Pragmatic Cluster-randomized Trial of Home-based Preventive Treatment for TB in South Africa (CHIP-TB)

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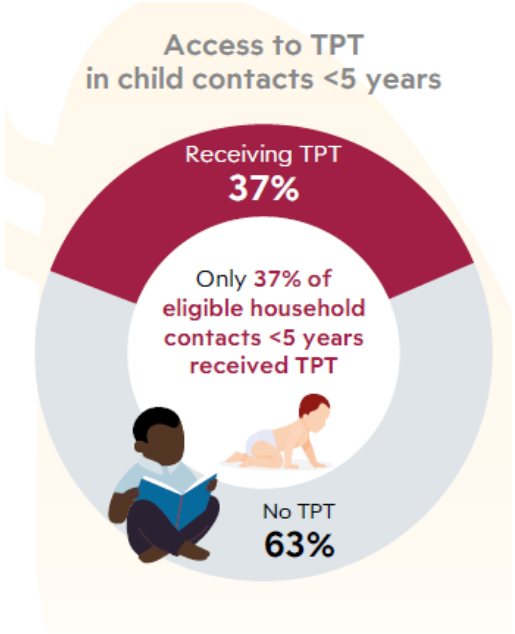
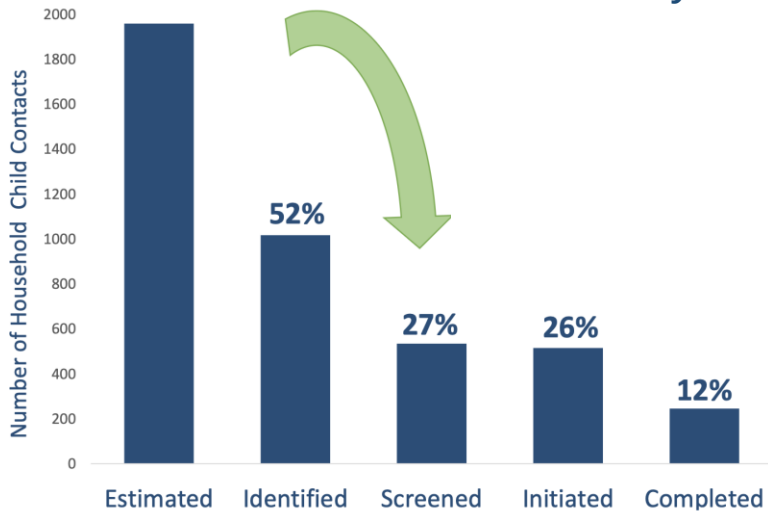
Implementation Gap for TB Preventive Treatment (TPT) among children



