8%); and one-off, 9/305 (3.0%). Common reasons for IPs to decline APT included: preferred face-to-face conversation 400/1832 (21.8%), partner already in clinic 388/1832 (21.2%), unwilling to engage with partner 206/1832 (11.2%), preferred partner to attend clinic 202/1832 (11.0%) and partner overseas 150/1832 (8.2%). Of 241 partners sent APT packs, 120/241 (49.8%) returned chlamydia and gonorrhoea testing samples, of which 78/119 (65.5%) were positive for chlamydia (no result in one), but only 60/241 (24.9%) HIV and syphilis samples (all negative). In an unplanned analysis, 2/106 (2.0%) IPs, who were offered APT and accepted it for one or more partners, tested positive for chlamydia at 12–24 weeks. Of IPs not selecting APT or whose partners refused, 29/560 (5.2%) had a positive result on repeat testing.

The process evaluation showed that overall intervention fidelity was good and APT was well liked by those who delivered and received it. Overall, we found a mixed picture of an intuitive, coherent intervention struggling to gain purchase within already pressured services. HCPs preferred RELAY to their clinic systems because it helped them standardise PN. However, many sites struggled to scale up the trial processes owing to continual external pressures to adapt services to achieve efficiencies.

In some services, APT was perceived as time-consuming and without palpable impact. This observation was related to the absence of a reduction in patient numbers in clinic waiting rooms. In this way, the 'invisibility' of the effectiveness of APT curtailed the establishment of positive feedback loops driving normalisation within services.

In the CCA, APT cost more than standard PN (£91.23 vs. £75.21). Where accepted, it was more effective than standard PN with an absolute effect difference of 5.26%.

B1 and B2. In the model, chlamydia positivity was highest for symptomatic index cases of low sexual activity, with infected partners who were typically asymptomatic and highly sexually active. Partner notification for this index–partner combination would prevent the most transmission. Increasing the number of treated partners from current levels in Britain (0.51, 95% credible interval, CI 0.21 to 0.80) by 25% would reduce chlamydia prevalence by 18% (95% CI 5% to 44%) in both women and men within 5 years. Reducing the time to partner treatment alone had a minor effect on reducing prevalence. Together, these results suggest that PN typically identifies sexual partners who are likely to further transmit chlamydia and that APT could further reduce prevalence if PN uptake increases.

B3. In the cost-effectiveness analysis, the base-case results showed APT cost less and was more effective than standard PN in terms of MOA and QALYs, and therefore cost-saving. The results were supported by deterministic sensitivity analysis and scenario analysis for most scenarios, with ICERs very low and well within accepted thresholds.

C1. There was very little published evidence on health economic aspects of PN in MSM. This supports the need for new interventions with parallel economic evaluation.

C2. Published models have not examined the impact on HIV diagnosis of PN for bacterial STIs, and interventions cannot be extrapolated between countries. There were challenges in fitting the model of gonorrhoea/HIV co-infection to data, including issues with parameter identifiability.

C3. We considered APT for MSM (and their more emotionally connected partners) and developed recommendations for a multilevel, multistakeholder intervention targeting MSM with other types of partners for whom PN is known to be more challenging. Key intervention elements included: a co-ordinated and coproduced mass and social media intervention to change norms and beliefs to challenge stigma and other barriers to PN; NGO peer-led work reducing STI-related stigma and persuading MSM to participate actively in PN to protect others and their communities; working with MSM to enable them to prepare for PN interactions and encourage HCP action, monitoring systems to directly address one-off PN outcomes; dating app providers promoting appropriate PN messaging.

Conclusions

The Programme provides findings about APT, which show promise for future PN. RELAY could be added to clinic systems for recording PN outcomes and processes. The Programme identified gaps in research about PN for one-off, and other partnerships with poor outcomes and high potential for onward sexual transmission. Data from the trial also suggested that APT uptake might be lower for people belonging to ethnic minority groups, although it was not powered to formally evaluate any such differences. The process evaluation and the work in Stream C identify a need for interventions that reach beyond sexual health services.

Future work

Future work should identify PN approaches for one-off partners; determine how to provide real-time or fast feedback for practitioners on the impact of interventions whose value is not obvious; further research is needed on how to increase uptake of APT, explore the pros and cons of immediate antibiotics, and optimise the uptake of self-sampling in partners, particularly people with mild learning disabilities; understand how services can use sex partnership-type information to improve PN methods, especially for hard-to-reach groups; develop and evaluate a system intervention to increase readiness in MSM for and engagement with PN for bacterial STIs, focusing on one-off partnerships and addressing economic factors and partnership type.

Trial registration

This trial is registered as ISRCTN15996256.

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