

Effectiveness and cost-effectiveness of traditional and new partner notification technologies for curable sexually transmitted infections: observational study, systematic reviews and mathematical modelling

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Declared competing interests of authors: Christian L Althaus received salary support from the Swiss National Science Foundation (PZ00P3_136737). Katherine M E Turner received salary support from the UK National Institute for Health Research Post-Doctoral Fellowship programme (project number: PDF 2009-02-055) and consultancy fees from the Department of Health Office for Sexual Health, University Hospitals Bristol NHS Foundation Trust and National Institute for Health and Care Excellence. Catherine H Mercer received funding from the UK Medical Research Council (grant number: G0601685). Sereina A Herzog received salary support from the Swiss National Science Foundation (grant numbers: PDFMP3_124952, 320030_135654). Jackie A Cassell received grant funding from the National Institute for Health Research Health Technology Assessment programme (project number: 07/42/01) and consultancy fees from the European Centre for Disease Prevention and Control. Peter J White received support from the UK Medical Research Council Centre for Outbreak Analysis and Modelling. Helen Ward received grant funding from the UK Medical Research Council (G0601699) and the Wellcome Trust (090285/Z/09/Z). Nicola Low received funding from the Swiss National Science Foundation (grant numbers: PDFMP3_124952, 320030_135654) and from GlaxoSmithKline to chair a scientific advisory board meeting about chlamydia vaccines in September 2010. She is on the editorial board of the Cochrane Sexually Transmitted Infections Review Group and co-author of a systematic review of partner notification strategies, which will be published in the *Cochrane Database of Systematic Reviews*.

Published January 2014

DOI: 10.3310/hta18020

Scientific summary

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Health Technology Assessment 2014; Vol. 18: No. 2

DOI: 10.3310/hta18020

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

Partner notification is essential to the comprehensive case management of people with sexually transmitted infections (STIs). As a multilevel process, the goals and outcomes of partner notification vary depending on the target level and on the sexual behaviour of the index case and type of sexual partnerships that he or she has. The sexual partners of index cases can be reached with a range of methods, each of which can be considered as a separate technology. Traditional methods of partner notification, including patient and provider referral, require sexual partners to attend a health-service setting to be assessed clinically before antibiotic treatment can be dispensed or prescribed. Patient referral methods can be separated into simple and enhanced, depending on the intensity of the intervention. New technologies have been developed to allow partners to receive treatment without a face-to-face assessment in a health-service setting. Expedited partner therapy (EPT) was developed in the USA and involves giving index cases antibiotics or prescriptions for their partners without the need for a consultation with a health professional. Its UK equivalent is accelerated partner therapy (APT), where the consultation can be done by telephone or with a pharmacist.

Objectives

The Health Technology Assessment (HTA) programme asked, 'What is the clinical and cost-effectiveness of providing treatment for the partner(s) of people with a STI without testing them for the STI first?' The project presented in this monograph addressed the question by investigating both traditional and new partner notification technologies for curable STIs. Methods were outlined in a protocol. Specific objectives were:

- to compare the effectiveness of different partner notification approaches to providing testing and treatment for the partners of people with curable STIs by
 - systematic reviews and analysis of secondary data to obtain estimates of outcome measures
 - mathematical modelling to estimate impact. The modelling studies considered chlamydia and gonorrhoea transmission in general heterosexual populations
- to determine the cost-effectiveness of different partner notification approaches to providing testing and treatment for the partners of people with curable STIs
- to provide recommendations for future research.

Methods

The authors used a range of research methods: analysis of secondary data, systematic reviews, and static and dynamic modelling studies.

Secondary data

The authors analysed clinical audit data about partner notification for chlamydia to estimate intermediate outcomes of partner notification for chlamydia in UK genitourinary medicine clinics. There were three outcome measures: the number of partners per index case who were tested for chlamydia; the number of

partners per index case with a positive chlamydia test; and the number of partners treated per index case. Shewhart control charts (R, The R Foundation for Statistical Computing, Vienna, Austria) were used to describe variability in outcomes across clinics and a hierarchical logistic regression model was constructed to examine factors associated with partner notification outcomes at the individual and clinic levels.

Systematic reviews

The authors performed two systematic reviews. The first examined the effects of traditional and new partner notification technologies in randomised controlled trials published from 1 January 1966 to 31 August 2012, searching MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials. The populations studied were patients with chlamydia, gonorrhoea, non-specific genital infection, trichomonas, pelvic inflammatory disease (PID), syphilis or co-infection with any of these STIs. The primary outcome was reinfection of the index case, measured as repeated detection at a follow-up visit. Meta-analysis was conducted where appropriate.

The second systematic review included published studies from 1 January 1980 to 31 December 2011 examining the evidence available for obtaining quality-adjusted life-year (QALY) estimates for female reproductive tract outcomes of bacterial STIs. The databases searched were MEDLINE, EMBASE, ISI Web of Knowledge, NHS Economic Evaluation Database (NHS EED), Database of Abstracts of Reviews of Effects (DARE) and HTA. The population of interest was women. Outcomes were measures of health-related quality of life (HRQL) and QALY weights. The analysis was descriptive.

