Smartphone-enabled video-observed versus directly observed treatment for tuberculosis: a multicentre, analyst-blinded, randomised, controlled superiority trial

Alistair Story, Robert W Aldridge, Catherine M Smith, Elizabeth Garber, Joe Hall, Gloria Ferenando, Lucia Possas, Sara Hemming, Fatima Wurie, Serena Luchenski, Ibrahim Abubakar, Timothy D McHugh, Peter J White, John M Watson, Marc Lipman, Richard Garfein, Andrew C Hayward

Summary

Background Directly observed treatment (DOT) has been the standard of care for tuberculosis since the early 1990s, but it is inconvenient for patients and service providers. Video-observed therapy (VOT) has been conditionally recommended by WHO as an alternative to DOT. We tested whether levels of treatment observation were improved with VOT.

Methods We did a multicentre, analyst-blinded, randomised controlled superiority trial in 22 clinics in England (UK). Eligible participants were patients aged at least 16 years with active pulmonary or non-pulmonary tuberculosis who were eligible for DOT according to local guidance. Exclusion criteria included patients who did not have access to charging a smartphone. We randomly assigned participants to either VOT (daily remote observation using a smartphone app) or DOT (observations done three to five times per week in the home, community, or clinic settings). Randomisation was done by the SealedEnvelope service using minimisation. DOT involved treatment observation by a health-care or lay worker, with any remaining daily doses self-administered. VOT was provided by a centralised service in London. Patients were trained to record and send videos of every dose ingested 7 days per week using a smartphone app. Trained treatment observers viewed these videos through a password-protected website. Patients were also encouraged to report adverse drug events on the videos. Smartphones and data plans were provided free of charge by study investigators. DOT or VOT observation records were completed by observers until treatment or study end. The primary outcome was completion of 80% or more scheduled treatment observations over the first 2 months following enrolment. Intention-to-treat (ITT) and restricted (including only patients completing at least 1 week of observation on allocated arm) analyses were done. Superiority was determined by a 15% difference in the proportion of patients with the primary outcome (60% vs 75%). This trial is registered with the International Standard Randomised Controlled Trials Number registry, number ISRCTN26184967.

Findings Between Sept 1, 2014, and Oct 1, 2016, we randomly assigned 226 patients; 112 to VOT and 114 to DOT. Overall, 131 (58%) patients had a history of homelessness, imprisonment, drug use, alcohol problems or mental health problems. In the ITT analysis, 78 (70%) of 112 patients on VOT achieved ≥80% of scheduled observations compared with 35 (31%) of 114 on DOT (adjusted odds ratio [OR] 5.48, 95% CI 3.10–9.68; p<0.0001). In the restricted analysis, 78 (77%) of 101 patients on VOT achieved the primary outcome compared with 35 (63%) of 56 on DOT (adjusted OR 2.52; 95% CI 1.17–5.54; p=0.017). Stomach pain, nausea, and vomiting were the most common adverse events reported (in 16 [14%] of 112 on VOT and nine [8%] of 114 on DOT).

Interpretation VOT was a more effective approach to observation of tuberculosis treatment than DOT. VOT is likely to be preferable to DOT for many patients across a broad range of settings, providing a more acceptable, effective, and cheaper option for supervision of daily and multiple daily doses than DOT.

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### Research in context

**Evidence before this study**

We searched PubMed for studies published before 22 March, 2018, using the search terms “tuberculosis” AND (“video” OR “mobile”) AND “observe/observation”. 11 studies described implementation of synchronous (six) or asynchronous (five) video-observed therapy (VOT). Most studies were pilot projects assessing feasibility and acceptability of using VOT. They showed that VOT is an acceptable, flexible, cost-effective and patient-friendly intervention. Two cohort studies compared treatment observation levels for directly observed treatment (DOT) and synchronous VOT; one, a study in South Australia, reported 87.9% of treatment events observed for VOT and 68.9% for DOT; the second, a study in New York City, reported 95% adherence for VOT and 91% for DOT. No comparative studies have been published for asynchronous VOT.

**Added value of this study**

This is the first randomised controlled trial comparing the level of treatment observation for DOT and asynchronous VOT. A higher proportion of patients on VOT completed 80% or more scheduled treatment observations over the first 2 months following enrolment than those on DOT. The study also showed that VOT was cheaper to deliver than DOT.

