

Accelerated partner therapy contact tracing for people with chlamydia (LUSTRUM): a crossover cluster-randomised controlled trial



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Summary

Background Accelerated partner therapy has shown promise in improving contact tracing. We aimed to evaluate the effectiveness of accelerated partner therapy in addition to usual contact tracing compared with usual practice alone in heterosexual people with chlamydia, using a biological primary outcome measure.

Methods We did a crossover cluster-randomised controlled trial in 17 sexual health clinics (clusters) across England and Scotland. Participants were heterosexual people aged 16 years or older with a positive *Chlamydia trachomatis* test result, or a clinical diagnosis of conditions for which presumptive chlamydia treatment and contact tracing are initially provided, and their sexual partners. We allocated phase order for clinics through random permutation within strata. In the control phase, participants received usual care (health-care professional advised the index patient to tell their sexual partner[s] to attend clinic for sexually transmitted infection screening and treatment). In the intervention phase, participants received usual care plus an offer of accelerated partner therapy (health-care professional assessed sexual partner[s] by telephone, then sent or gave the index patient antibiotics and sexually transmitted infection self-sampling kits for their sexual partner[s]). Each phase lasted 6 months, with a 2-week washout at crossover. The primary outcome was the proportion of index patients with a positive *C trachomatis* test result at 12–24 weeks after contact tracing consultation. Secondary outcomes included proportions and types of sexual partners treated. Analysis was done by intention-to-treat, fitting random effects logistic regression models. This trial is registered with the ISRCTN registry, 15996256.

Findings Between Oct 24, 2018, and Nov 17, 2019, 1536 patients were enrolled in the intervention phase and 1724 were enrolled in the control phase. All clinics completed both phases. In total, 4807 sexual partners were reported, of whom 1636 (34%) were steady established partners. Overall, 293 (19%) of 1536 index patients chose accelerated partner therapy for a total of 305 partners, of whom 248 (81%) accepted. 666 (43%) of 1536 index patients in the intervention phase and 800 (46%) of 1724 in the control phase were tested for *C trachomatis* at 12–24 weeks after contact tracing consultation; 31 (4.7%) in the intervention phase and 53 (6.6%) in the control phase had a positive *C trachomatis* test result (adjusted odds ratio [OR] 0.66 [95% CI 0.41 to 1.04]; $p=0.071$; marginal absolute difference -2.2% [95% CI -4.7 to 0.3]). Among index patients with treatment status recorded, 775 (88.0%) of 881 patients in the intervention phase and 760 (84.6%) of 898 in the control phase had at least one treated sexual partner at 2–4 weeks after contact tracing consultation (adjusted OR 1.27 [95% CI 0.96 to 1.68]; $p=0.10$; marginal absolute difference 2.7% [95% CI -0.5 to 6.0]). No clinically significant harms were reported.

Interpretation Although the evidence that the intervention reduces repeat infection was not conclusive, the trial results suggest that accelerated partner therapy can be safely offered as a contact tracing option and is also likely to be cost saving. Future research should find ways to increase uptake of accelerated partner therapy and develop alternative interventions for one-off sexual partners.

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Introduction

Partner notification (also referred to as contact tracing) is the process of identifying, informing, testing, and treating sexual partners of a person diagnosed with a sexually transmitted infection.¹ Contact tracing is a key element of sexually transmitted infection control, with potential

effects at several levels.² It should benefit the individual diagnosed with the sexually transmitted infection (the index patient) by preventing repeat infection, and the sexual partner who might be the source of infection or could transmit undiagnosed infections to new sexual partners. It should also help to reduce the spread of

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Research in context

Evidence before this study

Contact tracing (partner notification) for chlamydia is a key element of sexually transmitted infection control, but achieving even modest outcomes can be challenging. Accelerated partner therapy is a contact tracing method whereby health-care professionals assess sexual partners by telephone, before giving the index patient a package of antibiotics and sexually transmitted infection self-sampling kits to deliver to their sexual partner(s).

We searched MEDLINE and Embase on Jan 4, 2022, for publications in any language from Jan 1, 2000, to Dec 31, 2021, using the terms “accelerated partner therapy” AND “sexually transmitted infections” AND (“contact tracing” OR “partner notification”) in any field. An exploratory randomised controlled trial and a qualitative study in the UK showed that accelerated partner therapy was feasible, acceptable, and faster than standard contact tracing. A 2014 health technology assessment of traditional and new methods for sexually transmitted infection partner notification found that accelerated partner therapy could reduce index patient reinfection and recommended that randomised trials of accelerated partner therapy using biological outcomes of effectiveness should be done.

Added value of this study

This crossover cluster-randomised controlled trial showed that the offer of accelerated partner therapy as an additional contact tracing method with usual care is likely to cause a small reduction in repeat chlamydia infection by 12–24 weeks after

treatment, and an increase in the proportion of sexual partners treated, compared with usual care alone, but uptake of accelerated partner therapy was lower than expected. The accelerated partner therapy intervention had a slightly higher cost than standard contact tracing for the index patient, but partner testing and treatment were cheaper. Almost half of the sexual partners who accepted accelerated partner therapy returned swab or urine samples for chlamydia and gonorrhoea testing, but just less than one-quarter returned blood samples for HIV and syphilis testing.

Implications of all the available evidence

Accelerated partner therapy is likely to be a cost-saving contact tracing option for heterosexual people with chlamydia, and might reduce the risk of repeat infection. These trial findings confirm the potential of accelerated partner therapy to improve contact tracing outcomes, which had been suggested by earlier exploratory studies. Accelerated partner therapy can be used in jurisdictions where prescribing legislation requires a consultation with the sexual partner. Accelerated partner therapy appears to be well suited to emotionally connected sexual partnerships, but more effective interventions for one-off partnerships are needed. In linked economic and transmission modelling analyses, accelerated partner therapy would be less costly and more effective than usual contact tracing. Further implementation research should determine whether uptake can be increased in a post-COVID-19 setting, because of increased familiarity with self-sampling, self-testing, and contact tracing.

sexually transmitted infections in sexual networks and populations.³ *Chlamydia trachomatis* (chlamydia) is the most commonly reported bacterial sexually transmitted infection in the UK,^{4,6} with an incidence of 229 441 diagnosed cases in England alone in 2019.⁴ Most chlamydia infections are asymptomatic and easily treatable with oral antibiotics. However, untreated chlamydia can cause pelvic inflammatory disease, infertility, ectopic pregnancy, and chronic pelvic pain in women, and epididymo-orchitis in men.⁷ Chlamydia infections do not induce lasting immunity after antibiotic treatment, and therefore create a challenge for sexually transmitted infection control. In prospective studies, around 20% of women had a repeat diagnosis of chlamydia infection in the first year after treatment,^{8–10} with peak incidence at 2–5 months.¹¹ Mathematical modelling has shown that improving contact tracing for chlamydia would be more cost-effective than increasing the coverage of chlamydia testing.²

