



Stellenbosch

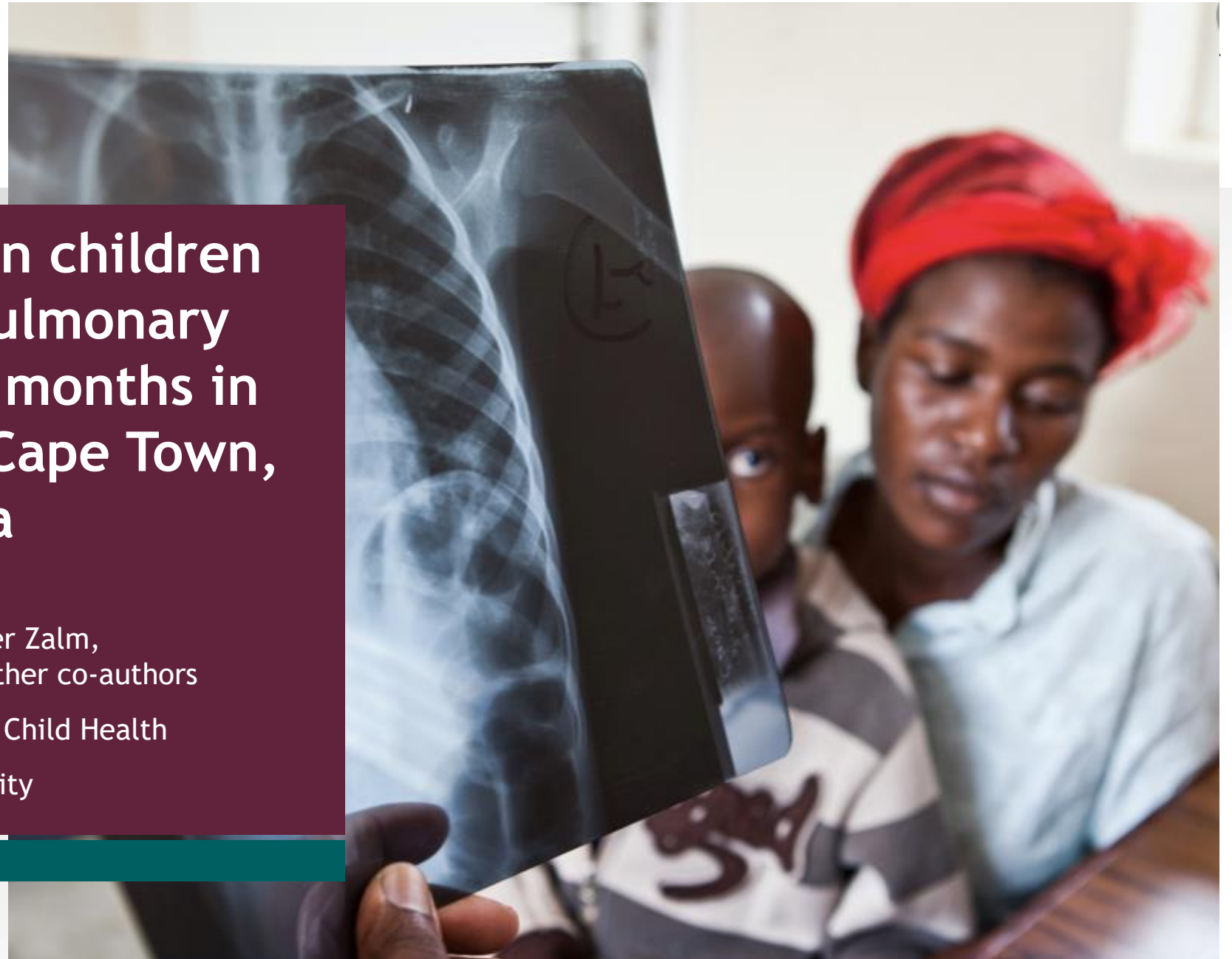
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Treatment response in children with presumptive pulmonary tuberculosis over six months in the UMOYA cohort in Cape Town, South Africa

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INTRODUCTION

- In 2022, an estimated 1.3 million children below 15 years developed tuberculosis (TB) worldwide
- NIH case definition to classify pediatric TB may include response to treatment, but the dynamics of TB-related symptoms in children remain understudied
- *Are symptom resolution and recurrence useful to inform TB diagnosis in children?*

RESEARCH QUESTIONS

- ❖ How many children resolve TB-related symptoms, and when?
- ❖ How many children have recurrence of TB-related symptoms after symptom resolution, and when?
- ❖ What are factors associated with symptom resolution and symptom recurrence?