TPT highly effective in preventing TB disease but remains poorly implemented

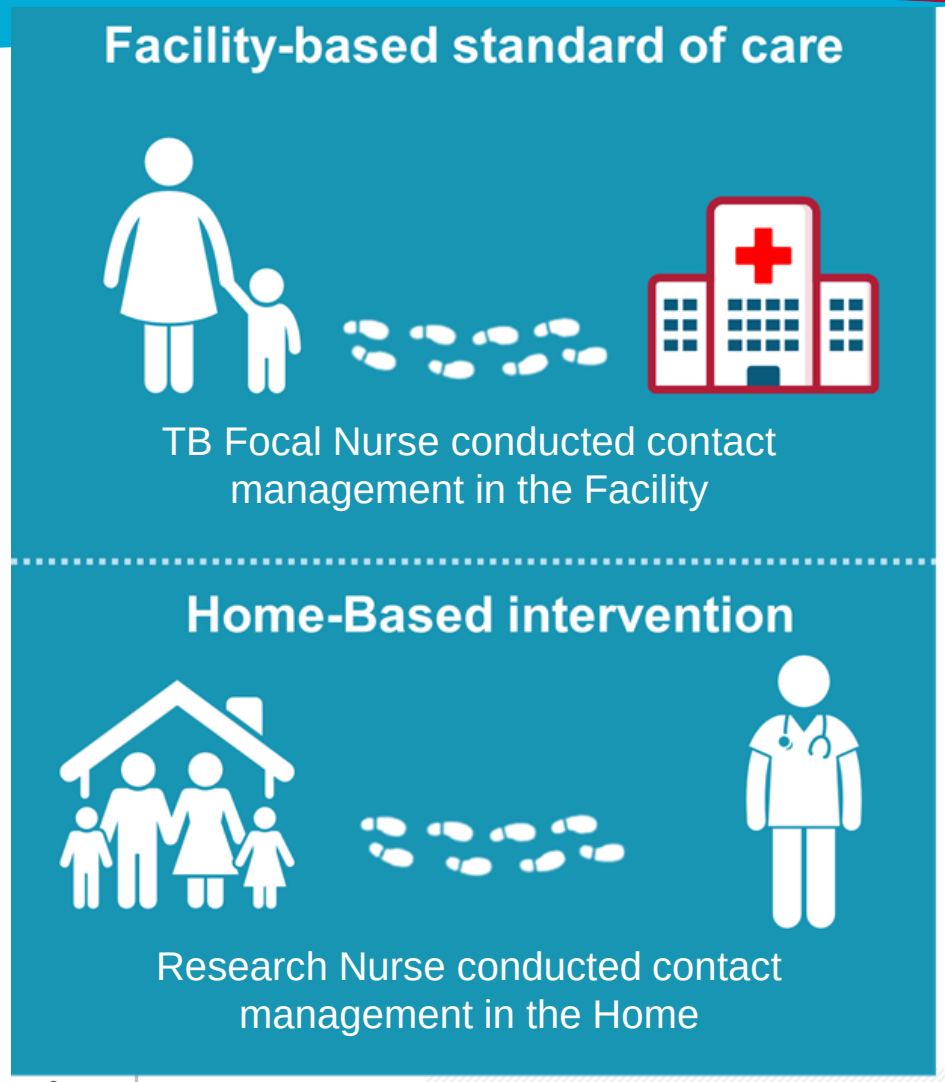
Paediatric TB Prevention Continuum of Care
Matlosana, South Africa
October 2015 – February 2017



Vast majority of child contacts are either not identified or not linked to facility-based care

Community-based contact management may improve identification of child contacts and increase the number of children initiated on TPT

Can community-based contact management improve TPT uptake compared with facility-based standard of care?



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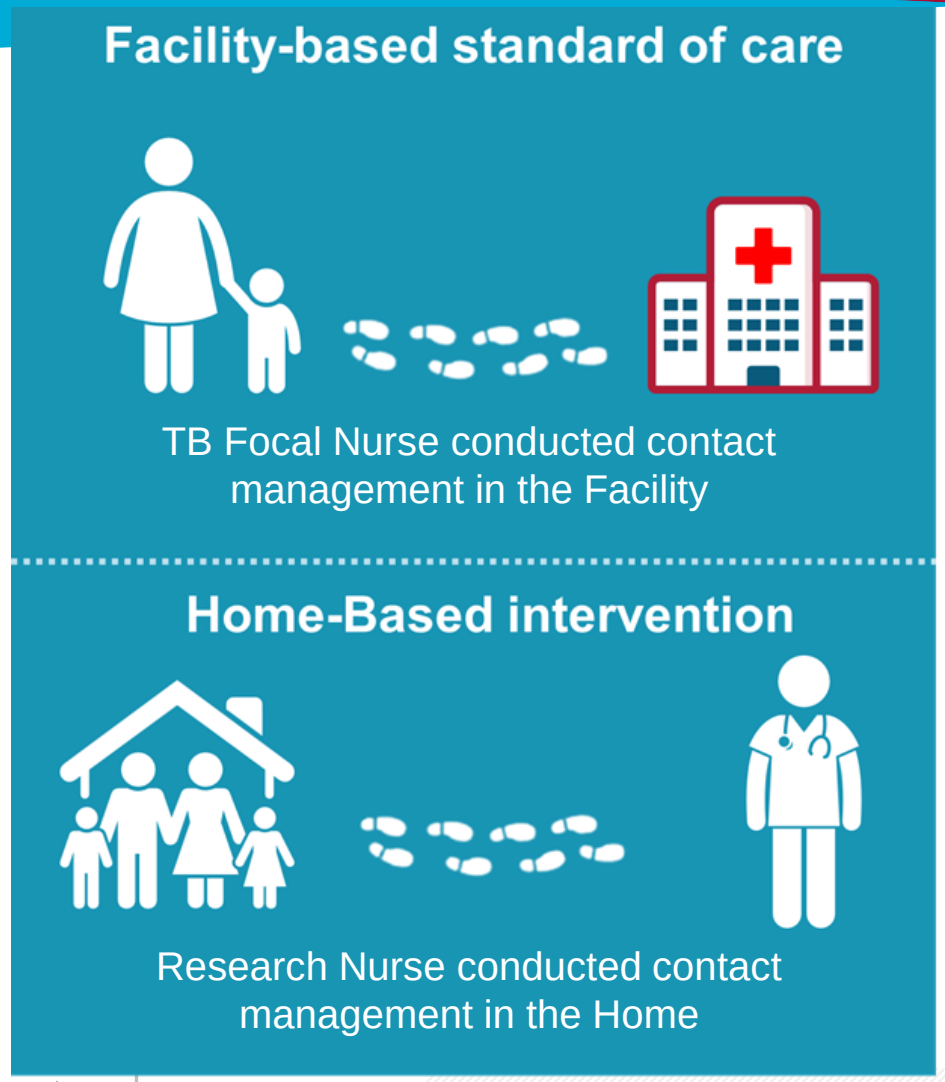


