Conclusion

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A Deeper Dive into TB Nurse Case Management

October 25th-27th, 2022

San Antonio, TX

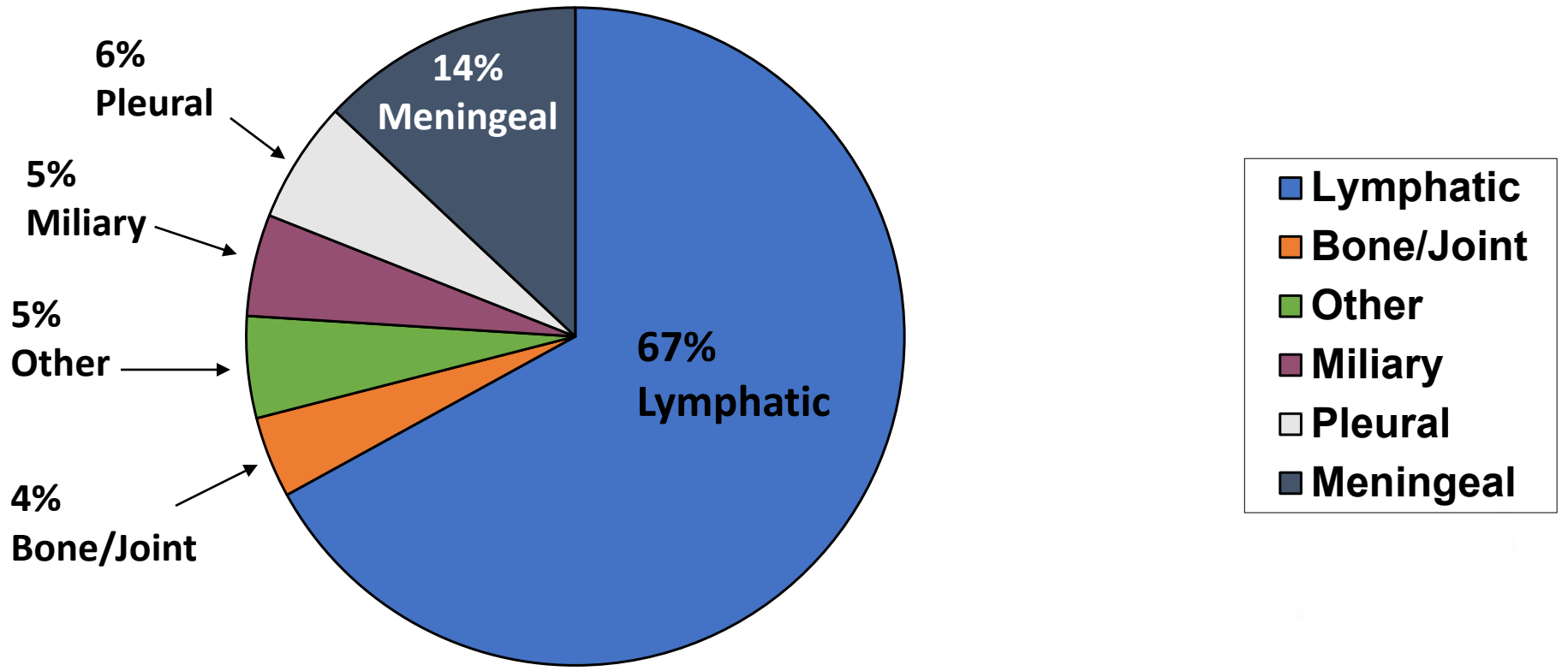
Percent Risk of Disease by Age

Age at Infection	Risk of Active TB
Birth – 1 year*	43%
1 – 5 years*	24%
6 – 10 years*	2%
11 – 15 years*	16%
Healthy Adults	5-10% lifetime risk
HIV Infected Adults+	30-50% lifetime

*Miller, Tuberculosis in Children Little Brown, Boston, 1963

+WHO, 2004

Extrapulmonary TB Disease in Children (25%)



