Cost-effectiveness of community-based household tuberculosis contact management for children in Cameroon and Uganda: a modelling analysis of a cluster-randomised trial

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Summary

Background WHO recommends household contact management (HCM) including contact screening and tuberculosis-preventive treatment (TPT) for eligible children. The CONTACT trial found increased TPT initiation and completion rates when community health workers were used for HCM in Cameroon and Uganda.

Methods We did a cost–utility analysis of the CONTACT trial using a health-system perspective to estimate the health impact, health-system costs, and cost-effectiveness of community-based versus facility-based HCM models of care. A decision-analytical modelling approach was used to evaluate the cost-effectiveness of the intervention compared with the standard of care using trial data on cascade of care, intervention effects, and resource use. Health outcomes were based on modelled progression to tuberculosis, mortality, and discounted disability-adjusted life-years (DALYs) averted. Health-care resource use, outcomes, costs (2021 US$), and cost-effectiveness are presented.

Findings For every 1000 index patients diagnosed with tuberculosis, the intervention increased the number of TPT courses by 1110 (95% uncertainty interval 894 to 1227) in Cameroon and by 1078 (796 to 1220) in Uganda compared with the control model. The intervention prevented 15 (–3 to 49) tuberculosis deaths in Cameroon and 10 (–20 to 33) in Uganda. The incremental cost-effectiveness ratio was $620 per DALY averted in Cameroon and $970 per DALY averted in Uganda.

Interpretation Community-based HCM approaches can substantially reduce child tuberculosis deaths and in our case would be considered cost-effective at willingness-to-pay thresholds of $1000 per DALY averted. Their impact and cost-effectiveness are likely to be greatest where baseline HCM coverage is lowest.

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Introduction

WHO estimates that 1·2 million children (aged <15 years) developed tuberculosis in 2021, of whom 220 000 died.[1] The WHO African region has the highest per-capita tuberculosis mortality rate in children, contributing around 38% of global child tuberculosis deaths.[2] Most of these deaths occur in children who do not receive treatment.[2] This situation highlights the importance of preventive measures that reduce the number of children developing tuberculosis, and approaches that increase the proportion of children with tuberculosis who are detected and treated.

Household contact management (HCM) targets both these pathways: using systematic tuberculosis screening for household contacts of patients newly diagnosed with tuberculosis (index patients) to identify and treat additional co-prevalent disease, and providing tuberculosis-preventive treatment (TPT) to decrease tuberculosis risk in those without disease. Although a minority of all tuberculosis transmissions are thought to occur within households,[3] in many settings, household contacts are nevertheless at high risk of tuberculosis disease and infection.[4,5] Children and people living with HIV are at high risk of subsequently developing tuberculosis once exposed, and TPT reduces this risk by up to 90% in those with immunoreactive evidence of tuberculosis infection.[6] Modelling work has suggested that moving from zero to complete coverage of HCM could have averted tuberculosis disease in nearly 160 000 children and deaths in over 100 000 children in 2016.[7]

WHO first recommended HCM for children younger than 5 years and people living with HIV in 2012,[8] and has subsequently broadened this recommendation to include all child contacts younger than 15 years.[9] However, global coverage of TPT in children younger than 5 years remains low; by the end of 2022, only 55% of the target of 4 million set for the 2018–22 period by the UN General

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Research in context

Evidence before this study

We searched PubMed with the terms ("child*" OR "paed*" OR "ped") AND ("TB" OR "tubercul*") AND ("household" OR "community") AND ("contact*") AND ("screen*" OR "invest*" OR "prevent*") AND ("model*" OR "cost-effect*" OR "CEA" OR "cost–utility analysis" OR "CUA" OR "economic analysis") for articles published before Nov 1, 2022. We found 124 studies, from which we identified four that had estimated the cost-effectiveness of household contact management (HCM) of tuberculosis and tuberculosis-preventive treatment (TPT) in children younger than 15 years. Mandalakas and colleagues used a model-based cost-effectiveness analysis of various infection screening strategies for HCM of children younger than 5 years in South Africa, finding an incremental cost-effectiveness ratio (ICER) of US$237 per life-year saved from a societal perspective for the no-test strategy. Using a model-based cost-effectiveness analysis of short-course TPT in household child contacts across 12 countries, Jo and colleagues found ICERs of US$100–1600 per disability-adjusted life-year (DALY) averted. In a cluster-randomised trial of a health-systems intervention for latent tuberculosis infection management, Oxlade and colleagues reported a cost per additional contact initiating treatment of CA$568 (range 329–2103) for TPT of all household contacts and $1174 (734–3064) when restricting TPT to children aged 5 years or younger. More recently, Dodd and colleagues modelled the potential country-level and global effects and cost-effectiveness of multidrug-resistant or rifampicin-resistant tuberculosis HCM for children younger than 15 years, finding ICERs of US$703–1208 per DALY averted.