Static models

Two studies used static models. In the first, the authors developed an algorithm to estimate the probability of chlamydia transmission from index cases to the next two generations of sexual partners. Data inputs included partnership numbers and types from a genitourinary medicine clinic audit, and estimates of chlamydia transmissibility, adjusted for partnership type. Two new measures of partner notification impact were derived: (1) the absolute reduction in onward transmission and (2) its reciprocal, the number of partners that need to be notified to interrupt one secondary transmission (NNTIT).

In the other study, a spreadsheet tool (Microsoft Excel, Microsoft Corporation, Richmond, WA, USA) was used to compare the cost per new case detected through partner notification and by increasing screening coverage in the National Chlamydia Screening Programme (NCSP) in England. Costs were obtained from a costing guidance initiative from the NCSP. The baseline programme was compared with one scenario with increased screening in men, and with another scenario with increased efficacy of notification of partners of index cases.

Dynamic models

The authors first conducted preparatory studies to improve parameter estimates and determine an appropriate modelling framework. First, they used a simple compartmental model of chlamydia transmission to examine the influence of different parameters on the predicted impact of an intervention programme. Based on the findings, new estimates of the average duration of asymptomatic chlamydia and the per-sex act and the per-partnership transmission probabilities of chlamydia were derived, based on reanalysis of previously published data. The authors then compared three published individual-based models of chlamydia transmission, using UK-population-based data about sexual behaviour and chlamydia positivity. As a result, a new individual-based modelling framework for STIs was developed. This was used to study the individual- and population-level effects of traditional partner notification methods for chlamydia, according to different numbers of partners traced or different look-back periods.

A new mathematical model of chlamydia and gonorrhoea co-infection was then developed, informed by a reanalysis of previously published epidemiological data. The model was used to examine the effects of traditional (partner attends clinic for treatment and STI testing) and new (APT, treatment without testing)

technologies among heterosexuals on the prevalence of each STI and on the frequency of outbreaks of gonorrhoea. Reinfection of index cases with chlamydia and gonorrhoea by their untreated partners, after different delays until partner treatment, was estimated using a simple probability model.

Results

The systematic review of randomised controlled trials provided strong evidence that EPT is more effective than simple patient referral in reducing reinfection in the index cases with curable STIs [risk ratio (RR) 0.71; 95% confidence interval (CI) 0.56 to 0.89]. There was no evidence that EPT was better than enhanced patient referral (RR 0.96; 95% CI 0.60 to 1.53). The evidence was insufficient to determine which method of enhanced patient referral was most effective in particular settings.

Analysis of UK clinical audit data showed a median of 0.47 partners tested for chlamydia per index case and 0.60 partners treated per index case. Partner notification outcomes were lower in London than elsewhere (median number tested per index case 0.30 vs. 0.52) and lower in men who have sex with men than in heterosexual men [adjusted odds ratio (OR) 0.34; 95% CI 0.17 to 0.68]. These levels of intermediate outcomes of partner notification are comparable with levels found in the randomised controlled trials in the systematic review.

The static model estimating the impact of partner notification for chlamydia in genitourinary medicine clinic attendees found that fewer casual than regular partners need to be traced and treated to prevent a secondary case. For example, the NNTIT for men aged < 25 years was 1.92 for casual partners and 3.25 for regular partners. The algorithm provides a basic tool to support public health decision-making at the local clinic level but a dynamic model is required for detailed analysis of the effects of partner notification on chlamydia transmission.

Modelling the transmission dynamics of *Chlamydia trachomatis* provides new estimates of the average duration of asymptomatic chlamydia infection in women (433 days; 95% CI 420 to 447 days); the heterosexual per-partnership transmission probability of chlamydia [55.5%; interquartile range (IQR) 49.2% to 62.5%]; and per-sex act probability (9.5%; IQR 6.0% to 16.7%). Comparison of three individual-based models of chlamydia transmission showed that differences in sexual partnership dynamics and in infection parameter estimates partly explained the differences in model predictions of preventative interventions. A new framework for individual-based models of STI transmission was developed to improve the modelling of the sexual partnership dynamics.

In an individual-based model of chlamydia transmission with baseline prevalence 3%, model predictions show that 68% of current partners of chlamydia-positive index cases would be infected. A look-back period of up to 18 months would identify > 10% positivity in notified partners. At chlamydia screening rates of 0.1 per year, prevalence was reduced to about 70% of the baseline prevalence after 5 years. An additional reduction in chlamydia prevalence is obtained with partner notification, to about 60% of the baseline. If each partner is successfully treated with a probability of 50%, notification of the current partner achieves most of the additional reduction.