Initial Household Visit with TPT Initiation

Research Nurse:

- Conducts contact tracing, clinical evaluation and counselling
- Initiates asymptomatic children on TPT
- Refers asymptomatic children to clinic

Monthly Follow-up Home Visits

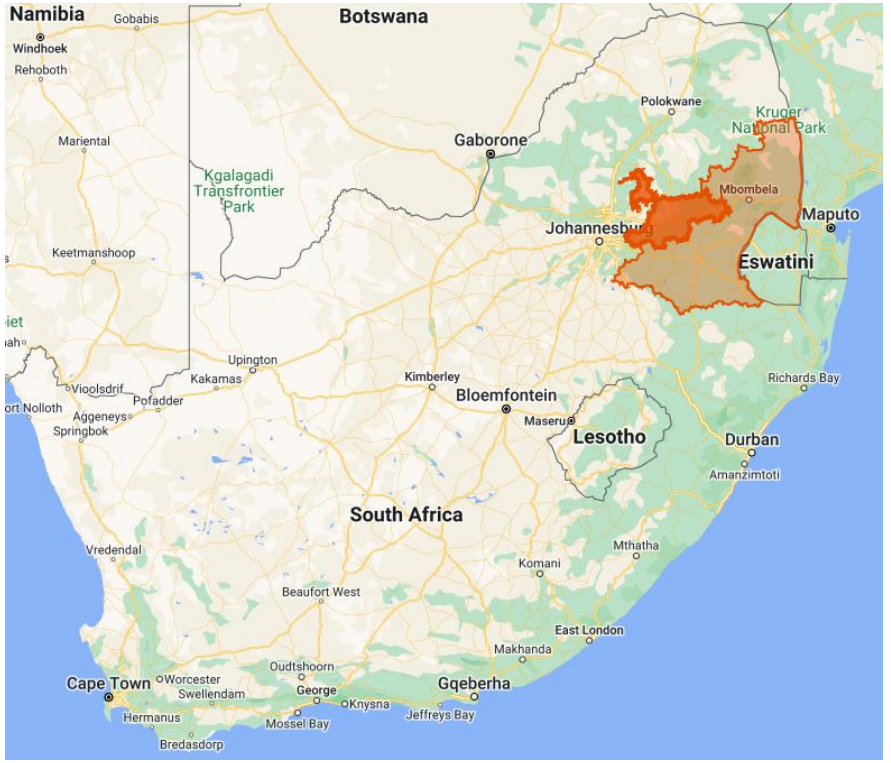
- Those on TPT**:**
  - Assess TB symptoms & side effects
  - Provide TPT refills monthly
  - Refer children with side effects
- Previously symptomatic children:
  - Ensure linkage to care