Added value of this study

To our knowledge, this study is the first cost–utility analysis of HCM for child tuberculosis contacts based on a randomised trial comparing a community-based (intervention) to a facility-based approach (the standard of care), and is also the first economic analysis of a TPT intervention delivered at household level by community health workers. Our estimates of costs and effects are based on results from a multicountry cluster-randomised trial.

Implications of all the available evidence

Community-based approaches to HCM are expected to avert tuberculosis disease and deaths in children. Our approach in Cameroon and Uganda would be considered cost-effective at willingness-to-pay thresholds of US$1000 per DALY averted. The impact and cost-effectiveness of such interventions would be greater in settings with higher tuberculosis disease prevalence among contacts and lower existing coverage of screening for child household contacts.

Assembly high-level meeting on tuberculosis had been reached.[10] Barriers to uptake vary by setting, but are likely to include perceived lower priority than treatment for tuberculosis disease; unclear perceived benefits among parents and health-care workers of long treatment for apparently well children; fear of generating resistance by use of TPT on undiagnosed tuberculosis disease; and use of facility-based models of screening that place the onus on household members to return with children to facilities.[11] For many households affected by tuberculosis, the opportunity costs of engaging with care seeking can lead to catastrophic costs of over 20% of annual household income.[12] Evaluation of practical strategies for HCM that use community health workers to visit households for screening and shorter 3-month TPT regimens are therefore priorities, as is generating evidence on the cost-effectiveness of strategies, which is currently sparse.[13]

Despite recommendations and anticipated benefits, no previous study has evaluated the effectiveness of community-based HCM compared with a facility-based standard of care. The Community Intervention for TB Active Contact Tracing and Preventive Therapy Management (CONTACT) study (NCT03832023) was a multicentre, parallel, open-label, cluster-randomised, controlled trial comparing facility-based and community-based models of HCM, delivered by community health workers. The study took place between 2019 and 2022 in Cameroon and Uganda, and the primary endpoint was the proportion of children younger than 5 years or children aged 5–14 years living with HIV who initiated and completed TPT among those declared by index patients. Ten clusters in each country were selected from health facilities that registered at least 50 patients with bacteriologically confirmed tuberculosis in the preceding year (from the Central and Littoral regions of Cameroon and the South-Western region of Uganda). The detailed design,[14] feasibility,[15] and results of the study have been reported elsewhere.[16] The intervention increased the coverage of child contact investigation and improved TPT initiation and completion rates. In this Article, we report the cost-effectiveness of the interventions to assist decision makers when considering implementation of HCM interventions. Our analysis combines empirical cost estimates from financial data and activity timings with mathematical models of care pathways to estimate the resource use and health benefits of different interventions.

Methods

Conceptual approach

We developed a conceptual model representing the care pathways for household child tuberculosis contacts enrolled and screened for tuberculosis symptoms in the CONTACT trial. Child contacts without tuberculosis-suggestive symptoms were evaluated for TPT eligibility

and initiated on TPT when eligible (children aged <5 years, or those aged 5–14 years and HIV positive). Child contacts with symptoms at initial screening or during TPT follow-up were referred for tuberculosis investigations at the facility in both care models. Tuberculosis investigations followed national guidelines, typically consisting of clinical assessment (with or without chest x-ray), sample collection (including sputum and nasopharyngeal aspirate), bacteriological assessment (mainly using Xpert MTB/RIF; Cepheid, Sunnyvale, CA, USA), antibiotic prescription, and hospitalisation if required. Sample referral to facilities with diagnostic capability was possible in both care models when Xpert MTB/RIF was not available on site. Child contacts diagnosed with prevalent or incident tuberculosis were initiated on anti-tuberculosis treatment following national guidelines. Children initiated on TPT received 3 months of a rifampicin–isoniazid fixed-dose combination (in a dispersible form that was suitable for children), in accordance with the WHO recommendation,[9] with monthly follow-up. Per Ministry of Health requirements in both countries, two additional monitoring visits were done by community health workers at 1 week and 2 weeks after starting TPT. The initial conceptualisation allowed all the cascade steps to take place at either households or facilities, except tuberculosis investigations, which took place at the facility only. Screening for tuberculosis in the household was part of national guidelines in Uganda, but not often done in the standard-of-care model. In the trial, screening for tuberculosis symptoms, TPT initiation, and follow-up were done at the facility in the standard-of-care (control) group and at the household in the intervention group by community health workers, except for TPT initiation, which was done by a nurse in the household. Simplified clinical care pathways for household child tuberculosis contacts are shown in figure 1 (see appendix 1 pp 1–7 for more details).