UMOYA COHORT STUDY

- Prospective observational cohort study
- Children aged 0-13 years with presumptive pulmonary TB
 - Confirmed TB case
 - Unconfirmed TB case
 - Symptomatic control (unlikely TB, did not receive TB treatment)
 - Healthy control
- Follow-up at week 0, 2, 8, 16, 24 (52, 108, etc)
- Sociodemographic questionnaire + medical history + chest X ray at enrolment
- Clinical assessment at enrolment and follow-up



METHODS (1)

- **Inclusion criteria:**

TB case/symptomatic control AND having a baseline visit* AND ≥ 1 follow-up visit

- **Definition of weeks**

- Baseline: enrolment visit (symptomatic controls) or visit within 7 days of start of TB treatment (TB cases)
- Week 2: 1-4 wks after baseline
- Week 8: 4-11 wks after baseline
- Week 16: 12-17 wks after baseline
- Week 24: 18-37 wks after baseline

METHODS (2)

TB-related symptoms: cough, wheeze, fever, low weight without improvement*, lack of appetite, reduced activity level, lymphadenopathy, tachycardia, tachypnoea, haemoptysis

- **Any symptom:** having ≥ 1 of the symptoms above
- **Symptom resolution:** having symptom X \rightarrow not having symptom X
- **Symptom (re-)occurrence:** not having symptom X \rightarrow having symptom X

*Acute weight loss, or weight-for-age Z, weight-for-height Z, or weight-for BMI Z score below -2 without evidence of weight improvement (i.e., Z score increase of ≥ 0.1 per two weeks since the last recorded Z score)

METHODS (3)

- Descriptives:
 - n(%) symptom resolution per symptom per timepoint
 - n(%) symptom (re-)occurrence per symptom per timepoint
- Statistical analysis
 - Factors associated with switching from symptomatic to asymptomatic state (and *vice versa*) using Markov switch modelling