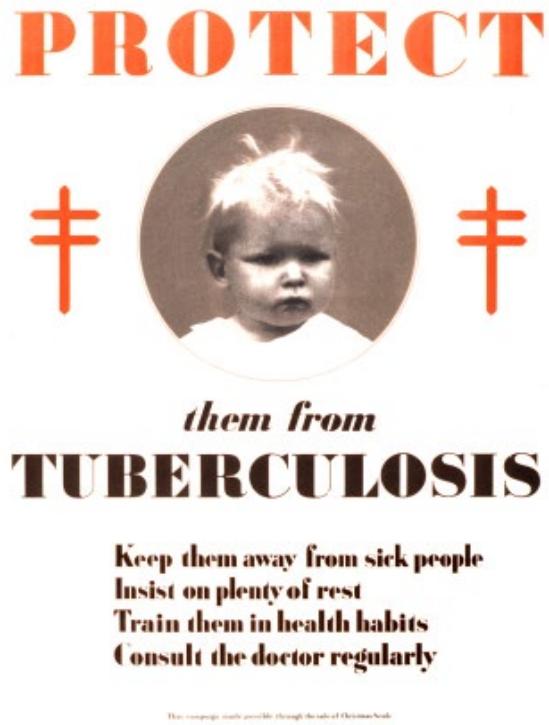
CDC

IGRAs and the 2021 AAP "RED BOOK"

- Can use IGRAs in immunocompetent children 2 y/o and older in all situations when a TST would be used
- Preferred test for children 2 years and older who have received a BCG vaccination
- Data shows IGRAs perform consistent well in children 2 years and older, some experts use down to 1 y/o
- Neither IGRAs nor the TST are perfect; always need clinical judgment!

TB Prevention After Exposure

- Household contact with contagious person
  - Teen or adult with pulmonary TB disease
  - Usually ≥ 4 hours of contact
- Initial TST negative
  - Window period for TST conversion
  - (8-10 weeks)
- CXR and physical exam normal
- **Window prophylaxis recommended:**
  - For children < 5 yrs of age
  - Immunosuppressed patients
  - Patients on tumor necrosis factor-alpha blockers or other biologic
  - May prevent progression to disease during window period
- Repeat TST 8-10 wks after exposure
- May stop medication if 2nd TST negative < 5mm in immunocompetent patients



Treating TB infection

- 3HP (approved for children ≥ 2 years old:

  INH:

  15 mg/kg rounded up to the nearest 50 or 100 mg
  20-30 mg/kg rounded up **ages 2-11 y/o** maximum 900 mg

  RPT:

  10.0–14.0 kg 300 mg
  14.1–25.0 kg 450 mg
  25.1–32.0 kg 600 mg
  32.1–49.9 kg 750 mg
  ≥ 50.0 kg 900 mg maximum

- Rifampin x 4 months [4R]
  - 10-20 mg/kg daily dose ages 2 years and older (max 600 mg)
  - 20-30 mg/kg daily
    - Infants and toddlers
    - Immunosuppressed
    - Disseminated disease, ESPECIALLY meningitis

- Isoniazid (INH) x 6-9 months [6H/9H]
  - 10-15 mg/kg single daily dose
  - 20-30 mg/kg twice weekly given by DOT
  - Duration: 9 months

- INH + rifampin [3HR] x 3 months

Therapy for TB Disease

- Start 4-drug therapy (a change from 2006 Red Book)
  - INH, rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB); INH/RIF are the backbone of therapy
- Use PZA only during 1st 2 months for susceptible TB
  - This is your 'shortening agent': consolidate from 9 to 6 months of therapy
- Stop EMB once culture results known, if have pan-susceptible TB
  - This is your insurance in case you have drug-resistant TB
- Anticipate minimum 6-month therapy, may need to extend it to longer periods, especially for extensive, CNS or bone disease
- Can dose BIW or TIW after first 2 weeks of daily dosing
- ***Always*** administered by directly observed therapy (DOT)

2018 Red Book

SHINE Trial

Shorter Treatment for Minimal Tuberculosis (TB) in Children

The NEW ENGLAND JOURNAL of MEDICINE

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Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children

A. Turkova, G.H. Wills, E. Wobudeya, C. Chabala, M. Palmer, A. Kinikar, S. Hissar, L. Choo, P. Musoke, V. Mulenga, V. Mave, B. Joseph, K. LeBeau, M.J. Thomason, R.B. Mboizi, M. Kapasa, M.M. van der Zalm, P. Raichur, P.K. Bhavani, H. McIlleron, A.-M. Demers, R. Aarnoutse, J. Love-Koh, J.A. Seddon, S.B. Welch, S.M. Graham, A.C. Hesseling, D.M. Gibb, and A.M. Crook, for the SHINE Trial Team*

Inclusion Criterion

- Age 0-16 years
- Weight ≥ 3kg.
- Clinician has decided to treat with standard first-line regimen
- Symptomatic but non-severe TB including:
  - extrathoracic lymph node TB; intra-thoracic uncomplicated (hilar) lymph node TB
  - minimal or no parenchymal abnormality on CXR
  - smear negative on gastric aspirate/other respiratory sample