Decision-analytical modelling approach

We used the clinical care pathways shown in figure 1 as the structure of a decision-tree model. Data on coverage of child contact investigation under the standard of care and intervention were obtained from the CONTACT trial and used to calculate care cascades. Cascade steps for tuberculosis symptom screening, TPT initiation and completion, investigations, and anti-tuberculosis treatment for co-prevalent and incident disease were modelled on the basis of proportions informed by trial data. These data were disaggregated by country, trial group (control or intervention), and age group (0–4 years or 5–14 years). Intervention effects were estimated by applying country-specific odds ratios derived from logit-link binomial-likelihood generalised linear mixed models for the main trial analysis for tuberculosis-suggestive symptoms, TPT initiation, TPT completion, and tuberculosis diagnosis. The risks of progression to incident tuberculosis depending on TPT initiation or not were modelled with use of estimates from a published systematic review and meta-analysis.[6]

Outcomes following tuberculosis disease were modelled on the basis of meta-analytic mortality risk estimates specific to first-line treatment, and were stratified by age group, HIV status, and antiretroviral therapy status.[17] The mean age-specific life-years lost (with and without 3% discounting),[18] over a lifetime horizon, were calculated using country-specific life expectancy from UN estimates.[19] We did not consider the contribution of morbidity to disability-adjusted life-years (DALYs) and did not model drug-resistant tuberculosis or mortality in children truly negative for tuberculosis.

Country-specific economic costs associated with resource use under the intervention and standard of care were calculated and applied to the model. We estimated unit costs for activities involved in tuberculosis contact screening, TPT delivery and follow-up, tuberculosis investigations, and anti-tuberculosis treatment using study and published data.[20–23] Where volunteers were involved, we included the economic cost of their time using incentives paid as a proxy. We applied these unit costs to individual-level resource use data from the study to estimate costs per child contact. There were no missing resource use data. Costs were summed over the main care cascade steps and mean costs (and SDs) were estimated by country and care model. All costs were estimated in 2021 US dollars and assumed to accrue in the present, with no discounting applied. These costs were applied to the relevant cascade step and modelled as following gamma distributions, with means and SDs corresponding to estimates.

All model parameters were considered uncertain and described by prespecified probability distributions. We used 1000 samples of all inputs for probabilistic uncertainty analysis, and report means and 95% quantiles (uncertainty intervals [UIs]) for all model estimates. Calculations were done with a previously described decision-tree modelling framework in R using the HEdtree package.[24] Additional details on the model structure, model parameters, and results are provided in appendix 1 (pp 1–22) and the health economic analysis plan.[25] All analysis code and data are available on GitHub.

See **Online** for appendix 1

For the **analysis code and data relating to this study** see https://github.com/petedodd/CONTACT

Health economic outcomes

For every 1000 index cases identified, we calculated the number of children screened, TPT courses, anti-tuberculosis treatments, tuberculosis cases, deaths, DALYs, and costs in both the control and intervention groups. We calculated the incremental cost-effectiveness ratios (ICERs) for each country in terms of the incremental cost per DALY averted and the probability of the intervention being cost-effective at different