Contact tracing can be challenging both for patients, who might face barriers to informing sexual partners, and for practitioners, who need time to elicit and discuss sensitive information. Outcomes are limited in British sexual health services,^{12–14} where enhanced patient

referral is the recommended standard for contact tracing of chlamydia infections^{15,16} (a health-care professional advises the person with a sexually transmitted infection [the index patient] to inform their sexual partner[s] of the need for testing [routinely, a comprehensive sexually transmitted infection and HIV screen¹⁷] and chlamydia treatment, and provides printed or website information). Sometimes, the health-care professional contacts the sexual partner directly (provider referral) without disclosing the identity of the index patient. Allowing patients to choose the most acceptable contact tracing method, which might differ for different sexual partners, is considered optimal practice,¹⁸ but pressures on UK National Health Service (NHS) sexual health services have deprioritised contact tracing and reduced patient choice.¹⁹

We developed accelerated partner therapy as a new intervention to improve and accelerate contact tracing.^{20–22} We adapted accelerated partner therapy from expedited partner therapy, which was developed in the USA and has been shown to improve contact tracing outcomes.^{12,23,24} Expedited partner therapy does not meet UK prescribing guidance,²⁵ however, because practitioners provide medication or a prescription

without any consultation with, or previous knowledge of, the sexual partner. In the early (and current) accelerated partner therapy intervention, the health-care professional would telephone the sexual partner, in private, during the index patient's clinic attendance,^{20,21} enabling the health-care professional to assess the safety of prescribing, to meet UK prescribing guidance. The index patient would then be given a pack containing antibiotics, chlamydia and gonorrhoea self-sampling kits, and an invitation to visit a sexual health clinic for syphilis and HIV testing (requiring venepuncture), to deliver to their sexual partner. Accelerated partner therapy resulted in faster sexual partner treatment and greater overall numbers of sexual partners treated compared with usual practice, but rates of testing for HIV and other sexually transmitted infections were low.^{20,21} Since these early studies, HIV and syphilis fingerprick blood self-sampling kits have been approved.²⁶ We aimed to investigate the effectiveness of accelerated partner therapy offered as an additional option with usual contact tracing, compared with usual practice alone, in heterosexual people with chlamydia, using a biological outcome measure.²⁷

Methods

Study design

We did an unmasked crossover cluster-randomised controlled trial (limiting undetected sexually transmitted infections to reduce morbidity [LUSTRUM] trial). This report follows the CONSORT statement²⁸ and relevant extensions.^{29,30} The protocol for the trial,²⁷ an integral process evaluation,³¹ and preliminary health economics analysis based on transmission dynamic modelling³² are presented elsewhere.³³ We chose this study design because individual randomisation carried a high risk of contamination of the intervention and was operationally unfeasible; service-level consent²⁷ aimed to make delivery of the intervention more realistic in busy clinical settings; and the crossover design allowed all clinics to test the accelerated partner therapy intervention and provided efficiencies in patient enrolment. All patients could opt out of the research through a novel pragmatic opt-out process,³⁴ but none did so, and none opted out of their data being used for research purposes.

The study was conducted in 17 NHS (publicly funded) sexual health clinics (clusters) across England and Scotland. Clinic selection was based on numbers of reported chlamydia diagnoses in the Public Health England GUMCAD (genitourinary medicine clinic activity dataset) sexually transmitted infection surveillance system³⁵ (in England) and geographical diversity (in Scotland), to ensure representation from clinics in London and other metropolitan cities and urban towns.

This trial received ethical approval from the London-Chelsea Research Ethics Committee (18/LO/0773).

Participants

Eligible participants (index patients) were heterosexual people aged 16 years or older with a positive *C trachomatis* test result or a clinical diagnosis of conditions for which presumptive chlamydia treatment and contact tracing are initially provided—ie, pelvic inflammatory disease or cervicitis (in women) or non-gonococcal urethritis or epididymo-orchitis (in men), with a report of at least one contactable sexual partner in the past 6 months. Index patients whose test results were subsequently negative for *C trachomatis* were excluded from analysis. We excluded men who have sex with men (whose contact tracing needs might differ), and people with complex circumstances (such as sexual assault), index patients who had paid for or been paid for sex in the past 6 months, or people with insufficient English language skills to safely engage in telephone consultations.

Eligible partners were defined as a sexual partner of the index patient, aged 16 years or older, within a period of the past 6 months for chlamydia, 3 months for pelvic inflammatory disease, and 1 month for non-gonococcal urethritis, according to national guidance.¹⁷

Randomisation and masking

We allocated phase order for clinics through random permutation within strata, using computer-generated random numbers.³⁶ 14 clinics were initially randomly assigned, including three strata that were pairs of clinics within one NHS trust (hospital group), one stratum containing five clinics from large cities, and another containing three clinics from smaller towns. A further pair and one final clinic (allocated through simple randomisation) were randomly assigned later, to boost enrolment. To remove the potential for allocation bias, one statistician generated the allocation codes and another randomly permuted clinic names within strata. A third person matched the allocation codes with clinic names to reveal the allocations.

After a 4-month rolling clinic setup (July–October, 2018), seven clinics entered the intervention phase and seven entered the control phase. At the end of the first 6-month period (November, 2018–April, 2019) clinics followed their usual contact tracing procedures for a 2-week washout period, before crossover to the alternative phase for May–November, 2019. Enrolment in the three clinics randomly assigned later (February, 2019) also ended in November, 2019 (two started the intervention phase and one started the control phase in March, 2019). Total trial duration was 19 months, allowing for a 3-month follow-up period to complete data collection.

A short washout period was appropriate because, for index patients (and their sexual partners) enrolled at the end of the first phase, their subsequent management and follow-up was unaffected by the clinic crossover. Furthermore, staff familiarisation and the delivery or removal of accelerated partner therapy packs could also be conducted rapidly.

Index patient

- (1) Index patient has contact tracing consultation with health-care professional, who assesses their eligibility for accelerated partner therapy.
- (2) Eligible index patient is offered accelerated partner therapy alongside the clinic's other standard contact tracing options; the patient can choose different methods for different partners.
- (3) Index patient telephones or messages sexual partner (with or without the health-care professional present, according to preference) to offer immediate telephone assessment by the health-care professional.
- (4) Index patient waits in clinic while the health-care professional conducts telephone consultation in private with sexual partner; if partner accepts accelerated partner therapy, the index patient is given an accelerated partner therapy pack (appendix p 8) to deliver to their partner and shows how it should be used, or sends the pack to the sexual partner directly.
- (5) Index patient is informed that they will receive a follow-up telephone call in 2 weeks and they will either receive a chlamydia self-sampling postal kit in 12–24 weeks (preferred), or they can re-attend the clinic for testing.
- (6) At 2-week follow-up: Research Health Adviser telephones index patient 2–4 weeks after the initial consultation to find out about contact tracing outcomes with partner(s), to remind them of the repeat test, and to invite them to be contacted about taking part in a telephone interview regarding their experiences of accelerated partner therapy (process evaluation).
- (7) At 12 weeks: index patient is sent a personalised text reminder about repeat test.
- (8) At 13 weeks: index patient is sent a self-sample kit by The Doctors' Laboratory, London, UK; index patient returns self-collected sample or attends clinic for repeat testing and receives results either via text message (for negative results) or using routine clinic systems (for positive or equivocal results). Positive results are managed according to routine clinic protocol. If the index patient does not return a self-sample or attend clinic for repeat testing, they receive a personalised text reminder 8 days after the self-sample kit is sent out, followed by a telephone call 13 days after the self-sample kit is sent out. Self-samples received more than 24 weeks after the contact tracing interview are excluded.