Study Objectives

1. To determine whether home-based TPT services can improve **TPT uptake** among household child contacts aged < 5 years compared to the facility-based standard of care
2. To determine the **effect** of home-based vs facility-based contact management on the TPT continuum of care
3. To describe **TPT outcomes** for children receiving care in the home-based vs facility-based arms
4. To evaluate the **acceptability and feasibility** of home-based contact management

Methodology

- **Pragmatic Cluster-Randomized Effectiveness Trial**
  - Unit of randomization: clinic
  - Arms
    - **Home-based:** TB prevention services provided by research nurses
    - **Facility-based:** standard of care by DoH clinic staff
- **Setting**
  - 18 clinics in Nkangala district, Mpumalanga
  - March 2022 – June 2023
  - TPT Regimen: **3RH** or **6H**



Study Outcomes

Primary Outcome

- The (cluster-level) ratio of household child contacts (< 5 years) **initiating** TPT per index patient comparing home-based to facility-based TPT initiation

Secondary Outcomes

- HCC Identified: The (cluster-level) ratio of household child contacts (< 5 years) **identified** per index patient comparing home-based to facility-based TPT initiation
- TPT continuum of care: child contact identification, screening, initiation and completion
- Acceptability/Feasibility:
  - Proportion of identified households who agree to/decline home visit
  - Number of household visits per index patient

Eligibility: TB Patients

TB Patient

Inclusion Criteria:

- Bacteriologically confirmed PTB disease (Xpert, smear and/or culture positive)
- Age 18 years or older
- Treated at one of the participating clinics & lives in the catchment area of that clinic
- Willing to have a home visit and disclose their diagnosis to household members
- Provides informed consent

Exclusion Criteria

- RIF and/or INH resistance
- Household already participating in study

Child contact

Inclusion Criteria

- Child less than 5 years old
- Close contact of the TB patient
- Caregiver willing to provide informed consent

Exclusion Criteria

- Child contact of a drug-resistant TB patient

Designed to align with South African National Guidelines for TPT eligibility

Statistical Considerations

- **Sample Size Calculation and Assumptions**
  - 18 clinics: > 80% power to detect 100% increase (double) the number of HHC < 15y initiating TPT per TB patient

- **Statistical Considerations for Primary & Secondary Outcomes:**
  - Primary & Key Secondary:
    - Cluster-level differences using an unpaired t-test
  - Secondary:
    - Summary statistics of TPT completion and discontinuation by study arm

Sample Size Assumptions

- 1.8 children < 15y per household (prior contact tracing studies)
- Proportion of children 5-14 years initiating TPT would be the same as those < 5 years
- Anticipated 20% TB patients would **refuse** home visit
- Harmonic mean of 40 patients per clinic per year
- Conservative coefficient of variation (k) = 0.35
- Power 0.8; Type 1 error 0.05
- **Assumed SA guidelines would change from TPT for children < 5 to < 15 years prior to study initiation**

Salazar-Austin, et al. CID 2020

Study Population

Facilities assessed for eligibility
26 facilities

Excluded clusters (n=8)
- 2020 TB notifications <38 per annum

Randomized (18 facilities)

Allocated to Home-based Screening (9 facilities)	Allocated to Facility-based Screening (9 facilities)
Recruited TB Patients and Child Contacts (9 facilities) Recruited TB patients: n=171 Excluded TB patients: n=73 Reasons for exclusion: - Not wanting to be part of research project (n=30) - Unwilling to have home visit (n= 15) - No PTB (n= 9) - Not living in catchment area (n= 9) - DR-TB (n= 1) - Other (n= 9) Excluded Child Contacts: n= 8	**Recruited TB Patients and Child Contacts (9 facilities)** Recruited TB patients: n=156 Excluded TB patients: n=47 Reasons for exclusion: - Not wanting to be part of research project (n= 6) - Unwilling to have home visit (n= 9) - No PTB (n=23) - Under 18y (n= 1) - Other (n= 8) Excluded Child Contacts: n= 2
Lost to follow up (0 facilities) 1 child contact withdrew consent	**Lost to follow up (0 facilities)** No TB patients or child contacts withdrew
Analyzed (9 facilities) TB patients in primary analysis – 98 Child Contacts in primary analysis – 58	**Analyzed (9 facilities)** TB patients in primary analysis – 109 Child Contacts in primary analysis – 24

