Management and control of tuberculosis control in socially complex groups: a research programme including three RCTs

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Declared competing interests of authors: Alistair Story leads the Find&Treat service that manages the video-observed treatment. Peter White reports grants from the Medical Research Council and NIHR during the conduct of the study and grants from Otsuka Pharmaceutical Co., Ltd (Tokyo, Japan) outside the submitted work. Richard Garfein established SureAdhere Mobile Technology, Inc. (San Diego, CA, USA), which provides a smartphone application for video-observed treatment. Ibrahim Abubakar is a member of the Health Technology Assessment Commissioning Board (2017 to present).

Published October 2020
DOI: 10.3310/pgfar08090

Scientific summary

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Programme Grants for Applied Research 2020; Vol. 8: No. 9
DOI: 10.3310/pgfar08090

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

Scientific summary

Background

Tuberculosis is the leading cause of death among curable infectious diseases globally. London has the highest rate of tuberculosis of any Western European capital. In London, rates are higher among people experiencing homelessness, prisoners and alcohol/substance misusers. These groups are also more likely to have delays in diagnosis and poor adherence to treatment, leading to poor clinical outcomes, the development of resistance and the spread of disease to others.

We established the Find&Treat service to respond to these problems. This pan-London service conducts mobile radiographic screening across venues that serve homeless populations, including hostels, day centres and drug treatment services. A multidisciplinary team helps to address the social needs of socially complex tuberculosis patients and to re-engage patients who have been lost to treatment follow-up. The NHS has also invested in static digital radiography in prisons to screen for tuberculosis.

Key challenges that needed to be addressed included measuring the prevalence of latent tuberculosis infection in these high-risk populations to inform screening and treatment programmes; measuring the prevalence of blood-borne viruses (hepatitis B, hepatitis C and human immunodeficiency virus) because both viral hepatitis and chemoprophylaxis can damage the liver and human immunodeficiency virus increases the chance of progressing to active disease; evaluating the effectiveness of NHS prison radiographic screening; maximising the uptake of the mobile radiographic service; speeding up diagnostic confirmation of tuberculosis in those with concerning radiographs to minimise the loss to follow-up associated with diagnostic delay; finding better ways to maximise adherence to tuberculosis, as the recommended approach of directly observed treatment whereby a health-care worker observes treatment doses three to five times per week is inconvenient for patients and services; and understanding the cost-effectiveness of approaches to inform NHS investment.

Work package 1: latent tuberculosis infection and blood-borne virus prevalence in people experiencing homelessness in London

Introduction

Urban homeless populations have high rates of active tuberculosis, but the prevalence of latent tuberculosis infection is unknown. This study measured the prevalence of latent tuberculosis infection among individuals using homeless hostels in London.

Methods

The method used was a cross-sectional survey with outcome follow-up in homeless hostels in London. The primary outcome was the prevalence of latent tuberculosis infection. Recruitment took place between May 2011 and June 2013.

Results

A total of 491 out of 804 (61.1%) individuals agreed to be screened. Latent tuberculosis infection prevalence was 16.5% (81/491; 95% confidence interval 13.2% to 19.8%). In UK-born individuals, a history of incarceration was independently associated with increased risk of infection (odds ratio 3.49, 95% confidence interval 1.10 to 11.04; $p = 0.018$). Only three participants met English treatment guidelines for latent tuberculosis infection, and none engaged with services after referral for treatment. Past hepatitis B infection prevalence was 10.4% (51/489; 95% confidence interval 7.7% to 13.1%), and 59.5% (291/489; 95% confidence interval 55.1% to 63.9%) of individuals were non-immune. Prevalence of current hepatitis C infection was 10.4% (51/489; 95% confidence interval 7.8% to 13.1%).

Conclusions

There is a high prevalence of latent tuberculosis infection and viral hepatitis in people experiencing homelessness and a large unmet need for treatment and hepatitis B vaccination.

Work package 2: evaluation of an NHS prison screening programme for active tuberculosis and survey of latent tuberculosis infection and blood-borne virus prevalence in prisoners

Introduction

We aimed to evaluate the effectiveness of a new prison programme that uses static digital radiographic units to screen for tuberculosis. We also aimed to measure the prevalence of latent tuberculosis infection and blood-borne viruses in a London prison and outcomes for participants who were referred to health-care services.