Sexual partner

- (1) Index patient telephones sexual partner to inform them about exposure to chlamydia and offer immediate telephone assessment (accelerated partner therapy).
- (2) If sexual partner agrees to accelerated partner therapy, health-care professional telephones them and conducts a clinical assessment in private. If appropriate, sexual partner is offered an accelerated partner therapy pack (delivered by the index patient or mailed directly). Sexual partners for whom accelerated partner therapy is inappropriate or who do not wish to accept will be advised by the health-care professional to attend clinic for further management. During the same telephone call, the health-care professional invites the sexual partner to be contacted about taking part in a telephone interview regarding their experiences of accelerated partner therapy (process evaluation).
- (3) Sexual partner receives accelerated partner therapy pack (appendix p 8), containing: antibiotics (either azithromycin or doxycycline, depending on local clinic practice); condoms; information about chlamydia, gonorrhoea, HIV, and syphilis; chlamydia and gonorrhoea self-sampling kit (urine or vulvovaginal swab), HIV and syphilis self-sampling kit (fingerprick blood sample), and information leaflet about how to take a sample (including link to an explanatory online video); request form for the sample to be processed by the laboratory; envelope for return of self-sampling kits; and packaging (envelope or small box, no branding or other identifiable markings, and which fits through a standard letterbox).
- (4) Sexual partner completes self-sampling, labels, and returns samples for testing.
- (5) Sexual partner takes antibiotic treatment.
- (6) Sexual partner informed of test results by text (for negative results) or routine clinic processes; positive results are managed according to routine care.

Figure 1: Overview of accelerated partner therapy and follow-up processes

Procedures

During initial consultations, health-care professionals assessed the eligibility of all potential index patients with a positive laboratory test result for *C trachomatis* or relevant clinical diagnosis. Health-care professionals were asked to record their consultations in real time, including a newly developed classification of sexual partner types, which categorises sexual partners into steady established, new, occasional, one-off, and sex work (excluded from the trial), broadly based on the degree of emotional attachment and likelihood of future sex.³⁷ Health-care professionals used RELAY, a web-based data collection platform developed for this trial on the basis of pilot studies, to collect data.^{20,21} The platform was hosted on secure servers and complied with NHS data storage requirements. RELAY was also intended for baseline data collection but, at almost all sites, health-care professionals prescreened index patients for eligibility and only created a RELAY record if the index patient met the eligibility criteria. Several sites restricted enrolment to a small number of clinic sessions per week.

Adverse events associated with the pathway of care were recorded because accelerated partner therapy is a novel intervention. Adverse events were recorded on a form detailing the person (or patient identification number) involved, date, person reporting, event and action taken, severity (low, moderate, or severe effect on the participant, based on the common terminology criteria for adverse events version 5.0,³⁸ which we adapted for the study), further action, and implications for analysis, and were reported to the trial steering committee. NHS services submitted their own Datix reports as required.

Accelerated partner therapy is a complex intervention,^{20–22,39,40} which was offered as an additional option in the intervention phase, alongside usual care, for index patients and their sexual partners (figure 1). Index patients could choose accelerated partner therapy or usual care for each sexual partner. In usual care, a health-care professional advised the index patient to inform their sexual partner(s) of the need for testing (routinely, a comprehensive sexually transmitted infection and HIV screen¹⁷) and chlamydia treatment (doxycycline) and provided printed or website information. In accelerated partner therapy, a health-care professional assessed the sexual partner(s) by telephone, then sent or gave the index patient antibiotics and sexually transmitted infection self-sampling kits for their sexual partner(s). Follow-up was the same in both usual care and accelerated partner therapy; all index patients were telephoned at 2 weeks and 12–13 weeks. If accelerated partner therapy was not feasible (eg, sexual partner could not be reached), usual care was offered instead.

During the control phase, clinics followed their standard protocols for usual care (enhanced patient referral). Follow-up telephone calls and repeat testing were the same as during the intervention phase.

Outcomes

The primary outcome was the proportion of index patients with a positive *C trachomatis* test result at 12–24 weeks after the initial contact tracing consultation. This measure is a proxy for repeat infection from an untreated partner, but also includes infections from new partners and antibiotic treatment failure, which cannot

be easily separated (figure 1). The outcome is widely used in trials of partner notification,¹² and the chosen period reflected a compromise between the optimum uptake of repeat testing⁴¹ and mathematical modelling of the most likely period of repeat infection.¹¹ The key secondary outcome was the proportion of sexual partners who had been treated at 2–4 weeks after the initial contact tracing consultation. Other secondary outcomes were one or more sexual partners treated per index patient; time to sexual partner treatment; proportion of sexual partners notified; and one or more sexual partners notified per index patient, ascertained during a telephone call with a research health adviser. The secondary outcomes of numbers of partners treated or notified per index patient were interpreted in the statistical analysis plan as one or more sexual partners treated or notified per index patient, to match UK reporting standards,¹⁷ and to make analysis more tractable with respect to missing outcome data at the partner level. We collected adverse events related to the intervention or trial participation.

The health economic evaluation included a cost-consequence analysis (appendix pp 11–18) and model-based cost-effectiveness analysis, reported separately.³³ We also did a process evaluation.³¹

Statistical analysis

The planned sample size was based on enrolment of a mean of 160 index patients per clinic per trial phase across the 17 clinical services (total 5440 patients) and a coefficient of variation in the number enrolled of 0.5. We expected that 10–25% of patients in the control phase would have a positive *C trachomatis* test result at 12–24 weeks of follow-up,^{12,41} and that 50% of enrolled patients (80 per clinic per phase; 2720 total) would contribute to the analysis of the primary outcome, assuming repeat sampling in 60% and excluding unconfirmed infections at baseline. This sample size would provide 80% power (at a 5% significance level) to detect a reduction in *C trachomatis* positivity from 10% to 5%, and 82% power to detect a reduction from 25% to 17% with the intervention. It would also provide 87% power to detect an increase in *C trachomatis* positivity from 60% to 70% with the intervention in index patients with one or more treated sexual partner(s).¹³ Sample size calculations were guided by Giraudeau and colleagues,⁴² but were performed conservatively as if the trial was a standard cluster-randomised controlled trial with 17 clinics in each randomly assigned group. Our calculations assumed a within-period intracluster correlation coefficient (ICC) of 0.02, in the absence of published data. The trial started in 14 clinics, before the protocol was amended on May 15, 2019. The original enrolment target, calculated in the same way with the same assumptions although assuming equal enrolment across clinics, was 210 index patients per clinic per trial phase (total 5880 patients).