1 cluster removed and replaced after randomization

IMPAACT4TB
PREVENTING TB TO END TB

Baseline Characteristics of Enrolled Participants

Baseline Characteristics of Enrolled TB Patients		Home-based N= 98	Facility-based N= 109	Total N= 207
Number of index/households reporting child contacts < 5 years (%)		44 (45)	39 (36)	83 (40)
Mean Age (years)		42	42	42
Male (%)		60 (61)	70 (64)	130 (63)
Bacteriologically confirmed PTB (%)		85 (88)	95 (87)	180 (87)
HIV Positive (%)		44 (45)	45 (41)	89 (43)
Baseline Characteristics of Enrolled Child Contacts		**Home-based N=58**	**Facility-based N=24**	**Total N=82**
Age	< 2 years	26 (45%)	9 (38%)	35 (43%)
	2 to < 5 years	31 (53%)	14 (58%)	45 (55%)
	Missing age	1 (2%)	1 (4%)	2 (2%)
Sex	Male (%)	26 (45)	11 (46%)	37 (45%)
Relationship to TB patient	Son/daughter	18 (31%)	14 (58%)	32 (39%)
	Grandchild	16 (28%)	3 (13%)	19 (23%)
	Niece/nephew	17 (29%)	6 (25%)	23 (28%)
	Sibling	3 (5%)	0	3 (4%)
	Other	2 (3.5%)	0	2 (2.4%)
	Not Reported	1 (1.7%)	0	1 (1.2%)
HIV Status	HIV Exposed	10 (17%)	4 (17%)	14 (17%)

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Primary Outcome: Ratio of Child Contacts Initiating TPT per Index Participant

Home-Based		Facility-Based	
Index Enrolled	Children < 5 years Initiated	Index Enrolled	Children < 5 years Initiated
98	54	109	20

	Home-based (95% CI)	Facility-based (95% CI)	Risk Ratio (95% CI)	P-value
Mean Number of Child Contacts < 5 years old INITIATED on TPT per index patient	0.52 (0.26, 0.78)	0.25 (-0.11, 0.62)	1.30 (0.86, 1.97)	0.19

30% more children were initiated on TPT per TB patient in home-based versus facility-based contact management, though this difference was not statistically significant