Note: GeneXpert may be positive or negative and a negative GeneXpert can be used as a substitute for a negative smear;

culture of respiratory sample may be positive or negative;

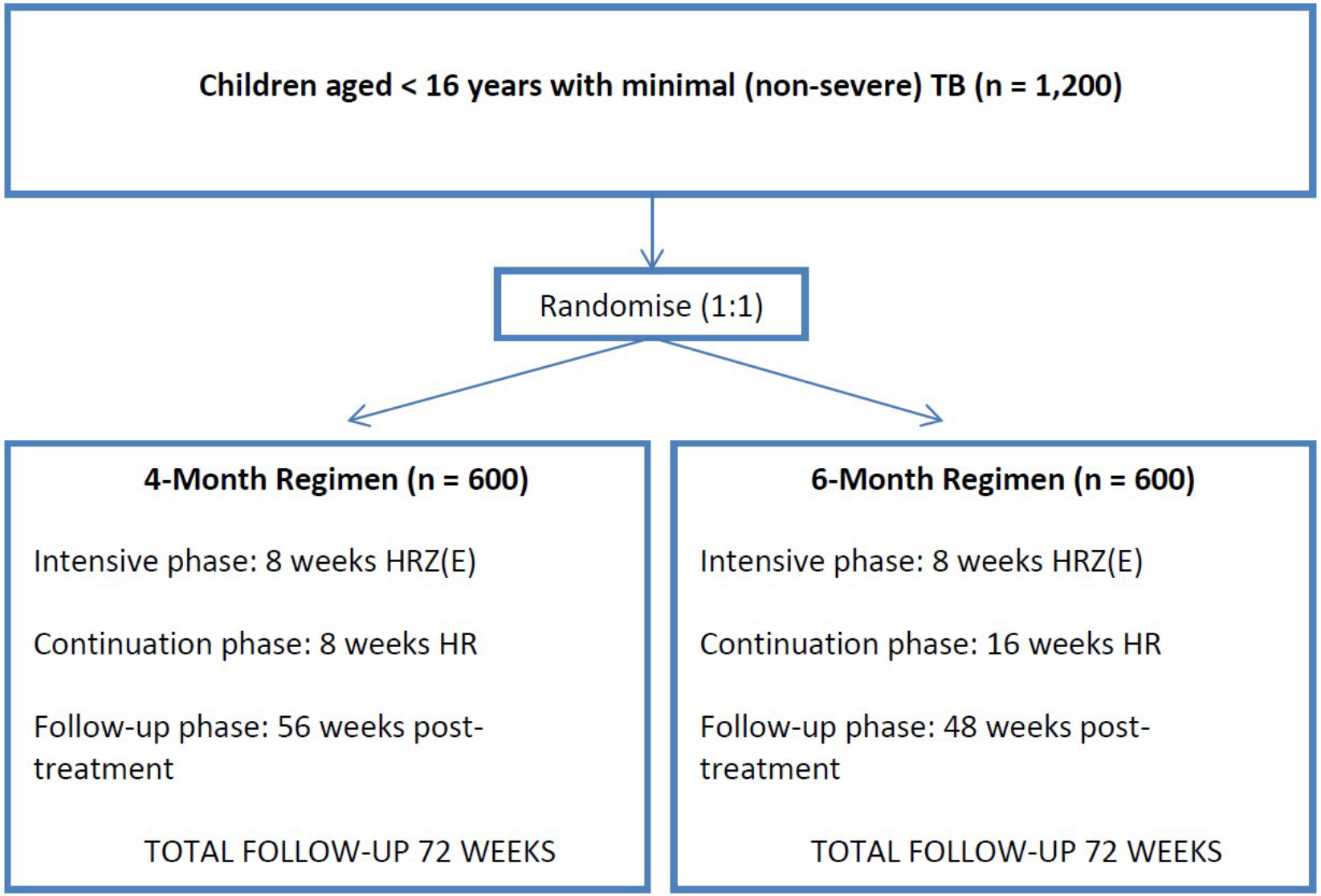
lymph node aspirate may be smear/culture/GeneXpert positive or negative)

- Not treated for previous TB unless successfully treated > 2 years since last completed treatment
- Known (or pending confirmation of) HIV status; HIV-infected or HIV-uninfected
- Willing and likely to adhere to 72 weeks follow up
- Informed written consent from the parent/legal caregiver(s) and assent in children
- Home address accessible for visiting and intending to remain within the recruitment area