An analysis plan was agreed before completion of data collection. The primary analysis was by intention-to-treat,

including all recorded eligible patients within study periods. For the primary outcome, and other quantitative outcomes, we fitted mixed effects logistic regression models with fixed effect for intervention phase and random effects to acknowledge the clustering of index patients for each clinic and each period nested within clinics.⁴³ The intervention effect is expressed as an odds ratio (OR) with 95% CIs. Models for secondary outcomes quantified for each sexual contact included additional random effects for each index patient. The primary outcome measures used the observed data, adjusted for patient characteristics. We conducted multiple imputation of sexual partner treatment status and index patient repeat test results under the missing-at-random assumption, using information on index patient sex, ethnicity, enrolment based on presence of non-gonococcal urethritis, and age, and did further sensitivity analyses in which we allowed patients who were lost to follow-up to be more, and then less, likely to have a positive *C trachomatis* result at repeat testing than those who were not lost to follow-up.⁴⁴ Analysis of the primary outcome and secondary outcome of one or more sexual partners treated per index patient were repeated in a sensitivity analysis after exclusion of clinics with very low uptake of the accelerated partner therapy intervention (defined after data collection as clinics where less than 15% of index patients accepted accelerated partner therapy for at least one sexual partner). A post-hoc per-protocol analysis was conducted comparing the primary outcome in index patients in the intervention phase who chose accelerated partner therapy, which was accepted by one or more sexual partner(s), with patients in the control phase. Further statistical analysis details are provided in the appendix (pp 9–10).

After the start of the trial, the protocol was amended on July 30, 2019, to allow inclusion and testing of index patient sexually transmitted infection samples up to 24 weeks, after we identified a computer server error that sent reminder texts to some index patients later than the scheduled 16 weeks, and to increase the number of clinics from 14 to 17.

This trial is registered with the ISRCTN registry, 15996256.^{45,46}

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Oct 24, 2018, and Nov 17, 2019, clinic administrative data showed that there were 16 445 chlamydia diagnoses in potentially eligible people. All 17 clinics completed both trial phases and a total of 1536 index patients were enrolled in the intervention phase and 1724 were enrolled in the control phase (figure 2), which was lower than our target of 2720 patients

See Online for appendix

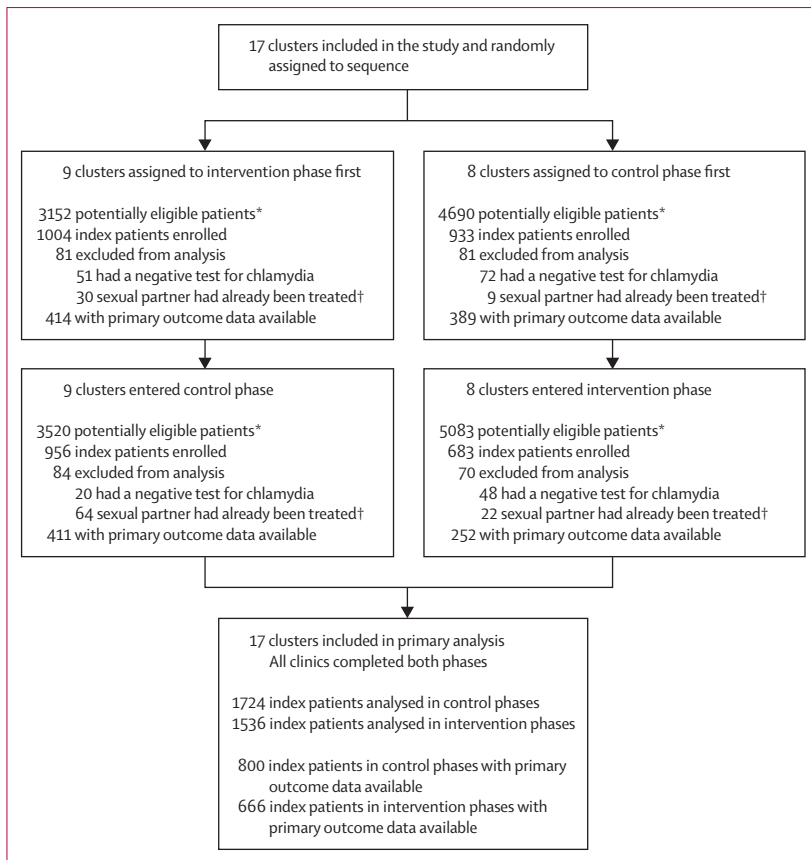


Figure 2: Flow diagram of enrolment by clinic randomisation status and period

*Administrative service data on all chlamydia diagnoses within trial period in heterosexual patients aged 16 years or older not attending as partner notification contact. †All potentially eligible sexual partners treated before clinic consultation of index patient.

in each phase. Baseline characteristics of participants were similar in the intervention and control phases (table 1; appendix p 3). In control phases, participants reported 2589 eligible sexual partners (median 1, IQR 1–2 [range 1–20]; 66% were male). 880 (34%) of these sexual partners were categorised as steady established, 342 (13%) as new relationship, 687 (27%) as occasional, and 680 (26%) as one-off partners (table 1). In intervention phases, participants reported 2218 eligible sexual partners (median 1, IQR 1–2 [range 1–10]; 64% were male). 756 (34%) of these sexual partners were categorised as steady established, 343 (15%) as new relationship, 610 (28%) as occasional, and 509 (23%) as one-off partners (table 1).

666 (43%) of 1536 index patients in the intervention phase and 800 (46%) of 1724 in the control phase returned a sample and were tested for *C trachomatis* at 12–24 weeks after the initial contact tracing consultation. Of those tested, 31 (4.7%) in the intervention phase and 53 (6.6%) in the control phase had a positive *C trachomatis* result (adjusted OR 0.66 [95% CI 0.41 to 1.04]; $p=0.071$; marginal absolute difference -2.2% [95% CI -4.7 to 0.3]; table 2). Analysis after missing-at-random multiple

imputation was consistent with the observed data analysis, but varying our assumptions led to stronger effect estimates both if those who did not return a sample were assumed to be more likely to have a positive result than those who did return a sample (adjusted OR 0.58 [95% CI 0.36 to 0.92]; $p=0.021$), and if those who did return a sample were assumed to be more likely to have a positive result than those who did not (0.57 [0.37 to 0.88]; $p=0.010$). Within-cluster between-period and within-cluster within-period formulations of the ICC were calculated based on a linear mixed model of the primary outcome with adjustment for intervention received and trial phase; both were estimated to be 0.00.

The proportion of index patients with one or more sexual partner(s) notified was 97.7% (1123 of 1150 patients) in the intervention phase and 97.3% (1185 of 1218) in the control phase (adjusted OR 1.18 [95% CI 0.70 to 2.00]; $p=0.54$), while the proportion of all partners notified was 95.0% in both phases (0.80 [0.49 to 1.29]; $p=0.35$). Among index patients with treatment status recorded, 775 (88.0%) of 881 patients in the intervention phase and 760 (84.6%) of 898 in the control phase had one or more treated sexual partners at 2–4 weeks after the initial contact tracing consultation (adjusted OR 1.27 [95% CI 0.96 to 1.68]; $p=0.10$; marginal absolute difference 2.7% [95% CI -0.5 to 6.0]; table 2).