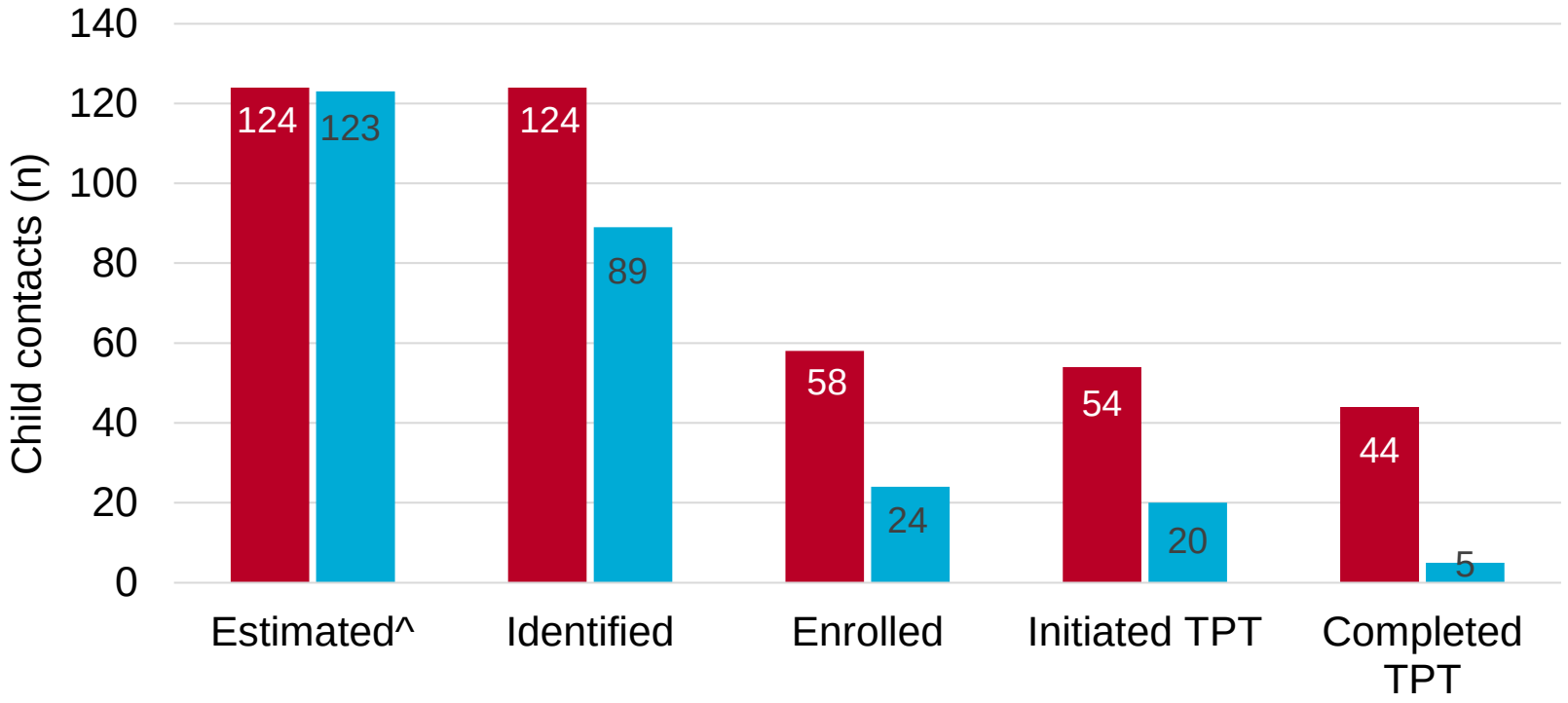
Secondary Outcome: Ratio of Child Contacts Identified per Index Participant

Home-Based		Facility-Based	
Index Enrolled	Children < 5 years Identified	Index Enrolled	Children < 5 years Identified
98	124	109	89

	Home-based (95% CI)	Facility-based (95% CI)	Risk Ratio (95% CI)	P-value
Mean Number of Child contacts < 5 years old IDENTIFIED per index patient	1.13 (0.61, 1.65)	0.94 (0.33, 1.56)	1.21 (0.58, 2.54)	0.59

21% more children were identified with home-based versus facility-based contact management, though this difference was not statistically significant

TB Prevention Continuum of Care



^ estimated number of children calculated based on average no of children < 5 per index household in home-based arm

More child contacts in the home-based than the facility-based arm were enrolled and completed TPT