**Implications of all the available evidence**

VOT is a more effective and cheaper approach to observation of tuberculosis treatment than DOT. The intervention has been acceptable when assessed in patients in various settings including North America, England (UK), Belarus, Kenya, and Vietnam.

### Methods

#### Study design and participants

We did a multicentre, analyst-blinded, randomised controlled, superiority trial at 22 clinics in England (UK; London [17 sites], Birmingham [three], Coventry [one], and Leicester [one]). Ethical approval was granted by the National Research Ethics Service East of England—Essex, Research Ethics Committee, 20/03/2014, ref: 10/H0302/51. The full trial protocol is published on the International Standard Randomised Controlled Trial Number Registry.

Eligible patients were identified by case managers at each participating clinic and referred to the study team. Inclusion criteria included patients aged 16 years or older with active pulmonary or non-pulmonary tuberculosis who were eligible for DOT according to UK national guidance. Patients were invited to participate regardless of whether they had previously agreed to treatment observation. Patients were excluded if they were not suitable for VOT because they did not have access to facilities to charge a smartphone. They were also excluded if they had less than 2 months remaining on their treatment regimen, because the primary study outcome required measurement of adherence over 2 months. Patients with MDR tuberculosis were excluded.

### Figure 1: Enrolment and randomisation

548 assessed for eligibility

322 excluded

- 98 did not meet inclusion criteria
- 127 declined to participate
- 45 other reasons*
- 27 not approached
- 25 MDR tuberculosis

226 randomised

114 allocated to DOT

- 56 ≥1 week of DOT
- 58 <1 week of DOT

112 allocated to VOT

- 101 ≥1 week of VOT
- 11 <1 week of VOT

114 intention-to-treat analysis

- 56 restricted analysis

112 intention-to-treat analysis

- 101 restricted analysis

*The most common other reason for not enrolling patients (32 of 45) was clinic staff considering that the patient needed intensive face-to-face support for emotional, medical, or physical reasons, or because of imminent risk of loss to follow-up. Characteristics of eligible patients who were approached but refused to take part in the study are in the appendix.

For the trial protocol see DOI:10.1186/ISRCTN26184967
because they require twice-daily treatment (these patients were recruited into a non-randomised study, that will be reported separately). All patients provided written informed consent to participate in the study.

Randomisation and masking
We randomly assigned participants to either asynchronous VOT or DOT based in a clinic, community (eg, pharmacy or hostel), or home setting. Randomisation was provided by SealedEnvelope, a telephone and online software application used for randomly assigning patients in clinical trials. The system used randomisation by minimisation to ensure balance across study sites and the stage of treatment at the time of enrolment (ie, within the first 2 months of treatment and after the first 2 months of treatment). Minimisation allocates patients to best maintain balance in the stratification factors by calculating an imbalance score at each randomisation. It then assigns with higher probability each patient to the treatment that will reduce the imbalance.

Procedures
DOT was delivered according to usual clinical practice. This involved treatment observation three to five times per week by a health-care or lay worker, with the remaining daily doses self-administered. VOT was provided by a centralised service in London (UK). Patients were trained to record and send videos of every dose ingested 7 days per week using a smartphone app developed by researchers at the University of California (San Diego, CA, USA). Trained treatment observers viewed the videos through a password-protected website. As a safety precaution, to address concerns that reduced face-to-face contact might lead to side-effects being undetected, patients were also encouraged to report adverse drug events on the videos. Smartphones (Samsung Galaxy S3/S4/Xcover3) and data plans (including UK calls and texts) were provided free of charge, paid by the study at commercial rates. Patients signed a form agreeing to return the phone at the end of treatment (details on returning the phones in the appendix). DOT and VOT observation records were completed by observers until treatment or study end. Full details of interventions are in the appendix.

Outcomes
The primary outcome was successful completion of 80% or more of scheduled treatment observations in the 2 months following randomisation. The proportion of scheduled observations (measured on a continuous scale) successfully completed in the 2 months following enrolment, and throughout treatment, was a secondary outcome.

Other secondary outcome measures were: sputum culture results at 2 months post-treatment initiation; treatment outcomes; occurrence of adverse events; numbers of hospitalisations; staff time spent observing or travelling to observe patients; staff time and cost of travel when re-engaging patients; cost of treatment observation; patient satisfaction, resource use, and health-related quality of life.