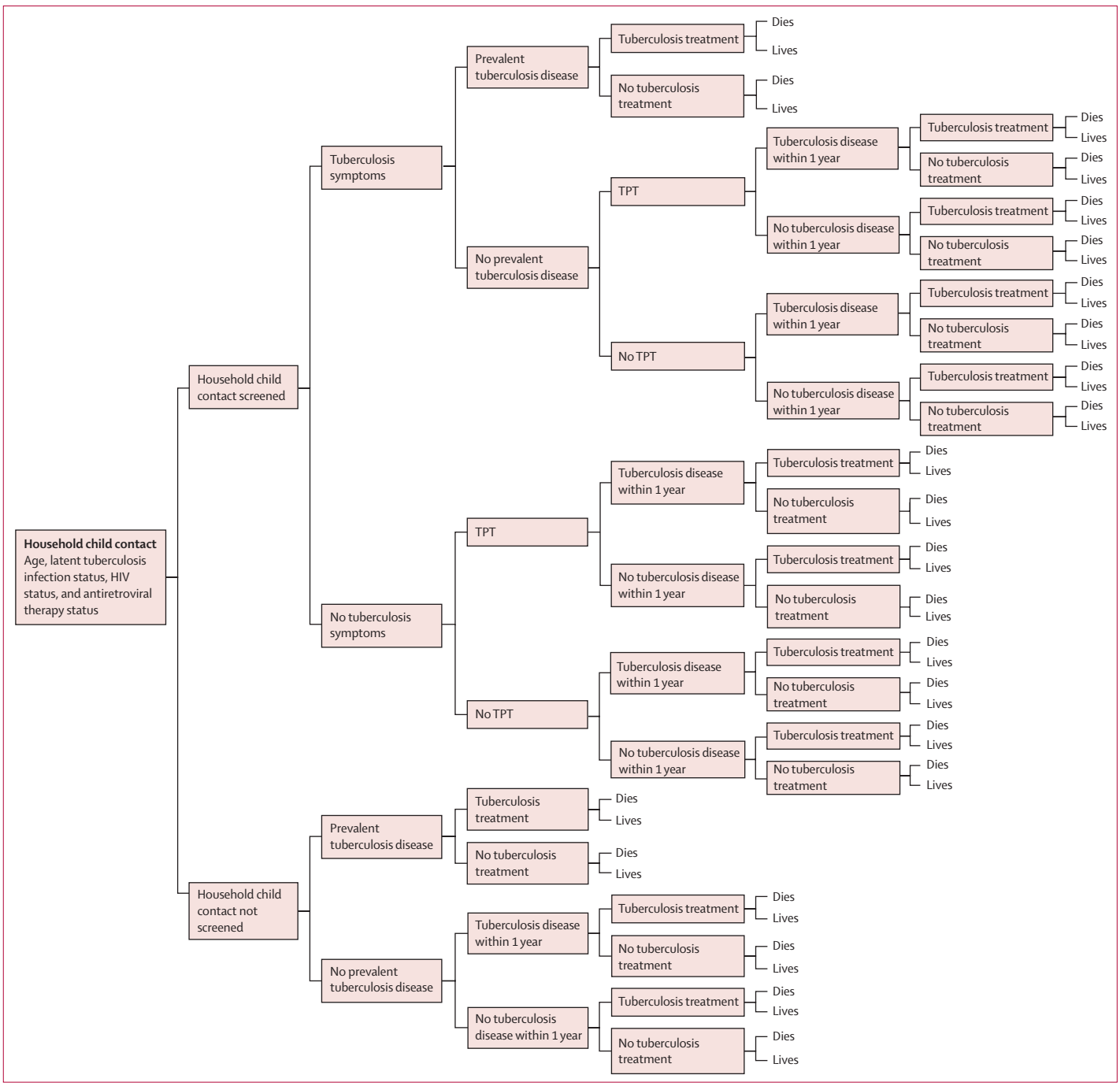

Figure 1: **Simplified diagram of decision-analytical model**
Diagram shows the pathways of care for household child contact screening, symptomatic child contact management (co-prevalent tuberculosis disease), asymptomatic child contact management (TPT cascade), and tuberculosis disease outcomes. Child contacts aged 5 years or those aged 5–14 years living with HIV were considered potentially eligible for TPT. TPT=tuberculosis-preventive treatment.

cost-effectiveness thresholds using a health-system perspective.

Sensitivity analysis

We evaluated the impact of assuming a higher tuberculosis prevalence (10%, based on a systematic review)[4] among household child contacts, removing the Ministry of Health-mandated extra visits in the intervention model (assuming similar visits as in the control model), assuming a 50% reduction in TPT regimen costs, and applying alternative discount rates of 0% and 5% for life-years.