However, of all sexual partners, only 842 (38.0%) of 2218 were known to be treated by 2–4 weeks in the intervention phase (400 [52.9%] of 756 steady established, 182 [53.1%] of 343 new, 162 [26.6%] of 610 occasional, and 98 [19.3%] of 509 one-off partners), and 859 (33.2%) of 2589 were known to be treated by 2–4 weeks in the control phase (400 [45.5%] of 880 established, 151 [44.2%] of 342 new, 175 [25.5%] of 687 occasional, and 133 [19.6%] of 680 one-off partners; table 3). Overall, less than one-fifth of reported one-off partners (231 [19.4%] of 1189) were known to be treated by 2–4 weeks.

A total of 1536 index patients with 2218 partners were enrolled in intervention phases, but accelerated partner therapy could not be offered by the clinic for 81 (4%) of these 2218 partners. Overall, 293 (19%) of 1536 index patients chose accelerated partner therapy for 305 (14%) of 2137 sexual partners, when available (table 4). Of these 305 partners, 166 (54%) were established, 85 (29%) were new, 45 (15%) were occasional, and nine (3%) were one-off partners (appendix p 4). Common reasons for index patients declining accelerated partner therapy included preference for face-to-face conversation (400 [22%] of 1832 patients), partner was already in clinic (388 [21%]), patient was unwilling to engage with partner (206 [11%]), patient preferred partner to attend clinic (202 [11%]), or partner was overseas (150 [8%]).

Following selection of accelerated partner therapy, sexual partner care largely followed all specified steps (table 4), but 49 (16%) of 305 sexual partners could not be contacted by telephone, eight (3%) declined accelerated

	Control phase	Intervention phase
Index patients		
Number of index patients	1724	1536
Age, years	24 (21–28, 17–62); 25.6 (6.4)	24 (21–28, 16–72); 25.7 (7.0)
Sex at birth*		
Male	547 (32%)	522 (34%)
Female	1177 (68%)	1014 (66%)
Basis for enrolment		
Diagnosis of chlamydia	1678 (97%)	1506 (98%)
Pelvic inflammatory disease	7 (<1%)	1 (<1%)
Cervicitis	0	0
Non-gonococcal urethritis	37 (2%)	27 (2%)
Epididymo-orchitis	2 (<1%)	2 (<1%)
Ethnicity		
White British or Irish	829 (48%)	707 (46%)
White other	199 (12%)	181 (12%)
Black or Black British	368 (21%)	377 (25%)
Asian or British Asian	100 (6%)	92 (6%)
Mixed	193 (11%)	134 (9%)
Other	35 (2%)	45 (3%)
Number of sexual partners per index patient		
Sexual partners in the previous 12 months	2 (1–3, 1–100); 3.1 (4.0)	2 (1–4, 1–60); 3.3 (4.5)
New sexual partners in the previous 12 months	2 (1–3, 0–99); 2.4 (3.9)	1 (1–3, 0–50); 2.4 (3.5)
Sexual partners in the previous 1, 3, or 6 months†	2 (1–2, 1–25); 2.1 (1.9)	1 (1–2, 1–39); 2.0 (2.0)
Sexual partners included in analysis	1 (1–2, 1–20); 1.5 (1.0)	1 (1–2, 1–10); 1.4 (0.9)

(Table 1 continues in next column)

partner therapy, and seven (2%) were transferred into face-to-face clinical care. Of 241 sexual partners who were sent accelerated partner therapy packs, 183 (76%) were male and 58 (24%) were female, and 120 (50%) returned chlamydia and gonorrhoea testing samples (among whom 78 [66%] of 119 had a positive test result for chlamydia [no result obtained for one returned sample]), but only 60 (25%) returned HIV and syphilis testing samples (all were negative; table 4; appendix p 1).

On sensitivity analysis excluding data from six clinics where less than 15% of index patients accepted accelerated partner therapy for at least one sexual partner, there was no significant intervention effect on index patient repeat chlamydia test results (appendix p 7), although there was a significant increase in the proportion of index patients with one or more treated sexual partners. In the per-protocol analysis, among 106 index patients who chose accelerated partner therapy, which was accepted by one or more sexual partners, and who had a repeat test for chlamydia at 12–24 weeks, only two (1.9%) patients were positive, compared with 53 (6.6%) in the control phase (adjusted OR 0.26

	Control phase	Intervention phase
(Continued from previous column)		
Sexual partners		
Number of sexual partners	2589	2218
Gender identity‡		
Male	1699 (66%)	1419 (64%)
Female	890 (34%)	799 (36%)
Partner type§		
Committed or steady established	880 (34%)	756 (34%)
New relationship	342 (13%)	343 (15%)
Occasional	687 (27%)	610 (28%)
One-off	680 (26%)	509 (23%)
Condom use with this partner		
Always	293 (11%)	202 (9%)
Sometimes	870 (34%)	800 (36%)
Never	1426 (55%)	1216 (55%)
Likelihood of future sex with this partner		
No	1066 (41%)	844 (38%)
Not sure	614 (24%)	458 (21%)
Yes	909 (35%)	916 (42%)

Data are n, n (%), or median (IQR, range); mean (SD). Sociodemographic data on sexual partners were provided by the index patients. *This was the same as current gender identity in all index patients in the primary analysis. †Dependent on basis for initial enrolment. ‡Response to question to index partner ("How does this partner describe their current gender identity?"; "What sex was the sex partner assigned at birth?" was also included in questionnaire but data were only recorded for 250 of 4807 partners). §Standardised assessment by health-care staff using the limiting undetected sexually transmitted infections to reduce morbidity (LUSTRUM) sex partner classification.³⁷

Table 1: Baseline characteristics of index patients and their sexual partners

[95% CI 0.06–1.07]; appendix p 6). In 560 index patients who did not select accelerated partner therapy or whose sexual partners did not accept, 29 (5.2%) were positive.

There were insufficient data to measure the prespecified outcome of time to sexual partner treatment because index patients were often unsure exactly when their sexual partners received care.

Full details of the cost-consequence analysis are provided in the appendix (pp 11–18). Briefly, total contact tracing cost per index patient was £71.26 in the control phase, £91.23 in the intervention phase with accelerated partner therapy, and £74.83 in the intervention phase without accelerated partner therapy. The differences were mostly driven by costs associated with estimated duration of initial consultation. The results suggest the accelerated partner therapy strategy is more costly but also more effective in preventing repeat infection in index patients compared with usual care. For sexual partners, total contact tracing cost was £33.17 in the intervention phase with accelerated partner therapy compared with £39.58 in the control phase, if we assume that sexual partners only returned samples for chlamydia testing. However, if we assume that some sexual partners had an additional test for HIV or syphilis, the costs