Semi-structured interviews were done with 16 patients selected to represent a range of backgrounds and VOT and DOT successes and failures. Full results of the qualitative analysis will be reported separately. Details of

| Directly observed treatment | Video-observed therapy |
|----------------------------|------------------------|
| As randomised (n=114)      | Restricted* (n=56)    |
| Age (years)                |                        |
| 16–34                      | 61 (54%)               |
| 35–54                      | 45 (40%)               |
| ≥55                        | 8 (7%)                 |
| Sex                        |                        |
| Male                       | 83 (73%)               |
| Female                     | 31 (27%)               |
| Born in the UK             |                        |
| No                         | 83 (73%)               |
| Yes                        | 31 (27%)               |
| Previous tuberculosis      |                        |
| No                         | 82 (72%)               |
| Yes                        | 30 (26%)               |
| Pulmonary                  |                        |
| No                         | 41 (36%)               |
| Yes                        | 73 (64%)               |
| Social risk factor†        |                        |
| Never                      | 48 (42%)               |
| >5 years ago               | 19 (17%)               |
| Within 5 years             | 47 (41%)               |
| Homeless                   |                        |
| Never                      | 77 (68%)               |
| >5 years ago               | 14 (12%)               |
| Within 5 years             | 23 (20%)               |
| Prison                     |                        |
| Never                      | 93 (82%)               |
| >5 years ago               | 9 (8%)                 |
| Within 5 years             | 11 (10%)               |
| Drug use                   |                        |
| Never                      | 96 (84%)               |
| >5 years ago               | 2 (2%)                 |
| Within 5 years             | 15 (13%)               |
| Alcohol problems           |                        |
| No                         | 91 (80%)               |
| Yes                        | 21 (18%)               |
| Mental health problems     |                        |
| No                         | 94 (83%)               |
| Yes                        | 18 (16%)               |

Data shown by allocated intervention and initial engagement (at least 1 week on allocated intervention). *Initial engagement with intervention (at least 1 week of observation in allocated arm). †History of homelessness, imprisonment, drug use or alcohol problems, or mental health problems.

Table 2: Baseline characteristics of the study population
the methods used for collection of the additional outcomes are in the appendix.

Statistical analysis
We determined that a sample of 200 patients per arm would provide a power of 90% to detect a 15% difference in the proportion of patients with the primary outcome (60% vs 75%). This was based on a two-sided significance level of 5%. Following a review of study progress, the funder’s study monitoring committee requested an interim analysis, the plan for which was published on the International Standard Randomised Controlled Trial Number Registry before analysis. It included a stopping rule using the Haybittle–Peto boundary of 0·001 for the primary outcome. We used the approach described in the interim analysis plan for the final analysis. This involved main and sensitivity analyses for intention-to-treat (ITT) and restricted groups, described below and summarised in the appendix.

In the main analysis, VOT treatment observations were classified as successfully completed if ingestion of all medicines was observed, or if video clips were received but not viewable because of a technical complication (since patients had no control over whether videos were corrupted). The sensitivity analysis considered only videos for which all medicines were observed as successfully completed. The ITT analysis included all patients, analysed according to the arm to which they were originally randomised. The restricted analysis excluded patients with less than 1 week of observation in the allocated arm. This was designed to include only those patients who had, at least initially, engaged with the allocated intervention.

We used logistic regression to analyse the primary outcome and linear regression for the secondary outcomes. Time since start of treatment, age, and sex were considered a priori as potential confounders and included in all models. For the restricted analysis, we also considered covariates that might have affected initial engagement with the allocated intervention (homelessness, imprisonment, drug use, alcohol problems, immigration concerns, mental health problems, previous loss to follow-up, and no recourse to public funds). All analyses accounted for clustering at the level of the clinic using robust standard errors. Likelihood ratio tests for interaction were used to assess evidence of differing effect size in population subgroups. Analyses were done using Stata (version 14) and R (version 3.3.2) software. This trial is registered with the International Standard Randomised Controlled Trials Number registry, number ISRCTN26184967.