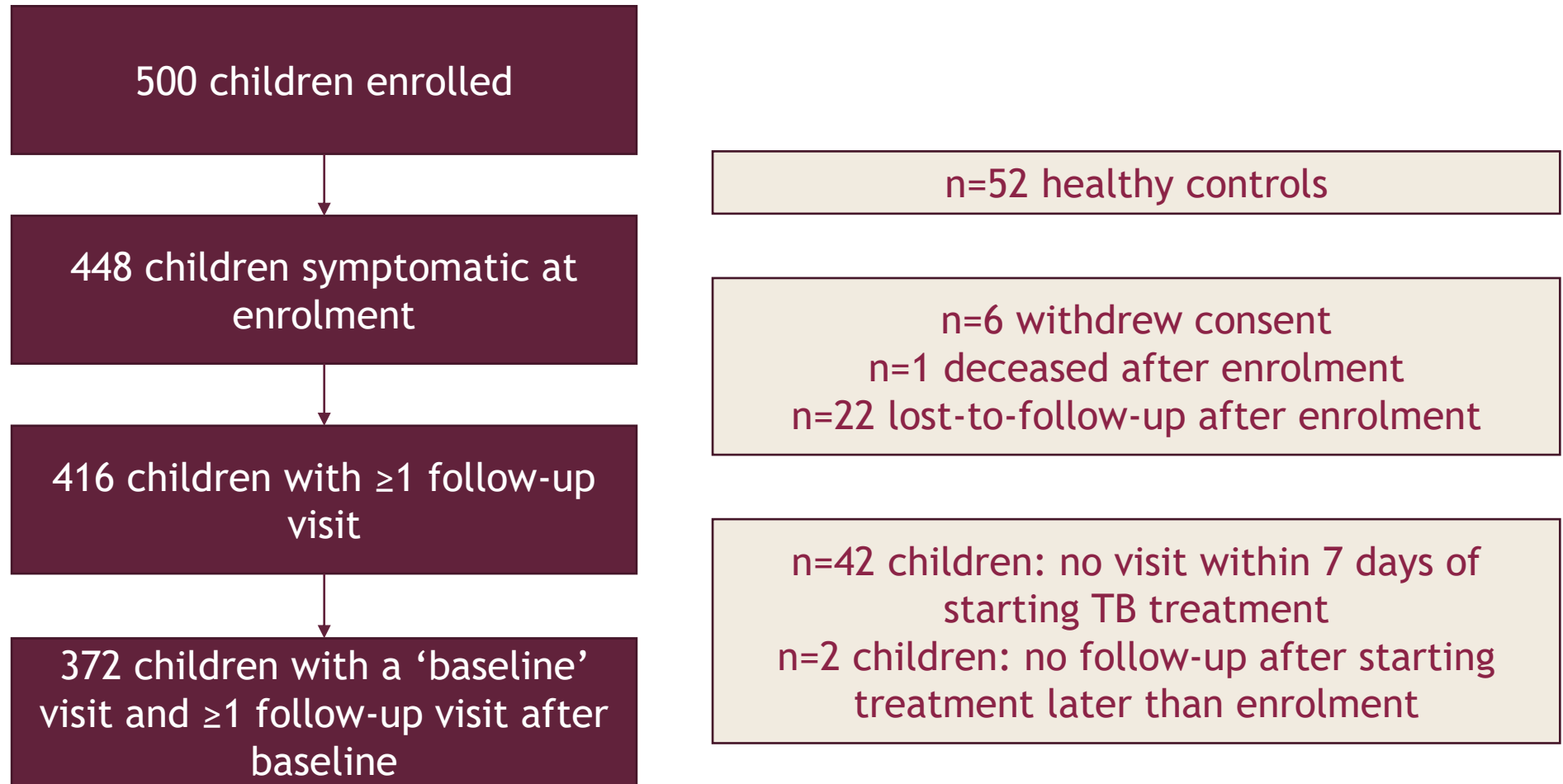
Any symptom



No symptoms

- Candidate determinants: TB diagnostic group, CXR, HIV status, age, symptom severity at baseline, smoking exposure, family history of allergy, informal housing, household size, family employment