	Cameroon			Uganda		
	Control	Intervention	Increment	Control	Intervention	Increment
Health-care resource use						
Household contacts screened	1203	3269	2066	1941	3311	1369
TPT courses	467 (460 to 473)	1577 (1360 to 1695)	1110 (894 to 1227)	987 (979 to 994)	2064 (1782 to 2209)	1078 (796 to 1220)
Anti-tuberculosis treatment courses	78 (44 to 128)	51 (5 to 175)	–28 (–106 to 83)	151 (78 to 246)	125 (38 to 249)	–26 (–123 to 91)
Health outcomes						
Prevalent tuberculosis	14 (14 to 14)	15 (5 to 77)	1 (–9 to 62)	15 (15 to 15)	20 (2 to 123)	6 (–13 to 108)
Incident tuberculosis	182 (99 to 291)	128 (65 to 220)	–54 (–95 to –23)	171 (91 to 269)	119 (61 to 194)	–52 (–91 to –22)
Prevalent tuberculosis deaths	3 (3 to 3)	0 (0 to 0)	–3 (–3 to –2)	1 (0 to 2)	0 (0 to 0)	–1 (–2 to 0)
Incident tuberculosis deaths	41 (23 to 67)	28 (3 to 56)	–12 (–46 to 5)	17 (5 to 39)	8 (1 to 35)	–9 (–31 to 21)
Total deaths	44 (26 to 70)	29 (3 to 56)	–15 (–49 to 3)	18 (5 to 41)	8 (1 to 35)	–10 (–33 to 20)
Discounted DALYs	1154 (676 to 1847)	752 (73 to 1474)	–401 (–1284 to 72)	494 (145 to 1120)	217 (37 to 953)	–278 (–890 to 548)
Costs and cost-effectiveness*						
Screening cost	18 120 (14 146 to 22 319)	106 589 (10 827 to 304 812)	88 470 (–6990 to 287 254)	28 954 (21 403 to 38 238)	75 134 (29 543 to 141 399)	46 180 (–586 to 112 850)
TPT cost	41 780 (10 184 to 92 136)	196 441 (32 668 to 534 666)	154 661 (–19 366 to 496 639)	80 567 (32 746 to 151 915)	302 971 (197 653 to 437 416)	222 403 (97 475 to 358 870)
Prevalent anti-tuberculosis treatment cost	4464 (2296 to 7259)	10 163 (2090 to 31 528)	5699 (–3144 to 27 573)	7428 (4796 to 10 582)	12 618 (1945 to 39 718)	5189 (–6348 to 33 224)
Incident tuberculosis cost	10 855 (4713 to 22 093)	10 825 (1512 to 30 472)	–30 (–13 677 to 15 124)	22 025 (8866 to 45 967)	17 427 (4327 to 36 509)	–4597 (–25 937 to 13 990)
Total cost	75 219 (41 379 to 128 047)	324 019 (102 490 to 693 221)	248 800 (24 428 to 616 748)	138 974 (86 314 to 215 498)	408 150 (287 817 to 546 959)	269 176 (130 434 to 418 399)
Incremental cost-effectiveness ratio†	..	..	620	..	..	970

Values in parentheses are 95% uncertainty intervals. All outcomes are presented per 1000 index tuberculosis patients. DALY=disability-adjusted life-year. TPT=tuberculosis-preventive treatment. *All costs are presented in 2021 US$. †The incremental cost-effectiveness ratio is presented as US$ per DALY averted.

Table 1: **Health-care resource use, health outcomes, costs, and cost-effectiveness**

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

For every 1000 index patients identified (table 1), 1203 household contacts younger than 15 years in Cameroon and 1941 in Uganda were screened for tuberculosis symptoms under the facility-based approach (control), compared with 3269 in Cameroon and 3311 in Uganda under the community-based approach to HCM (intervention). Of the 9724 screened, 4834 (49·7%) were girls 4890 (50·3%) were boys, and the mean age was 3·9 years (SD 1·7). The projected number of TPT courses required under the control model was 467 (95% UI 460–473) in Cameroon and 987 (979–994) in Uganda, compared with 1577 (1360–1695) in Cameroon and 2064 (1782–2209) in Uganda under the intervention model. The numbers of additional TPT courses required under the intervention model were 1110 (894–1227) in Cameroon and 1078 (796–1220) in Uganda. Under the control model, 78 (44–128) treatments for tuberculosis in Cameroon and 151 (78–246) in Uganda were required, compared with 51 (5–175) in Cameroon and 125 (38–249) in Uganda under the intervention.

An estimated 182 (95% UI 99 to 291) children in Cameroon and 171 (91 to 269) in Uganda developed incident tuberculosis, resulting in 41 (23 to 67) deaths in Cameroon and 17 (5 to 39) in Uganda under the control model (table 1). The intervention prevented 54 cases (23 to 95) of incident tuberculosis in Cameroon and 52 (22 to 91) in Uganda, thereby averting 12 deaths (–5 to 46) due to incident tuberculosis in Cameroon and 9 (–21 to 31) in Uganda. The intervention detected 1 (–9 to 62) additional child with prevalent tuberculosis in Cameroon and 6 (–13 to 108) in Uganda, resulting in the prevention of 3 (2 to 3) deaths in Cameroon and 1 (0 to 2) in Uganda. In total, the intervention resulted in 15 (–3 to 49) and 10 (–20 to 33) fewer deaths compared with the control in Cameroon and Uganda, respectively.