Methods

The method used was a cross-sectional survey with follow-up of clinical outcomes. Recruitment took place between January 2013 and June 2013. The setting was a London male prison with a static digital radiography facility for tuberculosis screening. Newly arrived prisoners were eligible for the tuberculosis radiographic screening. Existing prisoners were offered radiographic screening when possible. Any prisoner participating in the radiographic screening was eligible for latent tuberculosis infection/blood-borne virus screening. The primary outcomes were yield of chest radiographs suggestive of active tuberculosis, prevalence of latent tuberculosis infection, hepatitis C virus, hepatitis B virus and human immunodeficiency virus. The secondary outcomes were latent tuberculosis infection and blood-borne virus co-infection.

Results

The coverage of radiographic screening of new prisoners was 43%. A total of 1484 prisoners were screened, 87% of whom were new arrivals. A total of 2% (29/1484) of prisoners had further investigations for tuberculosis, and one prisoner began tuberculosis treatment. The overall tuberculosis prevalence was 67 cases per 100,000 prisoners (95% confidence interval 2 to 375 cases per 100,000 prisoners). Of those screened with a chest radiograph, 511 (34%) prisoners took part in the latent tuberculosis and blood-borne virus study. The estimated prevalence of latent tuberculosis infection was 13%. Of the 57% of prisoners who met the National Institute for Health and Care Excellence guidance for latent tuberculosis infection treatment, 46% were lost to follow-up or did not attend appointments, 43% started prophylaxis treatment and 56% of these completed their treatment. The prevalence of current hepatitis C virus was 4%; for hepatitis B virus, it was 2%. Sixty-five per cent of all participants had insufficient or no immunity to hepatitis B virus.

Conclusions

This study demonstrates a high prevalence of active and latent tuberculosis infection in a UK prison. There were high rates of non-attendance and loss to follow-up across latent tuberculosis infection, hepatitis B virus and hepatitis C virus. A high proportion of prisoners also had insufficient or no protection against hepatitis B. These results indicate very important unmet needs in this high-risk group. Further work is needed to develop effective systems of integrated screening and case management in prisons.

Work package 3: peer educators to increase uptake of mobile radiographic screening for tuberculosis in homeless hostels

Trial design

This was a cluster randomised controlled trial.

Objective
To compare current practice for encouraging people experiencing homelessness to be screened for tuberculosis on a mobile digital radiographic unit in London, UK, with volunteer peer educators who have direct experience of tuberculosis and homelessness.

Participants
Forty-six hostels in London took part between February 2012 and October 2013, with a total of 2342 residents eligible for screening.

Intervention
Volunteer peer educators agreed a work plan that involved moving around the hostel with staff and speaking to residents to encourage them to attend screening.

Randomisation
Randomisation was performed with minimisation on hostel size and historical screening uptake.

Blinding
The statistician was blinded to allocation to the intervention and control arms.

Primary outcome
The primary outcome was the number of eligible clients at a hostel venue screened for active pulmonary tuberculosis by the mobile radiographic unit.

Results
There were 59 hostels considered for eligibility and 46 were randomised. Control sites had 1192 residents, with a median uptake of 45% (interquartile range 33–55%). Intervention sites had 1150 eligible residents, with a median uptake of 40% (interquartile range 25–61%). There was no evidence that peer educators changed uptake (adjusted risk ratio 0.98, 95% confidence interval 0.80 to 1.20). The study team noted no adverse events.

Conclusions
This study found no evidence that volunteer peer educators increased or decreased client uptake of mobile radiographic unit screening for tuberculosis. Further qualitative work should be undertaken to explore the possible ancillary benefits to homeless peer volunteers and those living and working in hostels.

Work package 4: evaluating the impact of using polymerase chain reaction, Cepheid Xpert® MTB/RIF as a point-of-care diagnostic alongside mobile radiographic screening for tuberculosis

Methods
A randomised controlled trial was planned. Patients with radiographs that potentially indicated active tuberculosis were randomised to use of the rapid diagnostic or usual care (onward referral). The primary outcome was the number of clinic visits needed for exclusion or confirmation of tuberculosis.

Results
Owing to low recruitment and difficulties in follow-up, the trial was abandoned. The intention was to continue the evaluation as an observational study, but the mobile radiographic unit stopped using the technology soon after trial abandonment. Prior to abandoning the trial, 37 out of 95 eligible patients were recruited. Two out of 18 patients who were tested with Cepheid Xpert® MTB/RIF [mycobacterium tuberculosis/rifampicin] (Cepheid, Sunnyvale, CA, USA) were positive for *Mycobacterium tuberculosis* but six were ultimately diagnosed with active tuberculosis. In the control arm, 5 out of 19 patients were ultimately diagnosed with active tuberculosis. It did not prove possible to collect data on the number of outpatient visits needed to reach a diagnostic conclusion (primary outcome).