A new individual-based mathematical model of both chlamydia and gonorrhoea transmission was developed. To reproduce observed patterns of chlamydia and gonorrhoea prevalence and co-infection, an interaction has to be assumed, in which infection with either chlamydia or gonorrhoea increases susceptibility to the other. In the model, cotesting and treatment reduced the prevalence of both infections. The effect of APT compared with standard patient referral was minor in reducing the prevalence of both infections at the population level. Reductions in the time to treatment of partners, which could be achieved with APT, could reduce index case reinfection rates substantially.

Our systematic review of HRQL studies for chlamydia infection found few robust and validated tools. The only published QALY estimates were judged to be of too low quality to be used to study the cost-effectiveness of partner notification using this outcome. As a result, we did not estimate incremental cost-effectiveness ratios using cost per QALY in this project.

Measuring the costs of chlamydia screening and traditional partner notification technologies in the context of the NCSP in England suggested that doubling the efficacy of partner notification (from 0.4 to 0.8 partners per index case) would reduce the costs per infection diagnosed for a limited additional investment. In contrast, increasing the screening coverage of men to the same level as for women would require an investment of six times more money but lead to only twice as many additional infections being treated.

Conclusions

Implications for health care

- A range of enhanced patient referral methods is available. Genitourinary medicine clinics have staff with the skills and resources for conducting enhanced patient referral. Patients with curable STIs in primary care and community sexual health services should also be able to receive enhanced patient referral as part of their management. Support from health advisers in genitourinary medicine clinics and training for staff in primary and community health-care services might need to be strengthened.
- The findings of two studies in this monograph emphasise the importance of sexual history taking. First, sexual histories need to cover look-back periods that identify previous partners because our mathematical model predicted high percentages of sexual partners infected with chlamydia as far back as 18 months or three previous partners. Second, it is important to find out the type of sexual partnerships of index cases. The need for health adviser support for notifying casual partners should be considered because of the potential gains in interrupting transmission.
- The analysis of audit data shows that the outcomes of partner notification in genitourinary medicine clinics remain modest. The studies in this monograph show evidence of the gains of improving outcomes. The economic evaluation suggests that relative costs (per case identified) of increasing the success of partner notification are less than the costs of increasing the coverage of chlamydia screening.
- Although we examined the risk of gonorrhoea outbreaks as an unintended consequence of APT, this technology also has implications for the underdiagnosis and undertreatment of other STIs, which we did not consider. First, there are missed opportunities for diagnosing human immunodeficiency virus (HIV) infection and the importance of STI testing needs to be explained to partners receiving APT. Second, if an index case has chlamydia and gonorrhoea but is not tested for gonorrhoea or the test gives a false-negative result, the APT antibiotic will be a single 1-g dose of azithromycin, which is an inadequate treatment for gonorrhoea and could encourage antimicrobial resistance. Third, treatment for uncomplicated chlamydia and/or gonorrhoea will not be adequate treatment if a female partner has PID.
- The findings about the effects and impact of partner notification technologies cannot be generalised to men who have sex with men, as there is limited trial evidence and because the mathematical modelling studies modelled a general heterosexual population. However, the audit showed that partner notification outcomes were worse in men who have sex with men. We show findings for a population of high-risk individuals within a general population; these should be interpreted cautiously when applying these to specific populations at high risk or in high-prevalence areas.

Recommendations for research

1. A randomised controlled trial of the effects of APT compared with traditional partner notification technologies should be conducted, with follow-up measuring biological end points beyond 3 months. Determining whether or not the magnitude of benefit found in trials of EPT can be generalised to APT is a priority.
 - i. Randomised trials should include interventions to increase rates of testing for other STIs and HIV in partners notified by APT.
 - ii. Modelling studies of the effectiveness and cost-effectiveness of APT should be conducted alongside a clinical trial. This should build on the dynamic models for single and dual infections developed within this project.
2. Randomised trials to identify effective partner notification technologies for men who have sex with men should be conducted for both bacterial STIs and HIV.
3. Studies that use methods preferred by the National Institute for Health and Care Excellence (NICE) to collect HRQL data, including the development of appropriate tools, should be commissioned so that QALYs for temporary and permanent health states associated with bacterial STIs can be determined. This is a priority so that robust cost-effectiveness analyses of APT and of other interventions to prevent curable STIs and their consequences can be conducted.
4. Standard sets of disease-specific parameters for bacterial STIs should be developed to help researchers compare the performance of mathematical models and to help policy makers to interpret their outputs. Further research to develop these for gonorrhoea, trichomonas and syphilis is needed.
5. Basic science studies are needed to investigate the possible mechanisms for a biological interaction between the susceptibility to *C. trachomatis* and to *Neisseria gonorrhoeae*. Additional modelling studies of STI co-infections would be valuable.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Five-year impact factor: 5.804

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index and is assessed for inclusion in the Database of Abstracts of Reviews of Effects.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 07/42/02. The contractual start date was in March 2009. The draft report began editorial review in July 2012 and was accepted for publication in November 2013. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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