Exclusion Criterion

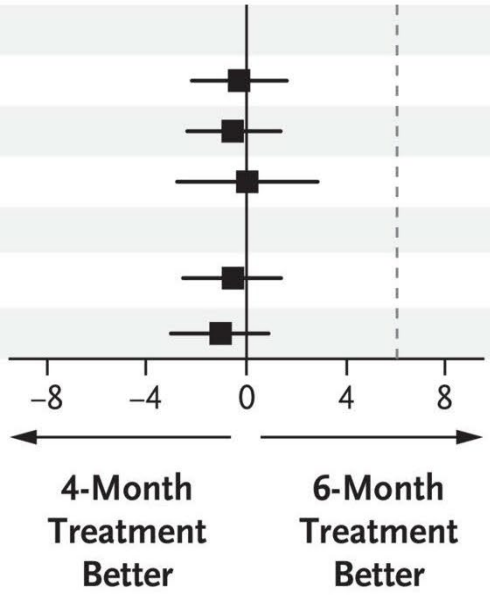
1. Smear-positive respiratory sample TB
   (note: smear-positive peripheral lymph node sample is allowed)
2. Premature (<37 weeks) **and** aged under 3 months
3. Miliary TB, spinal TB, TB meningitis, osteoarticular TB, abdominal TB, congenital TB
4. Pre-existing non-tuberculous disease likely to prejudice the response to, or assessment of, treatment e.g. liver or kidney disease, peripheral neuropathy, cavitation
5. Any known contraindication to taking anti-TB drugs
6. Known contact with drug resistant adult source case (including mono- resistant TB)
7. Known drug resistance in the child
8. Severely sick
9. Pregnancy

Methods


Children aged < 16 years with minimal (non-severe) TB (n = 1,200)
Randomise (1:1)
4-Month Regimen (n = 600)
Intensive phase: 8 weeks HRZ(E)
Continuation phase: 8 weeks HR
Follow-up phase: 56 weeks post-treatment
TOTAL FOLLOW-UP 72 WEEKS
6-Month Regimen (n = 600)
Intensive phase: 8 weeks HRZ(E)
Continuation phase: 16 weeks HR
Follow-up phase: 48 weeks post-treatment
TOTAL FOLLOW-UP 72 WEEKS

Unadjusted Analysis of the Primary Efficacy and Key Secondary Outcomes in the Trial Populations

	No. of Patients	4-Month Treatment	6-Month Treatment	Risk Difference (95% CI)
		no. of participants with event/total no. (%)		*percentage points*
Primary outcome				
Modified intention-to-treat population	1145	16/572 (3)	18/573 (3)	−0.3 (−2.3 to 1.6)
Per-protocol population	1121	14/563 (2)	17/558 (3)	−0.6 (−2.5 to 1.4)
Intention-to-treat population	1204	44/602 (7)	44/602 (7)	0 (−2.9 to 2.9)
Key secondary outcome				
Modified intention-to-treat population	910	10/450 (2)	13/460 (3)	−0.6 (−2.6 to 1.4)
Per-protocol population	895	8/445 (2)	13/450 (3)	−1.1 (−3.1 to 0.9)



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Primary Efficacy Analysis (Modified Intention-to-Treat Population)

Table 2. Primary Efficacy Analysis (Modified Intention-to-Treat Population).*

Outcome	4-Month Treatment (N=572)	6-Month Treatment (N=573)	Difference (95% CI)	
			Adjusted Analysis†	Unadjusted Analysis
			percentage points	
Unfavorable status — no. (%)	16 (3)	18 (3)	−0.4 (−2.2 to 1.5)	−0.3 (−2.3 to 1.6)
Death from any cause after 4 mo	7 (1)	12 (2)		
Loss to follow-up after 4 mo but during treatment period	0‡	1 (<1)		
Treatment failure				
Tuberculosis recurrence	6 (1)	4 (1)		
Extension of treatment	2 (<1)	0		
Restart of treatment§	1 (<1)	1 (<1)		
Favorable status — no. (%)	556 (97)	555 (97)		

Treatment Pearls

- Risk of drug toxicity very low
- Monitor weight (kids grow!)
- Routine blood work not necessary unless……
- Routine vitamin B_6 not necessary except breast-feeding, pregnant adolescents, poor diet
  - Vitamin B_6 doses 1-2 mg/kg
- Completion of therapy certificate!

Questions?

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Or

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