Point-of-care molecular diagnostics for community-based active case-finding: A multicentre randomised controlled trial on TB detection and treatment initiation

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Point-of-care Xpert in active case-finding is speeds up treatment initiation and lowers probability of treatment initiation failure

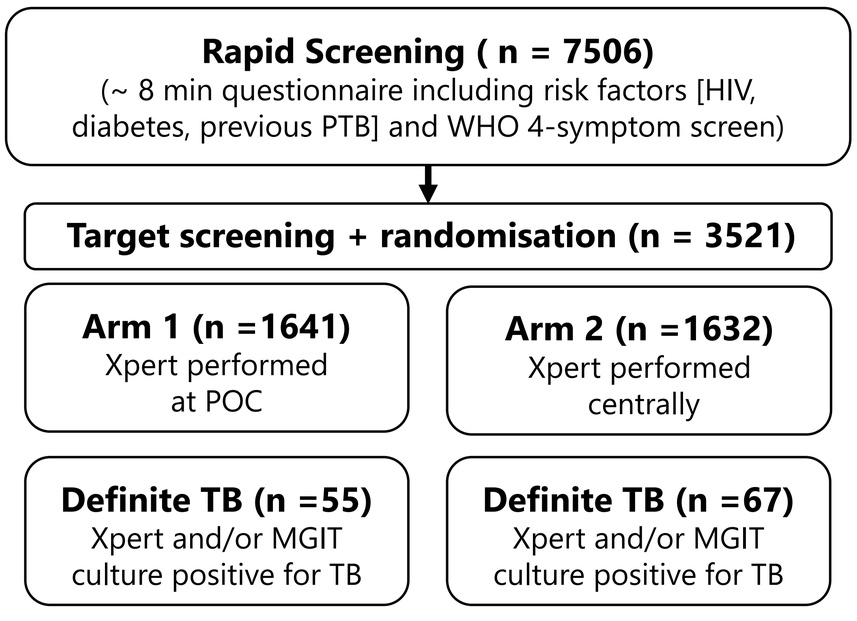

Figure 1: A consort diagram and overview

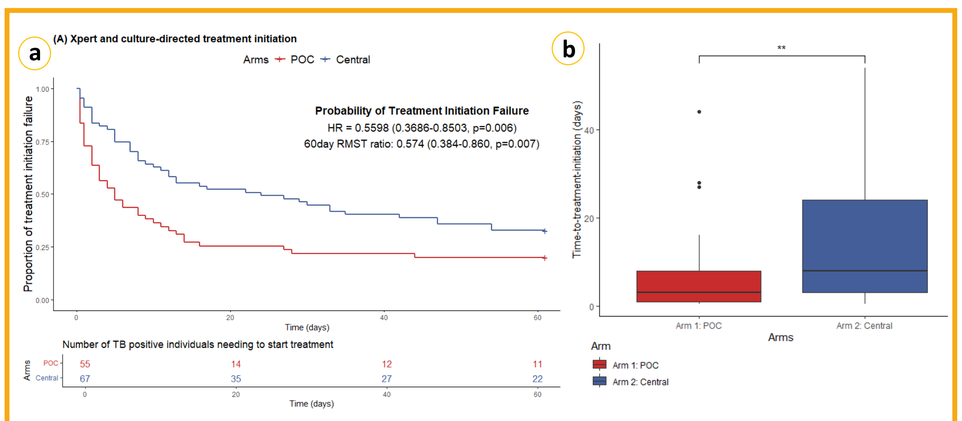

Figure 2: Survival analyses (a) showing faster treatment initiation and lower probability of treatment initiation failure over 60days in the POC arm (red) versus the central arm (blue). Boxplot (b) showing the median time-to-treatment-initiation in each arm.

