



### BACKGROUND

Outlined in its 'End TB Strategy'<sup>1</sup>, the World Health Organisation (WHO) has set out its aims to end the worldwide epidemic of Tuberculosis (TB) by 2035. Tuberculosis currently affects 1.8 billion people across the globe<sup>9</sup>; and its spread is associated with poor living conditions and overcrowding<sup>11</sup>. Standard treatment relies heavily upon daily adherence to four antibiotics: isoniazid, rifampicin, ethambutol and pyrazinamide, for the first two months. This is followed by pyrazinamide and ethambutol for a further four months<sup>10</sup>. The effectiveness of this treatment in curing TB and thereby reducing spread is challenging.

A combination of poor adherence to daily antibiotics, anti-tuberculous treatment side effects and the six-month duration of continuous therapy have fuelled the rise of treatment failure and multi-drug resistant TB as a public health crisis. As part of the 2015 WHO End TB strategy, global experts agreed upon using digital technology in addition to existing treatment strategies to improve compliance to anti-tuberculous treatment<sup>2</sup>. However, NICE recommends case management and Direct Observed Therapy (DOT) in the UK<sup>8</sup>.

### AIM

The aim of this evidence review was to assess the effectiveness of digital technology compared to usual intervention methods (Directly Observed Treatment therapy) in improving compliance to TB treatment.

### METHODS

A search strategy was devised and the electronic databases: NICE Evidence, Cochrane, PubMed, OVID MEDLINE and OVID EMBASE, were searched to identify three main sources of evidence to inform the review:

- I. Evidence-Based Guidelines
- II. Randomised Controlled Trials
- III. Systematic Reviews

Initial screening of search results was determined using title and abstract. Detailed screening was implemented using the strict inclusion criteria below:

- Population:** All adults or children in any setting undergoing DOT treatment for active or latent TB
- Intervention:** Addition of digital technology intended to increase compliance: SMS reminders, social media, video observed therapy, medication event monitoring systems, easy cure box
- Comparator:** Usual care
- Outcome:**
- I. **Primary outcome(s):**  $\geq 80\%$  Completion of treatment. Cure within 1 year measured by a negative sputum smear or culture.
  - II. **Secondary Outcome(s):** Isoniazid urine test. Identification of new drug resistance

The quality of included studies was assessed. Evidence-based guidelines were appraised using the AGREE II instrument. Systematic reviews and RCTs were appraised using their respective CASP framework.

### REFERENCES

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- (4) Bediang G, Stoll B, Elin N, Abena J, Geissbuhler A. SMS reminders to improve adherence and cure of tuberculosis patients in Cameroon (TB-SMS Cameroon): a randomised controlled trial. *BMC Public Health* 018;18(1):583.
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### FLOWCHART OF SEARCH PROTOCOL:

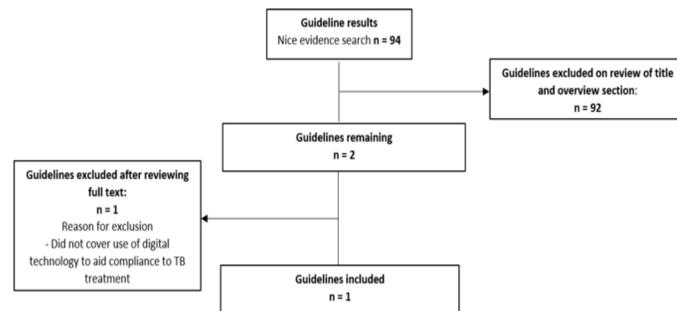


Figure 1. Search flow showing the number of guidelines included and excluded during the literature search process

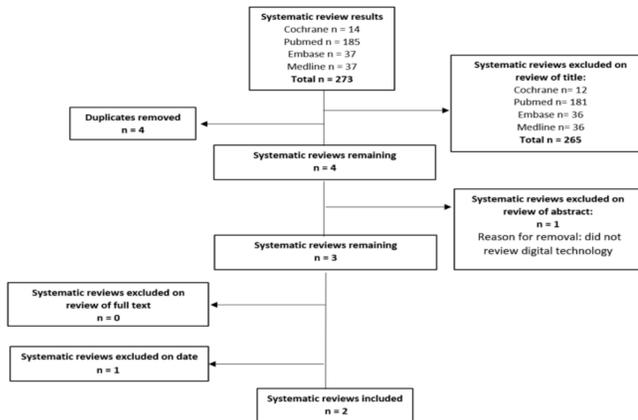


Figure 2. Search flow showing the number of systematic reviews included and excluded during the literature search process