RESULTS - PARTICIPANT INCLUSION



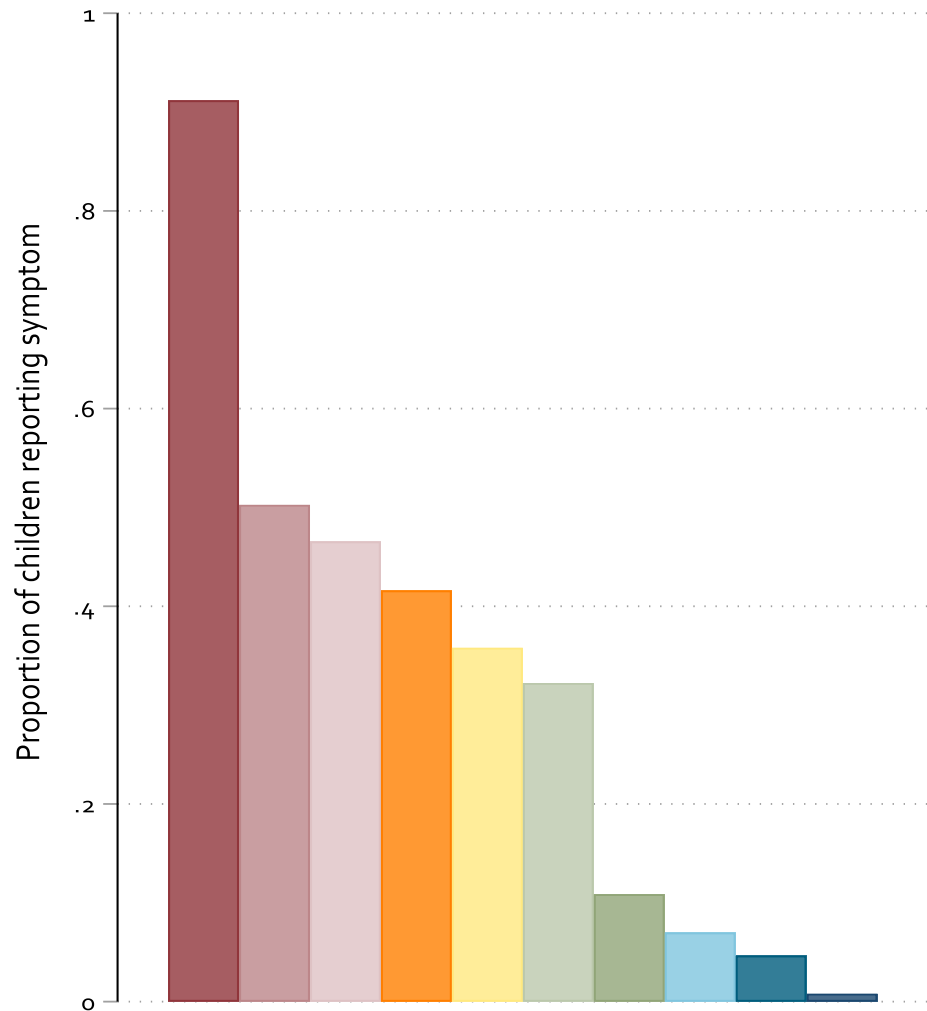
RESULTS - PARTICIPANT CHARACTERISTICS (n=372)

	Total N=372	Confirmed TB N=54	Unconfirmed TB N=99	Symptomatic control N=219	p-value
Age (months)	23 (11-47)	28 (13-47)	17 (9-35)	26 (11-55)	0.020
Male gender	186 (50.0%)	26 (48.1%)	43 (43.4%)	117 (53.4%)	0.25
HIV positive	32 (8.6%)	4 (7.4%)	12 (12.2%)	16 (7.3%)	0.34
Informal housing	124 (33.3%)	20 (37.0%)	35 (35.4%)	69 (31.5%)	0.66
Nobody in family employed	112 (30.1%)	15 (27.8%)	29 (29.3%)	68 (31.1%)	0.88
Abnormal chest X-ray	184 (50.8%)	45 (83.3%)	55 (57.9%)	84 (39.4%)	<0.001
Household smoking exposure	233 (62.6%)	35 (64.8%)	60 (60.6%)	138 (63.0%)	0.86
Child history of asthma	22 (6.2%)	2 (4.0%)	5 (5.3%)	15 (7.2%)	0.64
Family history of allergies	175 (47.9%)	18 (34.0%)	46 (46.9%)	111 (51.9%)	0.064