	Control phase (n=1724)	Intervention phase (n=1536)	OR (95% CI); p value	Adjusted OR (95% CI); p value; marginal difference (95% CI)
Primary outcome				
<i>Chlamydia trachomatis</i> test result at 12–24 weeks (observed data)				
Not tested*	924	870	NA*	NA*
Tested	800	666
Positive	53 (6.6%)	31 (4.7%)	0.67 (0.42 to 1.06); 0.083	0.66 (0.41 to 1.04); 0.071; -2.2% (-4.7 to 0.3)
Negative	747 (93.4%)	635 (95.3%)
<i>C trachomatis</i> test result at 12–24 weeks (MAR MI)				
Positive	116 (6.7%)	73 (4.8%)	0.67 (0.40 to 1.14); 0.14	0.67 (0.39 to 1.14); 0.14
Negative	1608 (93.3%)	1463 (95.2%)
<i>C trachomatis</i> test result at 12–24 weeks (MNAAR MI: $\delta = \log_e[0.5]$)				
Positive	154 (8.9%)	86 (5.6%)	0.58 (0.36 to 0.92); 0.021	0.58 (0.36 to 0.92); 0.020
Negative	1570 (91.1%)	1450 (94.4%)
<i>C trachomatis</i> test result at 12–24 weeks (MNAAR MI: $\delta = \log_e[2.0]$)				
Positive	98 (5.7%)	55 (3.6%)	0.57 (0.38 to 0.88); 0.010	0.57 (0.37 to 0.88); 0.012
Negative	1626 (94.3%)	1481 (96.4%)
Secondary outcomes				
At least one sexual partner treated for chlamydia at 2–4 weeks (observed data)				
Yes†	760 (84.6%)	775 (88.0%)	1.25 (0.94 to 1.64); 0.12	1.27 (0.96 to 1.68); 0.10; 2.7% (-0.5 to 6.0)
No‡	138 (15.4%)	106 (12.0%)
Not known*	826	655	NA*	NA*
At least one sexual partner treated for chlamydia at 2–4 weeks (MAR MI)				
Yes	1452 (84.2%)	1344 (87.5%)	1.29 (0.94 to 1.77); 0.12	1.30 (0.94 to 1.81); 0.12
No§	272 (15.8%)	192 (12.5%)
At least one sexual partner notified (observed data)				
Yes†	1185 (97.3%)	1123 (97.7%)	1.17 (0.69 to 1.97); 0.56	1.18 (0.70 to 2.00); 0.54; 0.4% (-0.8 to 1.7)
No‡	33 (2.7%)	27 (2.3%)
Not known*	506	386	NA*	NA*

Data are n or n (%) unless otherwise stated. Marginal percentage differences are shown for observed data analyses, averaging over fixed covariates of study population and integrating over random effects. For MNAAR analyses, δ is the OR that a positive case will have their outcome observed. Mean average values across imputations are reported where relevant. MAR=missing at random. MI=multiple imputation. MNAAR=missing not at random. NA=not applicable. OR=odds ratio. *Considered missing and not included in model estimation. †Determined by follow-up interview with index patient, or return of accelerated partner therapy self-test kits within 30 days. ‡Includes a mixture of no and unknown treatment outcomes for sexual partners listed for a single index patient. §Mixture of no and unknown treatment outcomes for sexual partners listed for a single index patient treated as observed no rather than imputed.

Table 2: Effect of offer of accelerated partner therapy on outcome measures in index patients

increased to £40.12 (with accelerated partner therapy) versus £46.53 (with standard contact tracing). This analysis presents disaggregated cost and consequence results only for the intermediate outcome of repeat infections avoided. A full economic impact for this outcome (based on pathways that follow this outcome) has to be modelled to estimate the cost-effectiveness of these alternative strategies. A full but preliminary economic evaluation, based on a population-based chlamydia transmission model comparing cost-effectiveness of accelerated partner therapy with standard

partner notification in terms of major outcomes averted and quality-adjusted life-years gained, is reported elsewhere.³³

Detailed findings of the process evaluation are reported elsewhere.³¹ Clinics operationalised the trial differently; some aimed to offer accelerated partner therapy to all potentially eligible patients, whereas others only offered accelerated partner therapy when certain staff were present. Staff found that the RELAY platform made it easier to document contact tracing processes and outcomes because it was intuitive and supported partner notification processes in both the intervention and control phases, as it guided health-care professionals through the full contact management process. Index patients commonly reported that accelerated partner therapy was only suitable within established relationships and not for one-off sexual partners, which is reflected in the trial findings (appendix pp 4–5). However, staff did not always offer accelerated partner therapy, citing multiple pressures, including lack of time to create RELAY records in addition to their clinical notes. Also, some sexual partners accompanied the index patients when they attended for treatment, or had already accessed face-to-face care. Participants who chose accelerated partner therapy felt it was acceptable and intuitive, worked well, and helped sexual partners overcome barriers to accessing care.³¹ Some sexual partners took the antibiotics immediately and used the self-sampling kits as a test of cure. Some sexual partners reported difficulties with fingerprick blood sampling and some did not understand the rationale for the full testing for sexually transmitted infections, although this was explained during their consultation. Most clinics were unable to provide sexual partners with direct links to the videos we had created to assist engagement with accelerated partner therapy and use of the packs.

Seven low-severity adverse events were reported, with no clinically significant harms to patients. In the first incident, results of self-sampling sexually transmitted infection tests for two patients were sent by post to site 1, instead of by secure email to named individuals. In the second incident, results of self-sampling sexually transmitted infection tests for two patients were sent by post to site 2, instead of by secure email to named individuals. In the third incident, one sexual partner was provided with antibiotics without assessment but tested negative and did not take them. In the fourth incident, 491 patients received reminder text messages later than intended, 52 patients received a message in error, and 78 patients did not receive a reminder text message. In the fifth incident, one sexual partner found an accelerated partner therapy pack intended for another sexual partner, which contained contact details. In the sixth incident, one index patient who had opted out of receiving a postal kit received one in error. In the final incident, one patient reported that they had not done any tests but had received

a text message with negative results. There were no adverse events relating to antibiotics taken.

Discussion

The offer of accelerated partner therapy in the intervention phase resulted in a reduction in the proportion of patients with repeat chlamydia infection at 12–24 weeks after initial consultation compared with those in the control phase, and an increase in the proportion of index patients with at least one treated sexual partner by 2–4 weeks. Overall, 293 (19%) of 1536 index patients chose accelerated partner therapy for a total of 305 partners, of whom 248 accepted. The accelerated partner therapy intervention cost slightly more than standard contact tracing per index patient, but sexual partner testing and treatment were cheaper with accelerated partner therapy.

We developed the accelerated partner therapy intervention following a stepwise framework for complex interventions,^{21,40,47,48} and measured the primary outcome with a biological marker of chlamydia infection.¹² The accelerated partner therapy intervention was theory-informed⁴⁹ and delivered with high fidelity,³¹ by trained health-care professionals in various sexual health clinic settings. Recognising the contribution of different types of sexual partnership to sexually transmitted infection transmission,⁵⁰ we also examined the effects of accelerated partner therapy using a novel classification of sexual partner type.³⁷

A limitation of the trial was the reduced statistical power because the prevalence of chlamydia infection at time of repeat testing was lower than in the studies on which we based our sample size (6·6% in the control phase vs 10·0–25·0% expected).^{11,27,41,51} Possible reasons for this lower prevalence include the potential for selection bias. The process evaluation suggested that the trial generated additional administrative work, with the need to create a RELAY record even when patients did not accept accelerated partner therapy.³¹ Overall chlamydia test positivity at follow-up might have been low if people who enrolled in the trial were more likely to follow recommendations to reduce repeat infection than those who did not enrol. It is also possible that full implementation of enhanced patient referral in both trial phases had real-world effects, or that the crossover design reduced community transmission and chlamydia incidence in both trial phases. Slightly less than half of the index patients returned a sample for repeat chlamydia testing, despite reminders, which reduced the precision of our estimates for the primary outcome. However, multiple imputation models under different assumptions showed findings that were consistent with the main analysis. Overall recruitment was also lower than our target because many eligible patients were not enrolled (figure 2), probably because of the additional administrative work, and recruitment also differed somewhat by trial phase, which could have introduced bias. The reduced power