Role of the funding source
The funder of the study had no role in study design, data collection, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results
Between Sept 1, 2014, and Oct 1, 2016, we screened 548 patients with tuberculosis for eligibility. Of these, 322 (59%) were ineligible and 226 (41%) were randomly assigned to the study groups (figure 1). Follow-up continued until Dec 31, 2016. ITT analyses included 112 to VOT and 114 patients assigned to DOT. Patients were mainly young adults born outside the UK (table 1). A high proportion had a history of homelessness, imprisonment, drug use, alcohol problems, or mental health problems. Baseline characteristics were similar between the two groups. Patients were substantially more likely to engage initially (ie, have at least 1 week of
follow-up) with VOT (101 [90%] of 112) than DOT (56 [49%] of 114). Levels of initial engagement with VOT exceeded 70% in all subgroups, but with DOT were particularly low (<50%) in younger adults, foreign-born patients and those without social risk factors or mental health problems (table 1). Amongst the 56 patients who initially engaged with DOT, 27 (48%) had home-based DOT, 20 (36%) clinic-based, and nine (16%) community-based (eg, a local pharmacy). DOT was scheduled three times per week for 14 patients, and five times per week for the remainder. The level of observation achieved in each study arm is in figure 2. In the ITT analysis, 78 (70%) of 122 patients on VOT successfully achieved the primary outcome (≥80% scheduled observations successfully completed during the first 2 months), compared with 35 (31%) of 114 patients on DOT: partially adjusted odds ratio (OR) 5.48, 95% CI, 3.10–9.68; p<0.0001 (table 2).

For the secondary outcome of the proportion of scheduled observations successfully completed over the first 2 months, in the ITT analysis, 5091 (79%) of 6474 scheduled observations were successfully completed on VOT, compared with 1774 (45%) of 3922 on DOT. The mean proportions of doses observed per patient were 78% (41%) for VOT and 36% (SD 31%) for DOT (adjusted mean difference in proportions 41%, 95% CI 29–53; p<0.0001). In the restricted analysis, the overall proportions were 5091 (86% [SD 17%]) of 5893 for VOT and 1774 (73% [27%]) of 2418 for DOT (adjusted mean difference in proportions 14%, 95% CI 7–20; p<0.0001). Full results for this secondary outcome are in the appendix.

High observation rates were maintained in the VOT arm, but they rapidly decreased in the DOT arm (figure 3). Over the full follow-up period (up to 6 months) 12422 (77%; 95% CI 76–77) of 16230 scheduled observations were completed in the VOT arm compared with 3884 (39%; 38–40) of 9882 scheduled observations in the DOT arm (p<0.0001). In the restricted analysis, over the full follow-up period 12422 (83%; 83–84) of 14907 of scheduled observations were completed in the VOT arm compared with 3884 (61%; 60–62) of 6351 in the DOT arm (p<0.0001). Observation completion rates were higher for VOT than DOT in all subgroups (table 3). There were no significant differences in positive sputum cultures at 2 months following treatment onset, treatment completion, loss to follow-up or numbers of hospital admissions between trial arms (appendix).

368 adverse events were reported by 32 patients on VOT and 184 reported by 15 on DOT (table 4). 169 unscheduled

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### Table 2: Numbers and proportions of patients and results of logistic regression analysis for the primary outcome

| n (%) with primary outcome* | Unadjusted | Partially adjusted† | Fully adjusted |
|----------------------------|------------|---------------------|---------------|
| DOT | VOT          | OR (95% CI) | p value | Adjusted OR (95% CI) | p value | Adjusted OR (95% CI) | p value |
|---------------------------|------------|-------------|---------|----------------------|---------|----------------------|---------|
| Intention to treat        |            |             |         |                      |         |                      |         |
| Total                     | 114        | 112         |        |                      |         |                      |         |
| Main†                     | 35 (31%)   | 78 (70%)    | 5.18 (2.94–9.12) | <0.0001 | 5.48 (3.10–9.68) | <0.0001 |                      |         |
| Sensitivity               | 35 (31%)   | 68 (61%)    | 3.49 (2.01–6.04) | <0.0001 | 3.60 (1.91–6.79) | <0.0001 |                      |         |

Restricted§

| Total                     | 56         | 101         |        |                      |         |                      |         |
| Main§                     | 35 (63%)   | 78 (77%)    | 2.03 (1.00–4.15) | 0.051  | 2.23 (1.16–4.27) | 0.016   | 2.52 (1.17–5.47) | 0.019  |
| Sensitivity               | 35 (63%)   | 68 (67%)    | 1.24 (0.62–2.45) | 0.542  | 1.29 (0.71–2.34) | 0.398   | 1.44 (0.75–2.75) | 0.273  |