The estimated total discounted DALYs were 1154 (95% UI 676 to 1847) in Cameroon and 494 (145 to 1120) in Uganda under the control model compared with 752 (73 to 1474) in Cameroon and 217 (37 to 953) in Uganda under the intervention model. The intervention averted 401 (–72 to 1284) DALYs in Cameroon and 278 (–548 to 890) in Uganda.

The unit costs for child contact screening and TPT use (table 2) were higher in the intervention model than in the control model, reflecting the additional investment in resources required for implementation. This included

	Cameroon		Uganda	
	Control	Intervention	Control	Intervention
Tuberculosis symptom screening	15·09 (1·76)	32·93 (24·02)	15·03 (2·14)	22·73 (8·32)
Prevalent tuberculosis investigations	46·83 (16·28)	39·61 (15·04)	35·42 (8·73)	30·54 (12·4)
Prevalent tuberculosis treatment	93·01 (10·85)	93·01 (10·85)	149·19 (22·29)	149·19 (22·29)
Tuberculosis-preventive therapy	90·44 (47·46)	123·65 (83·74)	82·3 (31·51)	147·86 (29·11)
Incident tuberculosis investigations	54·9 (34·26)	60·24 (39·88)	13·43 (NA)	13·43 (NA)
Incident tuberculosis treatment	93·01 (10·85)	93·01 (10·85)	149·19 (22·29)	149·19 (22·29)

All costs are presented as mean (SD) in 2021 US$. NA=not applicable.

Table 2: **Cascade of care unit costs (per child contact accessing that step)**

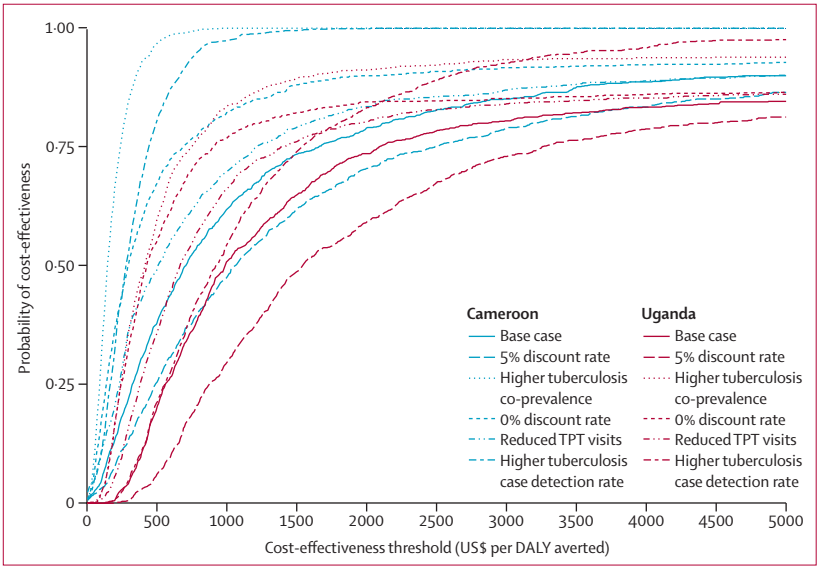

Figure 2: **Cost-effectiveness acceptability curves**
Curves show the probability that the intervention is cost-effective (y-axis) over various decision makers' willingness-to-pay thresholds (x-axis). Costs were measured in 2021 US$. Base case refers to the analysis done with the most likely or preferred set of assumptions and input values. DALY=disability-adjusted life-year. TPT=tuberculosis-preventive treatment.

staff time and travel costs to households to conduct intervention activities. The difference between the unit costs for prevalent and incident tuberculosis investigations arose from differences in resource use (eg, type of sample, test or no test, type and quantity of tests). Differences in costs between the two countries primarily reflect differences in unit costs applied and, to a lesser extent, resource use.

The increase in the number of household contacts screened and TPT courses under the intervention model increased the total costs per 1000 index patients compared with the control model, from US$75 219 (95% UI 41 379–128 047) to $324 019 (102 490–693 221) in Cameroon (increase $248 800 [24 428–616 748]), and from $138 974 (86 314–215 498) to $408 150 (287 817–546 959) in Uganda (increase $269 176 [130 434–418 399]; table 1).