	Control phase (n=2589)	Intervention phase (n=2218)	OR (95% CI); p value	Adjusted OR (95% CI); p value
Treated at 2–4 weeks (observed data)				
Yes*	859 (79.6%)	842 (83.6%)	1.31 (0.94–1.83); 0.11	1.25 (0.88–1.77); 0.20
No	220 (20.4%)	165 (16.4%)
Not known by index patient†	699	538	NA†	NA†
Follow-up not recorded‡	811	673	NA†	NA†
Known to be treated at 2–4 weeks				
Yes*	859 (33.2%)	842 (38.0%)	1.50 (1.08–2.10); 0.013	1.27 (0.99–1.65); 0.057
No	1730 (66.8%)	1376 (62.0%)
Notified at 2–4 weeks (observed data)				
Yes	1700 (95.0%)	1514 (95.0%)	0.93 (0.58–1.47); 0.75	0.80 (0.49–1.29); 0.35
No	89 (5.0%)	79 (5.0%)
Follow-up not recorded‡	800	625	NA†	NA†
Stratified by relationship type				
Treated at 2–4 weeks (observed data)				
Yes*, steady established‡	400/478 (83.7%) (n=880)	400/447 (89.5%) (n=756)	1.74 (1.04–2.91); 0.036	1.65 (0.96–2.82); 0.070
Yes*, new relationship‡	151/176 (85.8%) (n=342)	182/200 (91.0%) (n=343)	1.83 (0.79–4.24); 0.16	1.72 (0.72–4.14); 0.22
Yes*, occasional partner‡	175/232 (75.4%) (n=687)	162/207 (78.3%) (n=610)	1.19 (0.62–2.28); 0.59	1.16 (0.59–2.29); 0.66
Yes*, one-off partner‡	133/193 (68.9%) (n=680)	98/153 (64.1%) (n=509)	0.64 (0.32–1.27); 0.20	0.65 (0.32–1.32); 0.23

Data are n, n (%), or n/N (%) unless otherwise stated. NA=not applicable. OR=odds ratio. *Determined by follow-up interview with index patient, or return of accelerated partner therapy self-test kits within 30 days. †Considered missing and not included in model estimation. ‡The estimated effect of intervention group on the outcome is reported within each subgroup of sexual partner.

Table 3: Effect of offer of accelerated partner therapy on outcome measures in sexual partners

might, however, be partly offset by the lower than expected ICC (0.00 compared with 0.02), and we note our original power calculation conservatively assumed no correlation over time between phases within clusters. Accelerated partner therapy uptake was not considered within the power calculations; although accelerated partner therapy was not always offered, we expected more index patients to choose it when it was available.^{20,21}

This trial adds to the evidence from preliminary studies.^{20,21} Uptake of accelerated partner therapy in previous studies appeared to be associated with how the intervention was operationalised in individual clinics,²⁰ and varied between 40% and 80%. In this study, index patient uptake of accelerated partner therapy also differed between clusters (appendix p 3), largely influenced by the amount of enthusiasm for the trial but also possibly due to changes in how clinics provided usual care over time, such as by encouraging index patients to bring their sexual partners with them when attending for treatment (appendix pp 4–5). A separate mathematical modelling study showed the trial results to be consistent with an increased probability of successful partner treatment.⁵²

	Number
Per index patient	
Total index patients in intervention phase	1536
Accelerated partner therapy not selected for any partner	1243 (81%)
Accelerated partner therapy selected by index patient for ≥1 partner	293 (19%)
Accelerated partner therapy accepted by ≥1 partner	244 (16%)
Per sexual partner	
Total sexual partners in intervention phase	2218
Accelerated partner therapy not offered by clinic	81/2218 (4%)
Staffing limitations	68/81 (84%)
Drug supply issues	13/81 (16%)
Accelerated partner therapy not selected by index patient	1832/2137 (86%)
Patient preferred to have the conversation with the partner face to face	400/1832 (22%)
Partner was in clinic to be treated*	388/1832 (21%)
Patient did not want to talk to or see partner	206/1832 (11%)
Patient preferred for the partner to visit the clinic	202/1832 (11%)
Partner was overseas	150/1832 (8%)
Patient did not have partner's phone number	59/1832 (3%)
Patient was worried about partner's reaction	57/1832 (3%)
Patient did not understand how accelerated partner therapy works	1/1832 (<1%)
Other or missing	369/1832 (20%)
Accelerated partner therapy selected by index patient	305/2137 (14%)
No answer to phone call	49/305 (16%)
Sexual partner declined accelerated partner therapy	8/305 (3%)
Accelerated partner therapy accepted	248/305 (81%)
Accelerated partner therapy not clinically appropriate	7/248 (3%)
Receipt of accelerated partner therapy pack	
Not known	36/241 (15%)
Confirmed†	205/241 (85%)

(Table 4 continues in next column)

	Number
(Continued from previous column)	
HIV and sexually transmitted infection testing	
Chlamydia	
Test returned‡	120/241 (50%)
Positive	78/120 (65%)
No result obtained	1/120 (1%)
Gonorrhoea	
Test returned‡	120/241 (50%)
Positive	1/120 (1%)
No result obtained	1/120 (1%)
Syphilis	
Test returned‡	60/241 (25%)
Positive	0/60
No result obtained	0/60
HIV	
Test returned‡	60/241 (25%)
Positive	0/60
No result obtained	0/60

Data are n, n (%), or n/N (%). *Partners were excluded from analysis if there was evidence that they had been treated before the index patient's consultation. †Confirmed by index patient at 2-week follow-up or by return of self-sample test kit within 30 days. ‡With self-sampling within 30 days of accelerated partner therapy consultation.

Table 4: Summary of accelerated partner therapy uptake and HIV and sexually transmitted infection testing during intervention phases

Accelerated partner therapy is a UK adaptation of expedited partner therapy.³³ In a systematic review, expedited partner therapy resulted in lower proportions of index patients with repeated curable sexually transmitted infections (any of gonorrhoea, chlamydia, or trichomoniasis) than simple patient-referral contact tracing.¹² Golden and colleagues²⁴ used a randomised step-wedge design to evaluate expedited partner therapy in Washington, USA, and found some evidence of lower chlamydia positivity and gonorrhoea incidence at the population level. There are important differences between the UK and US settings and between accelerated partner therapy and expedited partner therapy. First, baseline and repeat infection rates were considerably higher in US studies than in our trial and pre-existing contact tracing outcomes were poorer than those

routinely observed in the UK. Second, expedited partner therapy trials did not include sexual partner sexually transmitted infection and HIV testing, so sexual partners who were found to have an infection did not receive contact tracing services. Of note, in our trial, almost two-thirds of sexual partners who returned a sample had a positive chlamydia test result and so onward contact tracing outside the trial might have wider, but unmeasured, effects on community transmission. Third, accelerated partner therapy treatment is limited to chlamydia, because current recommended first-line treatment for *Neisseria gonorrhoeae* in the UK is parenteral. Although expedited partner therapy guidance still allows oral cefixime treatment for gonorrhoea, an update in 2021 suggested that providers should limit treatment to people who cannot access prompt clinical evaluation.²³