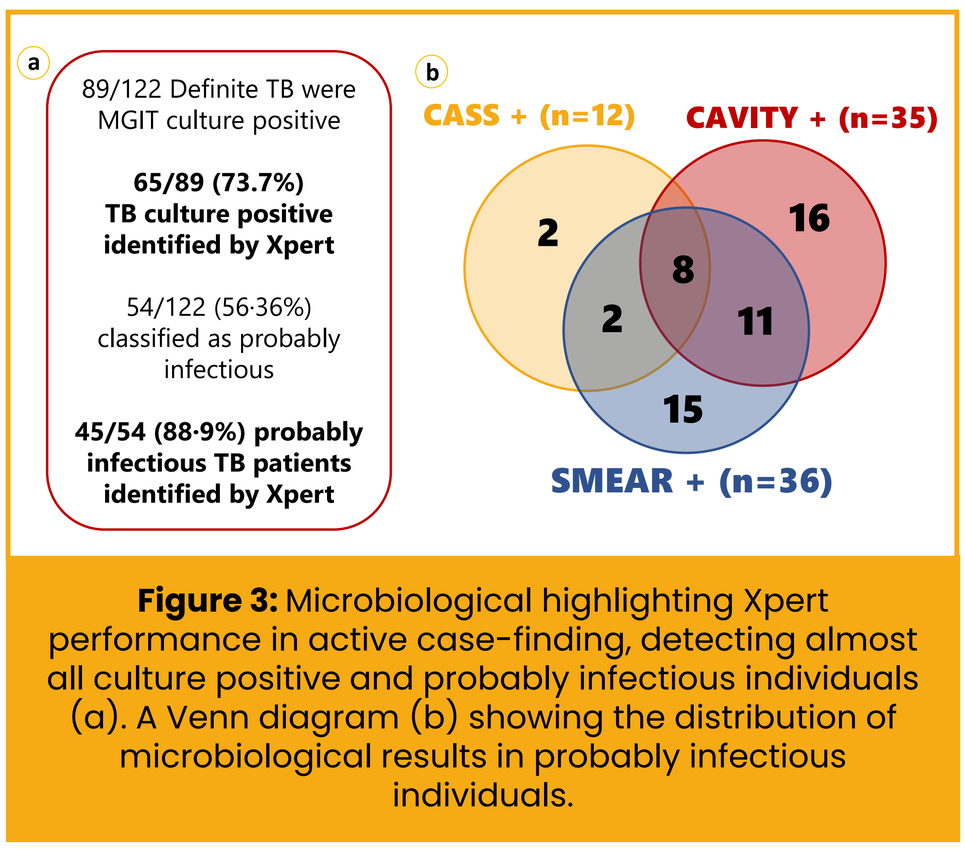

Figure 3: Microbiological highlighting Xpert performance in active case-finding, detecting almost all culture positive and probably infectious individuals (a). A Venn diagram (b) showing the distribution of microbiological results in probably infectious individuals.

1. Introduction

Identifying the ideal active case-finding (ACF) strategy for TB is critical to improve detection and hasten treatment initiation. We investigated a point-of-care (POC) Xpert-driven ACF strategy – the XACT model – in an open-label, international randomised controlled trial to ascertain whether POC diagnostics are a critical component of ACF strategies.

2. Methods

We performed ACF using a low-cost mobile clinic fitted with a portable Xpert system in peri-urban informal settlements of major cities of four African countries (South Africa, Zambia, Zimbabwe and, Mozambique). We compared time-to-treatment initiation between those randomised to Xpert done at (1) POC or (2) centralised laboratory. Liquid sputum culture was used as a reference standard. Those with microbiologically confirmed TB received infectiousness studies, including smear microscopy, chest x-ray (CXR) and cough aerosol sampling (CASS).

3. Results

Of screened 7506 individuals, 3273/3523 participants at risk for TB were randomised and included in the analysis. Xpert as a diagnostic tool in ACF performed well - detecting 73·03% (65/89) of culture-positive TB. 54/122 (56·36%) participants with definite TB were identified as probably infectious (cavities on CXR [n=35] and/or smear-positivity [n=36] and/or CASS-positivity [n=12]). Xpert identified almost all probably infectious cases (48/54 [88·9%]). POC Xpert time-to-treatment-initiation (median, interquartile range [IQR]) was significantly shorter than the centralised Xpert (3 [1-8] versus 8 [3-24]; p<0·001). POC Xpert was associated with lower probability of treatment initiation failure (primary outcome) by 60days (HR 0·5598 [0·3686-0·8503, p=0·006] and 60-day RMST 0·574 [CI 0·384-0·860, p=0·007]).

4. Conclusion

Community-based active case-finding using portable molecular-based diagnostic tools reliably detects probably infectious, minimally symptomatic TB patients. And significantly improves the speed and the uptake of treatment initiation. These data inform key elements of ACF strategies needed to bridge the gap to find, treat and end TB.

Acknowledgments

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