The ICER for implementing the intervention in comparison to the control was $620 per DALY averted in Cameroon and $970 per DALY averted in Uganda. The probability of the intervention being cost-effective compared with the control over a range of willingness-to-pay thresholds (representing decision uncertainty) is shown in figure 2. Assuming a cost-effectiveness threshold of 0·5×gross domestic product (GDP), equivalent to $750 in Cameroon and $410 in Uganda, results in a probability of the intervention being cost-effective of 53% in Cameroon and 12% in Uganda. This probability exceeds 50% at a cost-effectiveness threshold of $706 per DALY averted in Cameroon and $986 per DALY averted in Uganda.

A higher co-prevalence of tuberculosis disease (10%) reduced ICERs by more than 60% (to $155 per DALY averted in Cameroon and $356 per DALY averted in Uganda). Removing extra TPT follow-up visits reduced TPT costs by 30% resulting in a more than 25% reduction in ICERs (to $457 per DALY averted in Cameroon and $629 per DALY averted in Uganda). A 50% reduction in TPT drug costs decreased ICERs to $600 per DALY averted in Cameroon and $915 per DALY averted in Uganda. The ICERs dropped to $257 per DALY averted in Cameroon and $416 per DALY averted in Uganda with no discounting, and increased to $934 per DALY averted in Cameroon and $1514 per DALY averted in Uganda with 5% discounting.

Discussion

In our analysis of a community-based approach to HCM for tuberculosis, for every 1000 index patients, the intervention would prevent 10–15 tuberculosis deaths in children. The intervention would be cost-effective from a health-system perspective compared with the facility-based standard of care at thresholds of $700 per DALY averted in Cameroon and $1000 per DALY averted in Uganda. The choice of cost-effectiveness threshold ultimately lies with the decision maker, and guidance on appropriate thresholds lacks consensus. Historically, a threshold of 1×GDP to 3×GDP per capita was commonly suggested as a guide in countries where explicit thresholds are lacking (GDP per capita is $1500 in Cameroon and $820 in Uganda). However, this threshold has been widely criticised in recent years for its failure to reflect health opportunity costs.[26,27] More recent work estimating implicit thresholds from health spending suggests thresholds are in practice closer to 0·5×GDP per capita.[26,28] Under this rule of thumb, the intervention would remain cost-effective in Cameroon, but not in Uganda.

The country difference in the intervention's cost-effectiveness is primarily driven by higher numbers of child contacts screened per index patient under the standard of care and the assumed higher background case detection rate in Uganda. Higher baseline screening is likely to reduce the headroom for the intervention to improve screening rates, and the better passive case detection reduced the mortality impact of each additional instance of tuberculosis disease treated

or prevented. This intervention is likely to have higher impacts and to be more cost-effective in settings where HCM has low coverage and detection of tuberculosis in children is poor.

The relatively low contribution to averted mortality from the screening component of HCM was due to the low co-prevalence of tuberculosis disease (0·5%) among child contacts. The co-prevalence found in CONTACT is comparable to that found by the Vikela Ekhaya programme in Eswatini.[29] However, a systematic review of the co-prevalence of tuberculosis disease among child household contacts previously found values of 10% for children younger than 5 years in low-income and middle-income countries, and around 5% in high-income countries.[4] Updated reviews found a co-prevalence of tuberculosis disease in child contacts closer to 4% across all country income groups.[5] A lower-than-anticipated co-prevalence of tuberculosis disease in child household contacts might reflect earlier diagnosis of adult disease, leading to reductions in household exposure, or a reluctance to diagnose tuberculosis in children without bacteriological confirmation. Our findings were sensitive to the co-prevalence of tuberculosis disease: our sensitivity analysis, assuming values from a review, reduced ICERs by more than 60% to $155 per DALY averted in Cameroon and $356 per DALY averted in Uganda. This important determinant of impact could vary by context and should be monitored when implementing HCM interventions.

Under the intervention model, more child contacts were screened for every index tuberculosis patient: a mean of 3·4 versus 2·0 overall. This difference might reflect an increased willingness to engage with community-based HCM approaches that are more convenient and less costly to households than facility-based approaches, and is an important driver of impact. Our cost-effectiveness analysis took a health-systems perspective which excludes patient costs. Community-based HCM approaches are more likely to be favoured under economic evaluations that take a societal perspective, or those that consider equity. Findings from an auxiliary patient cost survey in the CONTACT study (unpublished) showed the potential for community-based HCM approaches to reduce costs to households with children receiving preventive therapy (Mafirakureva and colleagues, unpublished).