Data shown by trial arm for intention-to-treat and restricted analyses. DOT=directly observed treatment. VOT=video-observed therapy OR=odds ratio. *Primary outcome: patients who had ≥80% observations successfully completed in the first 2 months following randomisation. †Partially-adjusted models adjusted for time since start of treatment, age, sex, and treatment. Fully-adjusted models (for restricted analysis only) additionally adjusted for current social risk factor (homelessness, imprisonment, drug use, alcohol problems, immigration concern), ever lost to follow-up, no recourse to public funds, mental health problems. ‡Main analysis: VOT treatment observations were classified as successfully completed if ingestion of all medicines was observed, or if video clips were received but not viewable due to a technical complication. Sensitivity analysis: only videos for which ingestion of all medicines was observed were classified as successfully completed. §Restricted analysis included only patients who engaged initially (had at least 1 week of observation) on the allocated treatment arm.
outpatient appointments were made by 47 patients on VOT, compared with 233 by 42 patients on DOT. Average staff time per dose observed was 56 min (SD 54) for community based DOT (including travel time); 15 min (12) for clinic-based DOT, and 3.2 min (0.5) for VOT. Patients on DOT spent a mean 29 min (SD 48) per week on treatment observation (including travelling to or from clinics, waiting for appointments, and appointment time). Those on VOT spent a mean of 1.8 min (2.2) setting up and recording each video.

The costs of providing DOT over 6 months were estimated at £5700 per patient for observations five times per week, and £3420 for observations three times per week. For daily VOT over 6 months, costs were estimated at £1645 per patient (in a service managing 50 patients; appendix).

The sensitivity analysis excluding corrupted videos showed similar effects (table 2), as did the main restricted analysis.

**Discussion**

In this trial, VOT enabled higher levels of treatment observation for patients with tuberculosis, both over the first 2 months of treatment and throughout treatment, than DOT. VOT also supported daily dosing, was effective for socially complex populations, and had a lower drop-out rate than DOT. The absence of face-to-face contact did not reduce the identification of adverse events or lead to more unscheduled appointments. VOT reduced staff time requirements, especially compared with home-based DOT, making VOT cheaper than DOT even after taking into account the costs of the telephones and data plans provided by the study.

Systematic reviews and meta-analyses draw differing conclusions about the effectiveness of DOT. However, one review showed that DOT increased treatment success, adherence, and 2-month sputum conversion, and decreased loss to follow-up and acquired drug resistance compared with self-administered treatment. Community based DOT was more effective than hospital-based or clinic-based DOT, highlighting the importance of making DOT convenient for patients.

![Table 3: Numbers and proportions of patients with more than 80% of scheduled doses observed over the first 2 months](image-url)
The review also showed that DOT was more effective when delivered by health staff or lay workers than by family members. VOT provides the technology to support professional treatment observation that is more convenient and cheaper than in-person DOT. In this study, VOT had a much higher uptake rate than DOT (91% vs 46%). This is a clear indication that providing treatment observation in a more convenient, flexible, and less intrusive way makes VOT a more acceptable mode of treatment for many patients.

VOT, as used in this study, has a wide range of components beyond convenience of observation. The intervention included personal support, where patients met the VOT observer for training, and received regular personalised messages as reminders, confirmation of receipt of video clips, or to follow up when clips were not received. Patients were specifically asked to report any adverse events after each clip and the observers also supported onward referral to deal with reported adverse events. Numerically more adverse events were reported in the VOT group than in the DOT group, which was likely due to the systematic reporting, although it could also have resulted from better compliance. Patients were provided with a smartphone with a data plan, and free domestic calls and text messages. This acted facilitated easy communication and improved access to care providers, and was a material incentive that was valued by patients although patients were asked to return the smartphone on completion of the study. On average, fewer than one phone was needed per patient because phones were re-used throughout the trial.

The trial had several limitations. It was not possible to blind patients or treatment observers to the intervention, although the investigators and statistician were blinded during the analysis. We could not distinguish between doses that were not observed and doses that were not taken. Case managers reported that many of the unobserved scheduled doses for DOT had previously been negotiated with clinic case managers because of patients having conflicting appointments or priorities, or case managers choosing to trust patients to self-administer scheduled doses. Approximately 7% of video clips submitted during the first 2 months of treatment were corrupted because of a software bug that was subsequently fixed (appendix). In our main analysis we assumed that submission of a corrupted clip represented pill ingestion since patients were not aware that the videos they submitted were corrupted. We tested the potential impact of this assumption in sensitivity analysis A (appendix) which regarded corrupted clips as unobserved. This sensitivity analysis produced similar results to the main analysis.