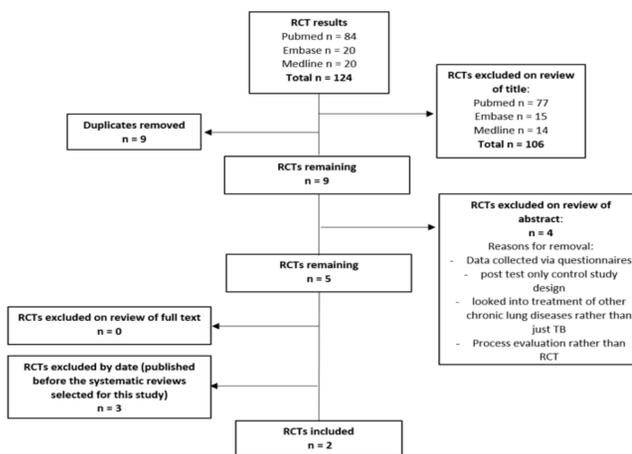


Figure 3. Search flow showing the number of RCTs included and excluded during the literature search process

**Flowchart:** The search strategy yielded 94 guidelines, 273 systematic reviews and 124 RCTs.

Of these, 92 guidelines, 265 systematic reviews and 106 RCTs were excluded on title and abstract. 13 duplicates were excluded overall. 1 guideline was excluded on review of full text because it contained no information on use of digital technology for compliance. 1 systematic review and 4 RCTs were excluded due to date of publication. Reviewers agreed on inclusion of the most recent guideline (Figure 1), the two most recent systematic reviews (Figure 2) and two RCTs published after the systematic review searches (Figure 3) for appraisal.

### RESULTS: TREATMENT GUIDELINES

One guideline was suitable for full review (WHO 2017)

- I. The WHO<sup>5</sup> updated their guidelines in 2017, highlighting that compliance interventions such as digital health technology should be used as a tool alongside a suitable treatment option, such as Directly Observed Treatment.
- II. The intended benefits of digital health technology are to maintain a good level of communication between the patient and health care provider; thereby improving compliance to treatment
- III. However, the recommendation to use digital health communications alongside a suitable treatment option such as DOT was based upon poor quality evidence.

### RESULTS: RANDOMISED CONTROLLED TRIALS

Two Randomized Controlled Trials were suitable for full review (Johnson et al, Bediang et al)

- I. 'SMS Messaging' - Johnston *et al*<sup>3</sup> did not find a statistically significant difference in compliance when implementing SMS messaging compared to the control. In the SMS messaging and control groups, compliance was 79.4% and 81.9% respectively (RR=0.97, 95% CI 0.88-1.07). Complete compliance was defined as >80% completion of medication at either 4 or 9 months
- II. 'SMS Messaging' - Bediang *et al*<sup>4</sup> did not find a statistically significant difference in compliance when implementing SMS messaging compared to the control. The two arms had compliance values of 63.5% and 62% respectively (OR=1.06, 95% CI 0.65-1.73). Complete compliance was defined as negative TB smear test at either five months or six months.

### RESULTS: SYSTEMATIC REVIEWS

Two systematic reviews were suitable for full review (Ngwatu et al, Alipanah et al)

- I. 'SMS Messaging' - Ngwatu et al<sup>6</sup> did not report a statistically significant increase in completion of TB treatment, and cure, in the SMS intervention group compared to the control (95% CI 0.65-2.56).
- II. 'Video Observed Therapy (VOT)' - Alipanah *et al*<sup>7</sup> did not report a statistically significant increase in completion of TB treatment when VOT was implemented compared to the control (RR 1.17, 95% CI 0.79-1.72).
- III. 'Video Observed Therapy (VOT)' - Similarly Ngwatu *et al*<sup>6</sup> did not reveal a statistically significant difference when using VOT (RR 0.99, 95% CI 0.93-1.05).
- IV. 'Medication Monitoring' - Ngwatu *et al*<sup>6</sup> did not find increased compliance when medication monitoring was introduced compared to the control group (RR 0.58, 95% CI 0.42-0.79).
- V. 'Medication Monitoring and SMS' - Ngwatu *et al*<sup>6</sup> did not find increased compliance when adopting education monitoring and SMS compared to the control group (RR 0.49, 95% CI 0.27-0.88).

### CONCLUSION

Untreated, tuberculosis is a major cause of morbidity and mortality globally. A major barrier to improving tuberculosis treatment, cure and cessation of transmission is poor compliance to treatment.

This evidence review attempted to answer the question: Is digital technology an effective tool in improving patient compliance to TB treatment?

Our review has shown that there is uptake of various new digital technologies globally, however the findings do not reveal statistically significant improvements in compliance. However, this is an actively evolving field, and more research is needed to identify which digital treatment strategies improve patient outcomes and would be economically feasible across all resource settings.