Affordability is also an important consideration. While our analysis did not consider scale-up costs or savings and cannot be interpreted as a budget impact analysis, incremental costs of approximately $250 per child notified with tuberculosis would translate to full implementation costs equivalent to a substantial fraction of national tuberculosis programme budgets. For countries such as Cameroon and Uganda with over 80% of their national tuberculosis programme budgets funded internationally, a decision to adopt such strategies would require sourcing additional funding.

In addition to these epidemiological and health-system features, other contextual factors that warrant local assessment and adaptations might influence the generalisability of the intervention approach. Feasibility research for CONTACT identified community health worker motivation, and incentive systems to cover transport and communication as key;[15] strengthened referral systems for symptomatic children are also important.[30] A value-of-information analysis could help motivate and design studies informing key parameters to help to reduce decision uncertainty.

Our analysis has some limitations. Modelling in this analysis was used to project outcomes beyond the study follow-up period; thus, assumptions related to incidence and mortality were based on the best available evidence from literature, which might not fully apply to these populations for a variety of reasons. The use of community health workers to deliver care has previously been shown to save health-system costs.[31] Shifting tasks to community health workers in the community-based HCM approach could result in health-system cost savings, which are not considered here. Unit costs for core health-care services under the standard of care were estimated from publicly available sources. Although historical costs were inflated using GDP price deflators and costs derived from other countries were adjusted by applying purchasing-power-parity conversion factors (see appendix 1 p 14), more recent country-specific costs would be preferable. The study overlapped with the COVID-19 pandemic, and related disruptions might have affected measured impact and increased some costs. However, these effects were not quantified precisely enough to include in the model. Finally, our analysis does not account for costs and potential benefits of screening adult household contacts, including any indirect benefits from reduced transmission.

Few other studies have reported on the cost-effectiveness of HCM approaches for child tuberculosis, and none have analysed HCM approaches using community health workers for TPT follow-up. Mandalakas and colleagues[32] considered TPT in children in South Africa in 2012 and found an ICER of $237 per DALY averted from a societal perspective for children aged 0–2 years. Sekandi and colleagues,[20] considering HCM in children younger than 15 years in Uganda in 2015, found ICERs of $444–1494 per additional tuberculosis diagnosis, depending on strategy. Jo and colleagues,[33] considering HCM in children younger than 15 years for 12 countries in 2018, found ICERs of $100–1600 per DALY averted. Dodd and colleagues,[34] considering HCM for child contacts of rifampicin-resistant tuberculosis globally, found ICERs of around $1000 per DALY averted, depending on regimen, strategy, and country. However, these studies have all been model-based rather than evaluating an implemented intervention. In a cluster-randomised trial, Oxlade and colleagues[35] reported the cost per additional contact

initiating TPT of $1174 (range 734–3064) in children younger than 5 years and $568 (329–2103) in all household contacts. This study did not project long-term health impacts beyond TPT initiation. Lung and colleagues[36] evaluated a randomised HCM trial in Viet Nam ending in 2015 that compared facility-based active case finding with passive case finding, finding an ICER of $544 per DALY averted. However, this intervention included adults. A key strength of our work is, therefore, that it is the first cost-effectiveness analysis of HCM strategies specifically for children that is based on a randomised trial.

Community-based approaches to HCM have the potential to make a substantial contribution to paediatric tuberculosis control, especially in settings with lower existing coverage. We found the approach used was cost-effective at thresholds of above $1000 per DALY averted. Cost-effectiveness improves markedly with a higher co-prevalence of tuberculosis disease among child contacts, which might influence the generalisability of these results to other settings.

Contributors

NM and PJD designed and implemented the modelling analysis. MB, AV, and MC contributed to the interpretation and analysis of study data. NM and PJD wrote the first draft of the Article. All authors critiqued the methods and results, and revised and edited the Article. NM and PJD had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

MB has received grants (paid to her institution) from Unitaid and Expertise France for the TB-Speed project on childhood tuberculosis diagnosis, from ANRS for a COVID-19 prevalence study in children with presumptive tuberculosis, and from EDCTP-2 for two therapeutic trials for the treatment of adults with tuberculosis meningitis (INTENSE-TBM) and adults with advanced HIV-TB co-infection (DATURA). All other authors declare no competing interests.

Data sharing

All code and data to reproduce this analysis are publicly available on GitHub at https://github.com/petedodd/CONTACT.

Equitable partnership declaration

The authors of this paper have submitted an equitable partnership declaration (appendix 2). This statement allows researchers to describe how their work engages with researchers, communities, and environments in the countries of study. This statement is part of *The Lancet Global Health*'s broader goal to decolonise global health.

See **Online** for appendix 2

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