Accelerated partner therapy is a safe and acceptable intervention that could be used as a contact tracing option, allowing sexual partners to receive treatment after exposure to chlamydia without the need for a clinic appointment. The preliminary analysis suggests that accelerated partner therapy might be cost-saving compared with usual care.³³ Of note, the linked modelling study suggests that there is potential for reduction in prevalence of chlamydia at the population level.³² We attribute the modest effect sizes, in part, to the smaller than expected numbers of index patients choosing accelerated partner therapy for their partners. It is also

possible that the use of RELAY, which appealed to clinic staff (as had been the case with earlier versions²¹), systematically enhanced contact tracing processes and outcome recording in usual care, reducing any difference associated with accelerated partner therapy.

Different types of sexual partners contribute differentially to onward transmission of sexually transmitted infections; one-off partnerships are likely to contribute disproportionately.⁵³ In almost all instances where index patients chose accelerated partner therapy, this was for an established or ongoing partner, which suggests that appropriate targeting of accelerated partner therapy will be needed for optimal impact. The types of (untreated) partner most likely to be responsible for repeat infection are therefore those with whom sex is ongoing, such as the steady established partner category in this trial. We found it was mostly these established partners with higher repeat infection risk who accepted accelerated partner therapy, which is likely to explain the effect seen despite the low uptake of accelerated partner therapy overall. Almost half of the sexual partners accepting accelerated partner therapy returned a sample (urine or vulvovaginal swab) for chlamydia and gonorrhoea testing, which was a much higher proportion than in our earlier feasibility study.²⁰ However, only about one-quarter returned samples for HIV and syphilis testing. By contrast, almost all sexual partners who attend sexual health services in person receive comprehensive testing.

In the UK, the COVID-19 pandemic has accelerated the shift to remote, self-managed health care. Accelerated partner therapy is likely to be a cost-saving approach,³³ which uses elements of self-management and contains all recommended elements of usual care.¹⁷ Uptake might increase in a post-COVID-19 setting, because of increased familiarity with self-sampling, self-testing, and contact tracing, as well as the rationale of making individual health decisions for both personal and public benefit. Sexual health services should therefore start to integrate accelerated partner therapy into their usual contact tracing practices, promoting it for index patients with established or ongoing sexual partners, accompanied by research focusing on normalisation, scale-up, and skills acquisition.

However, the well described, long-term pressures on UK sexual health services⁵⁰ will make it hard for services to facilitate immediate, and possibly unscheduled, assessment of sexual partners. Accelerated partner therapy will need to be audited alongside all other contact tracing approaches, so data collection practices, including recording of partnership type,³⁶ should be established now. More work is needed to increase uptake of self-sampling for sexually transmitted infections as part of accelerated partner therapy, so that opportunities for screening and control of syphilis, HIV, and other blood-borne viruses among those at higher risk of infection are not lost. Additionally, the potential harms of accelerated

partner therapy should continue to be assessed, because universal epidemiological treatment of sexual partners of people with chlamydia, in the absence of positive test results (current UK national guidance), leads to overuse of antibiotics.²⁶ When implemented into routine services, the trial-associated administrative work would not exist and staff might offer accelerated partner therapy, and sexually transmitted infection and HIV testing, more assertively.

More broadly, we need to consider sexual partners who are less likely to be reached by accelerated partner therapy, such as one-off partners with whom future sex is not anticipated. Although these partners do not pose a risk of repeat infection in the index patient, they are likely to make an important contribution to community transmission. Further research is needed to improve contact tracing and management options for other groups with higher prevalence of sexually transmitted infections and blood-borne viruses, including men who have sex with men, transgender people, and gender-diverse people. These options could include anonymous web-based services.

Accelerated partner therapy might lead to overuse of antibiotics, potentially increasing antimicrobial resistance. However, this is not unique to accelerated partner therapy as this type of empirical partner treatment is part of routine UK practice, irrespective of method of contact tracing used. Further work is needed to explore the optimal usage of empirical antibiotics in these situations.

To maximise the impact of accelerated partner therapy for individuals and their sexual partners, there needs to be a focus on increasing uptake. This will require health-care professionals to promote accelerated partner therapy for emotionally connected sexual partners where future sex is likely to occur, and flexibility in clinic capacity and workflows to accommodate immediate sexual partner management during the index patient's attendance. Accelerated partner therapy can be safely offered as a potentially cost-saving contact tracing option for heterosexual people with *C trachomatis* infection and might reduce the risk of repeat infection.

Contributors

CSE (principal investigator), AC (statistical lead), NL (mathematical modelling lead), JS, CHM, PF (qualitative and health psychology lead), TR (health economics lead), MS, RN, AMJ, and JAC conceived and designed the study and secured funding. OS and FM contributed to study design after funding was acquired. CSE, OS, AC, FM, PF, ARH, MS, MWO, SB, CO, EW, AC-S, AT, and JAC contributed to data collection. Data analysis was led by AC and OS with CSE, NL, FM, JS, CHM, PF, TR, RN, MWO, SB, CLA, AMJ, CO, EW, AT, and JAC. OS, AC, AT, ARH, and CSE have directly accessed and verified the underlying data reported in the manuscript. All authors contributed to interpretation of findings, and reviewed and approved the final manuscript. OS conducted the statistical analyses. CO and EW conducted the health economic analyses. CLA conducted the mathematical modelling. PF and FM conducted the process evaluation. FM led the development of RELAY and shared trial coordination and operationalisation with ARH, assisted by MWO. AT was data manager. MS, SB, and AC-S helped develop trial processes. JAC made substantial

conceptual contributions throughout the programme and specifically to the trial.

Declaration of interests

CSE reports honorarium for lectures at the 2020 Joint Australasian HIV & AIDS and Sexual Health Conferences; and is a Trustee to the Board of the British Association for Sexual Health and HIV (BASHH). JS reports BASHH 2022, 2021, and 2020 annual conference registration covered by BASHH, as an invited speaker (no honoraria received), with registration (all years) and accommodation (2022) paid by BASHH; attendance at the International Society STD Research (ISSTD) conference 2021 as an invited speaker (no honoraria received), with registration paid by ISSTD; is a BASHH National Audit Group committee member; and is a BASHH Bacterial STI special interest group committee member. RN reports sexual health and blood-borne virus clinical support from the Scottish Government; and is a non-executive Director on the Board of Public Health Scotland. JAC reports that BASHH has supported implementation work in other institutions within the LUSTRUM consortium, aiming to embed partnership type specifications into audits of partner notification, including work preparatory to a publication in *Eurosurveillance*. All other authors declare no competing interests.

Data sharing

The trial dataset is available at https://rdr.ucl.ac.uk/articles/dataset/LUSTRUM_Accelerated_partner_therapy_APT_cross-over_cluster_randomised_controlled_trial_data/14724669.

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