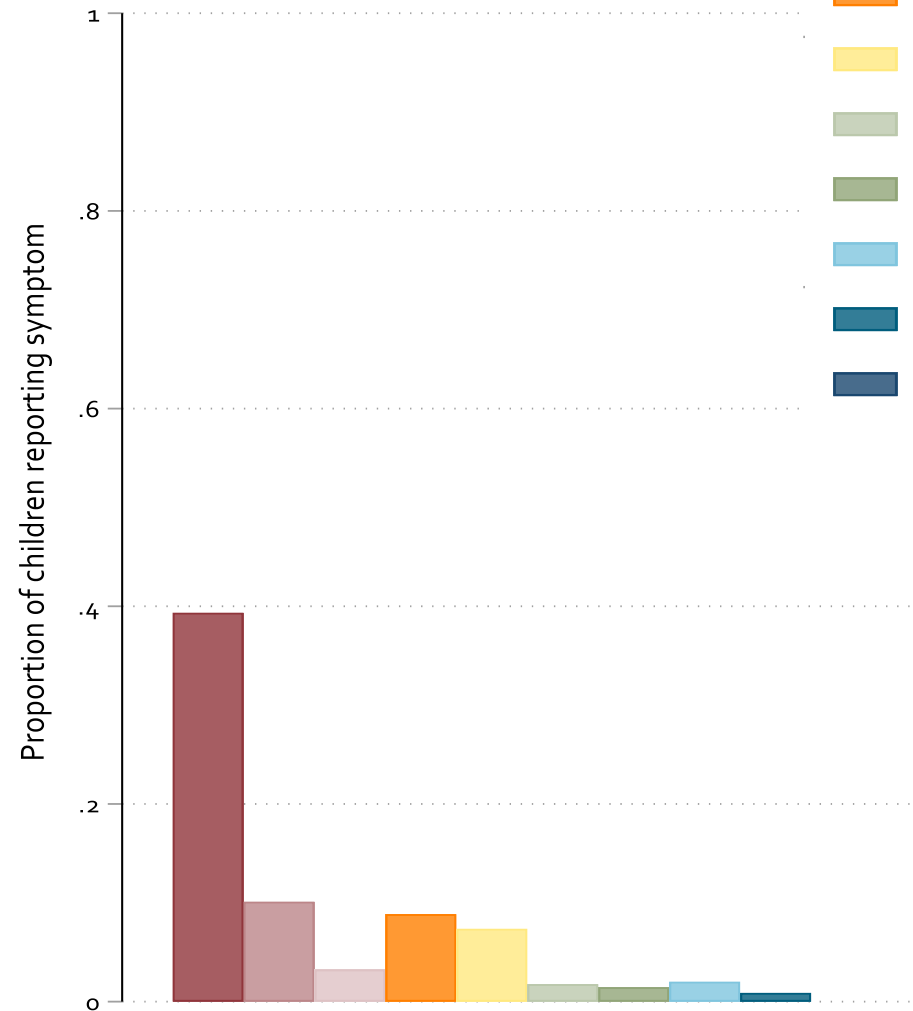
RESULTS - SYMPTOM PREVALENCE

- Cough
- Weightloss/underweight
- Fever
- Lack of appetite
- Wheeze
- Reduced activity
- Tachypnoe
- Lymphadenopathy
- Tachycardia
- Haemoptysis