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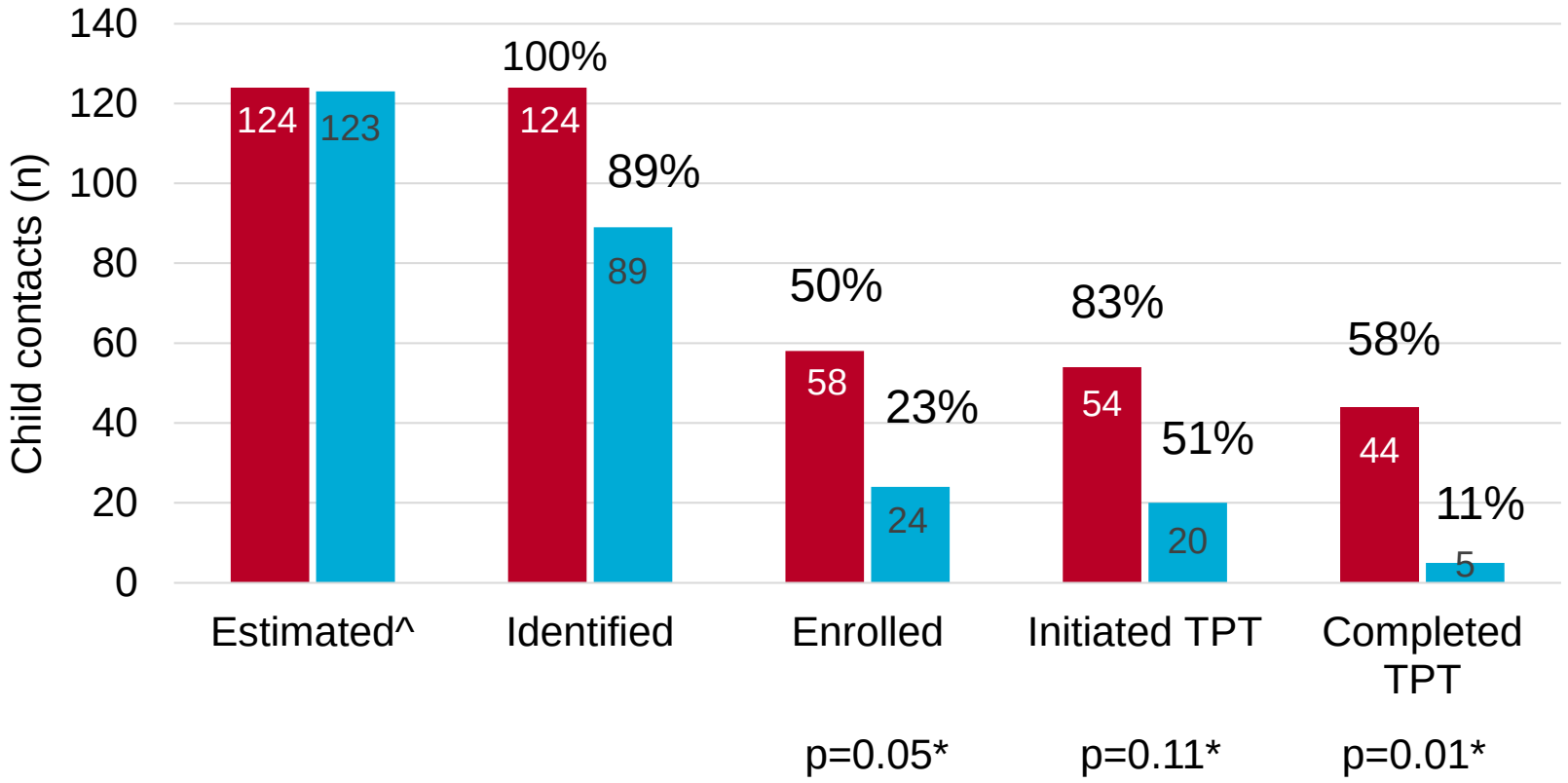

^ estimated number of children calculated based on average no of children < 5 per index household in home-based arm

*all proportions are cluster adjusted

More child contacts in the home-based than the facility-based arm were enrolled and completed TPT

TPT Outcomes

TPT Outcome	Home-based N= 54	Facility-based N=20	Total N=74
Treatment Completed	44	5	49
3RH	32	1	33
6H	2	4	6
3RH/6H	10	0	10
Treatment Discontinued or Changed	8 (15%)	0 (0%)	8 (11%)
Due to toxicity	1*	0	1
Due to patient/family preference	6	0	6
Other not specified	1	0	1
Lost to follow up	2 (4%)	15 (75%)	17 (23%)

*emesis with first three doses, likely reflects poor tolerability and not hepatotoxicity

Acceptability and Feasibility of Home-Based Intervention

Acceptability

54 out of 171 (32%) index patients that were assessed did not take part in the study

- 15 (9%) did not want a home visit
- 9 (5%) did not live in the catchment area of the clinic
- 30 (18%) did not want to be involved in research

Feasibility

- 96% of households were reached on the first visit
- ~75% of households were reached on the first follow-up visit

Conclusions

- This intervention was acceptable to some but not all people undergoing treatment for TB
- There was an indication of an increase in the number of children identified (21%) and initiated on TPT (30%) in the home-based care arm compared to the standard of care
- The proportion of children completing TPT was higher in the home-based care arm
- Additional interventions will be needed to reach households of index participants not living within the catchment area of their clinic for both facility-based and home-based TB prevention services
- Home-based interventions to find contacts and provide TPT within households should be further investigated

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