Conclusions

Despite overcoming a range of technical challenges to implementing polymerase chain reaction-based rapid diagnostics alongside a mobile radiographic screening service, we found recruitment and follow-up highly challenging in this setting.

Work package 5: a randomised controlled trial comparing smartphone-enabled video-observed treatment with face-to-face directly observed treatment

Aim

The aim was to compare smartphone-enabled video-observed treatment with face-to-face directly observed treatment.

Method

This was a randomised controlled trial.

Eligibility criteria

Adults (aged $\geq$ 16 years) with active tuberculosis who were eligible for directly observed treatment to support adherence were eligible for the trial. Groups eligible for directly observed treatment included patients with social risk factors (including alcohol or drug use, history of imprisonment and homelessness), mental health problems, evidence of poor adherence, previous tuberculosis treatment and clinically complex disease requiring extra support.

Exclusion criteria

The exclusion criteria were (1) need for intravenous treatment, (2) no access to the facilities needed to charge a smartphone, (3) patients with $<$ 2 months of treatment remaining and (4) multidrug-resistant tuberculosis patients.

Intervention

Video-observed treatment clips were submitted using a smartphone application via upload to a secure server. Video-observed treatment clips were read by a study nurse/video-observed treatment observer at a central location.

Control

A trained health professional, or a responsible layperson supported by a trained health professional, observed the patient swallowing scheduled doses of their medication.

Primary outcome measures

The primary outcome measure was $>$ 80% of scheduled video-observed treatment/directly observed treatment sessions successfully completed in the 2 months following randomisation.

Results

We randomly assigned 226 eligible patients (video-observed treatment, $n = 112$; directly observed treatment, $n = 114$). A total of 131 (58%) patients had social risk factors. The primary outcome was achieved by 78 (70%) out of 122 patients on video-observed treatment, compared with 35 (31%) out of 114 patients on directly observed treatment (partially adjusted odds ratio 5.48, 95% confidence interval 3.10 to 9.68; $p < 0.0001$).

Conclusions

Video-observed treatment is a more effective approach to observation of tuberculosis treatment than directly observed treatment.

Work package 6: cost-effectiveness studies

Aim 1

To evaluate the cost-effectiveness of latent tuberculosis infection screening among people experiencing homelessness screened alongside radiographic screening for active tuberculosis in the mobile radiographic unit.

Methods

The method employed was an integrated transmission dynamic and health economic model comparing current practice (radiographic screening for active tuberculosis in homeless populations) with radiographic screening for active tuberculosis plus screening for latent tuberculosis infection. The cost-effectiveness of different options was compared using incremental cost-effectiveness ratios relative to current practice.

Results

Screening for and treating latent tuberculosis infection had a net cost. When a quality-adjusted life-year is valued at £30,000, the latent tuberculosis infection screening was cost-effective provided treatment uptake was $\geq$ 25%. When a quality-adjusted life-year is valued at £20,000, the latent tuberculosis infection screening was cost-effective provided treatment uptake was $\geq$ 50%.

Conclusions

Screening for latent tuberculosis infection in people experiencing homelessness alongside radiographic screening for active tuberculosis in the mobile radiographic unit is potentially cost-effective, provided adequate treatment uptake can be achieved.

Aim 2

To compare the costs of face-to-face, directly observed treatment with those of video-observed treatment.

Methods

Comparison of NHS costs of directly observed treatment provision with costs of video-observed treatment.

Results

The minimum cost of directly observed treatment (three observations per week) is £3420 for 6 months per patient. The per-patient cost of video-observed treatment depends on the number of patients. If 50 patients are observed, the costs for 6 months' daily observation is £1645.

Conclusion

Video-observed treatment is cheaper than directly observed treatment.

Trial registration

This trial is registered as ISRCTN17270334 and ISRCTN26184967.

Funding

This project was funded by the National Institute for Health Research (NIHR) Programme Grants for Applied Research programme and will be published in full in *Programme Grants for Applied Research*; Vol. 8, No. 9. See the NIHR Journals Library website for further project information.

Programme Grants for Applied Research

ISSN 2050-4322 (Print)

ISSN 2050-4330 (Online)

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

Editorial contact: journals.library@nihr.ac.uk

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This report

The research reported in this issue of the journal was funded by PGfAR as project number RP-PG-0407-10340. The contractual start date was in September 2008. The final report began editorial review in September 2018 and was accepted for publication in January 2020. As the funder, the PGfAR programme agreed the research questions and study designs in advance with the investigators. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The PGfAR editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

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