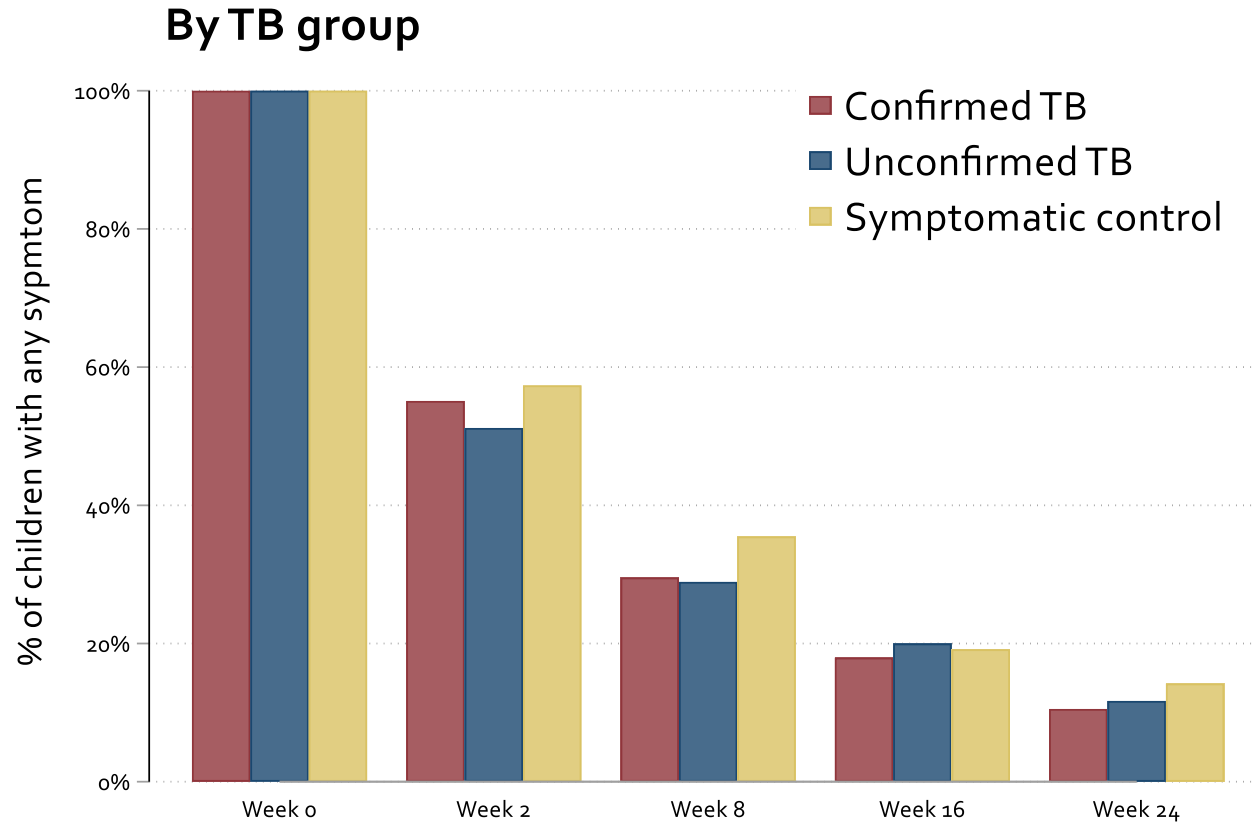
Week 0



Week 2



RESULTS - SYMPTOM PREVALENCE, across diagnostic groups



- ‘Any symptom’ prevalence similar between TB groups at each timepoint
- Number of symptoms also similar between TB groups at each timepoint

RESULTS - SYMPTOM RESOLUTION AND REOCCURRENCE

N=433 times



Having any symptom

N=356
times



N=157
times

Having no symptoms



N=321 times

- TB diagnostic group, chest X ray (ab)normality, age category, and HIV status were not associated with symptom resolution or symptom recurrence
- Household smoking exposure was associated with a 2.4x higher rate of becoming symptomatic (95% CI: 1.1-5.3)

RESULTS - SYMPTOM PERSISTENCE

- Among 242 children who attended all five follow-up visits...
 - n=43 had any TB-related symptom at each of those visits
 - n=18 had a cough and n=3 a wheeze at each of those visits
 - n=6 was underweight without weight improvement at each of those visits
 - n=1 had lymphadenopathy at each of those visits
- Persistence until week 24 did not differ between TB groups

DISCUSSION - SUMMARY OF RESULTS

- The majority of TB-related symptoms resolve within two weeks. 17% of children had at least one TB-related symptom at each follow-up visit until 6 months
- The rate of symptom resolution did not differ by TB diagnostic group, chest X ray results, HIV status, or age.
- The rate of symptom recurrence was higher for children exposed to smoking

LIMITATIONS

- Nuance of symptom presentation not fully accounted for
- Limited number of children with HIV (n=34)
- Possible need for a larger sample size to identify determinants of symptom resolution

CONCLUSION

- Generally, treatment response occurs early
- More research is needed on the usefulness of symptom resolution as a diagnostic marker for paediatric pulmonary TB

ACKNOWLEDGEMENTS

- **Children and their families who participate in UMOYA!**
- All doctors, nurses, counsellors and drivers contributing to UMOYA at the Desmond Tutu TB Center
- Co-authors on this study (Eline Wijstma, Vita Jongen, Carla McKenzie, Isabelle Dewandel, Rory Dunbar, Anders Boyd, Margaret van Niekerk, Marieke van der Zalm)



QUESTIONS?