ORs reported through logistic regression should not be regarded as accurate estimates of relative risk. For example, our adjusted OR for the main analysis is 5.48 but the corresponding unadjusted relative risk would be 2.27. The primary outcome (observing 80% scheduled doses) could be considered to be biased in favour of DOT, because it required substantially more VOT doses (scheduled 7 days per week) to be observed than DOT doses (scheduled three or five times per week). The restricted analysis further favoured DOT, because it included only the highly selected subset of patients allocated to DOT who were willing to be observed. That VOT still outperformed DOT under these constraints, especially when considered over 6 months, adds to the robustness of the findings.

The study was not powered to detect differences in culture conversion rate, treatment completion, loss to follow-up, relapse, or development of drug resistance. Nevertheless, it is reasonable to assume that improved adherence might improve all these outcomes. VOT might also improve treatment outcomes and reduce the risk of adverse events compared with DOT, because clinicians do not need to schedule intermittent high dose regimens to ensure observation.

Another limitation was the exclusion of patients with MDR tuberculosis from the randomised trial. This was done because these patients had a range of treatment regimens, some of which included injectable medications or multiple scheduled doses to be observed per day. It would be impractical for all these observations to be made through face-to-face DOT and we therefore did not consider there to be equipoise between VOT and DOT for these individuals. Patients with MDR tuberculosis were recruited into a separate non-randomised arm of the study that will be reported separately.

The patients in this study were distributed across multiple sites and had many complex social needs. The findings are therefore likely to be generalisable to similar settings where patients with risk factors for non-adherence are offered support. Although the study was done in a low-incidence, high-income setting, we think it plausible that the intervention would also be effective in high-incidence, low-income settings, provided that good internet and cellular data connections are available, as is the case in many urban areas in LMICs. Relative and
absolute costs of smartphones, data plans, and staff time differ between countries, but the large savings in staff time mean that VOT is likely to be cheaper than DOT in such settings. There is a need for more research in this area, including comparative studies between different digital adherence interventions in high-burden settings to measure effectiveness, feasibility with respect to technological infrastructure, and acceptability and cultural appropriateness of the interventions. Given the effectiveness of VOT for patients with complex social needs, the intervention could also be effective in treating other conditions that are prevalent in these populations; eg, hepatitis C.

There is an urgent global need for more effective and cheaper alternatives to DOT to enable effective ambulatory care of both drug-sensitive and MDR tuberculosis. In particular, it is important that new opportunities for shorter regimens for MDR tuberculosis are not lost because of insufficient attention to adherence. WHO now recommends that VOT can be a suitable alternative to DOT and has published guidance on its implementation. VOT is, in fact, likely to be preferable to DOT for many patients across a broad range of settings, providing a more acceptable, effective, and cheaper option for supervision of daily and multiple daily doses than DOT.

Based on the experience of this trial, VOT has been adopted by the UK National Health Service in London (UK), provided by the Find and Treat service. Most patients with MDR tuberculosis in London are now treated using VOT, and many of these patients require multiple daily dosing (Joe Hall, Find and Treat, personal communication). The intervention has also been used successfully in children aged as young as 12 years and is being provided to an increasing number of patients outside London, particularly those with complex social needs. In settings such as this where mobile-internet connectivity makes VOT feasible, it is likely to make an important contribution to tuberculosis eradication.

Contributors
AS and ACH led the study design and implementation, and contributed to the analysis and interpretation. RWA led the analysis and contributed to study implementation and interpretation. CMS did the analysis and contributed to data interpretation. EG, JH, GF, LP, and SH contributed to data collection, study implementation, and data analysis and interpretation. PJW did the analysis and contributed to study design and implementation, and data interpretation. IA, TDM, JMW, ML, and RG contributed to the study design and implementation, and data analysis and interpretation. ACH and CMS wrote the manuscript and all authors reviewed the final version.

Declaration of interests
AS is clinical lead for the Find and Treat service that manages Video-observed therapy. PJW has received research funding from Otuska for a retrospective study of multidrug-resistant tuberculosis treatment in several eastern European countries. RG reports involvement with SureAdhere Mobile, but no funding was received from the company for work on this study. All other authors declare no competing interests.

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