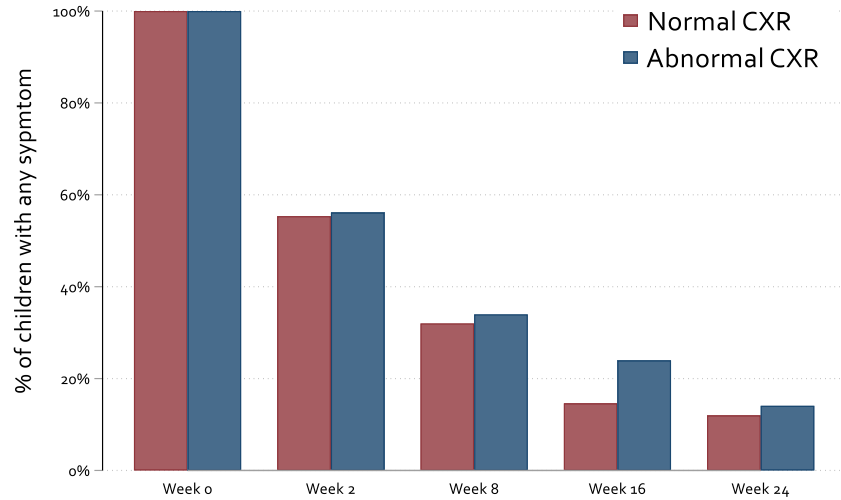
THANK YOU

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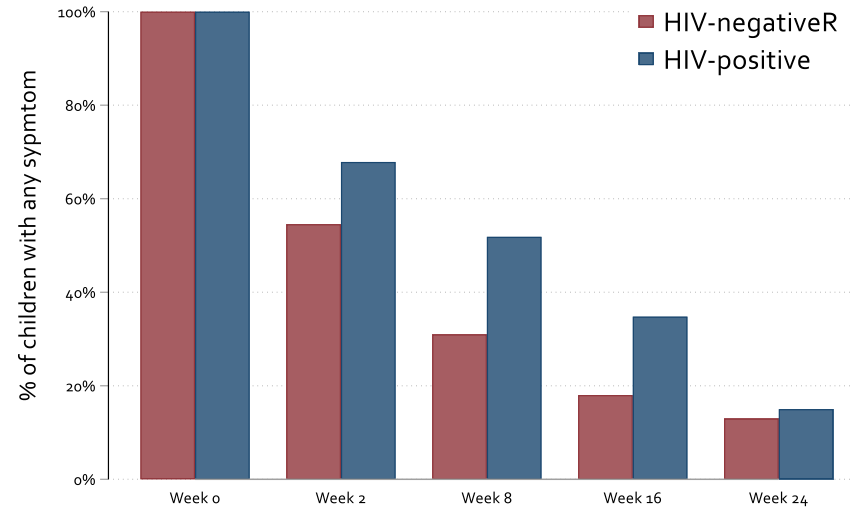
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EXTRA SLIDES - Symptom prevalence over time

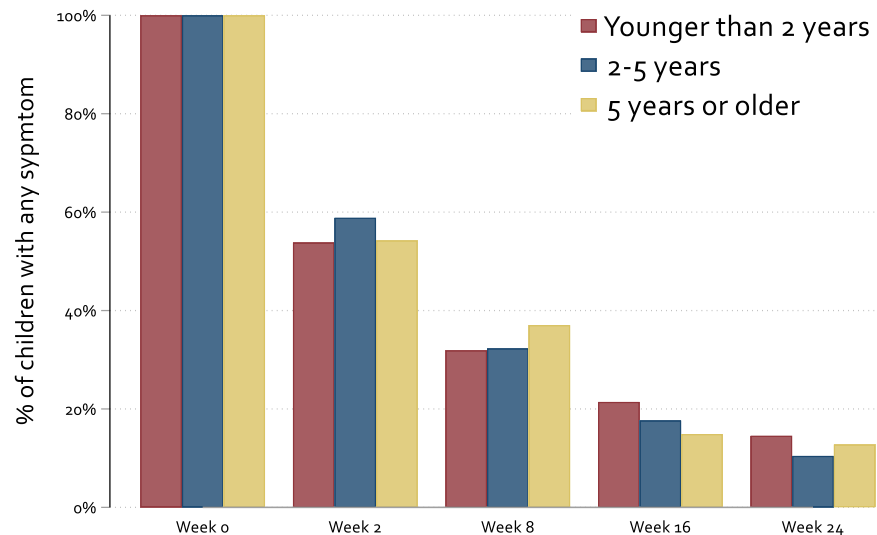
By chest X-ray result



By child's HIV status



By age category



By TB group

