



Pediatric MDR-TB

BENEFIT-KIDS – Better Evidence and Formulations for Improved MDR-TB Treatment for Children

Children with MDR-TB are a neglected population

Each year, ~30,000 children contract MDR-TB

Treatment for MDR-TB is longer, more complicated, and less effective than for DS-TB — especially for children

Fewer than 15% of children with MDR-TB are diagnosed and start treatment every year

If they start treatment, nearly 80% are successfully cured

Children need access to MDR-TB treatment that is effective, safe, well tolerated, and palatable

Evidence gaps about how to optimally dose existing medicines

- Puts children increased risk of SE if dose too high or increased risk of poor treatment response if dose too low

Despite access to child-friendly formulations, adult medicines need to be cut, broken, crushed, and mixed

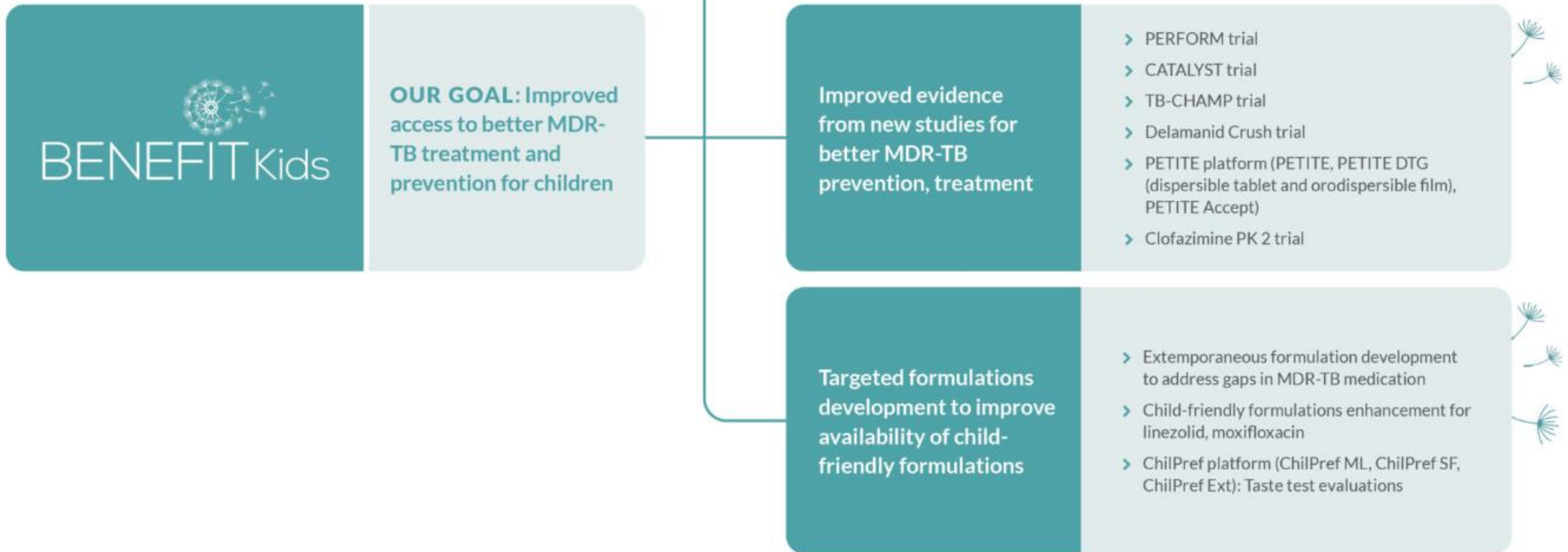
Breaking or crushing adult medicines can lead to dosing errors or make the medicines taste bitter

Even some newly available child-friendly formulations still have a bad taste

Pediatric MDR-TB treatment

Although adults are benefitting from treatment advances, children are not

Key evidence and product gaps — as well as lack of economic incentive for pharmaceutical companies — jeopardizes the potential of new innovations to truly transform pediatric MDR-TB treatments



Children's preferences between six novel moxifloxacin and linezolid formulations (the ChilPreF ML study): a 'swish-and-spit' taste panel evaluation in children in South Africa

- **Overall aim:** To inform pragmatic recommendations about which formulation(s) of moxifloxacin and linezolid to recommend for commercial manufacturing based on palatability profile:
- **Primary Objective:** To characterize the relative (ranked) taste preferences between formulation blends each of moxifloxacin and linezolid amongst children and disaggregated by manufacturer

Study Design

- Cross-sectional 'swish-and-spit' taste panel evaluation .
- At two sites in South Africa.
- Eligible healthy child volunteers between ages 5 and 17 years.
- Six different versions each of moxifloxacin and linezolid (i.e., 3 from each of the 2 manufacturers).
- Evaluation of moxifloxacin and linezolid will take place on separate days.

Sample and sampling

Table 1. Target stratification of enrollment by ethnicity, location, and age: Western Cape and KwaZulu Natal

	5-8-years		9-12-years		13-17-years		Total
	Female	Male	Female	Male	Female	Male	
Black urban	4	4	4	4	4	4	24
Black rural	4	4	4	4	4	4	24
Mixed	4	4	4	4	4	4	24
Indian	4	4	4	4	4	4	24
Total	16	16	16	16	16	16	96

Exclusion criteria

- Current TB disease (suspected or confirmed)
- Current contact with an infectious TB patient
- Undergoing dental care or treatment in the past 14 days
- The use of mouthwash within 24 hours of the study visit
- Smoking in the preceding 48 hours
- Known drug allergies or history of hypersensitivity to antibiotics , or intolerance to saltine crackers
- Children with any current condition that influences taste or smell sensation
- Inability to perform ranking activity

Relative (ranking) preferences

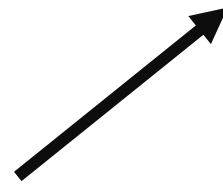
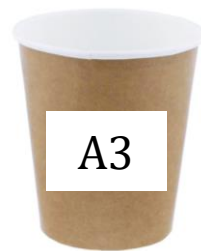
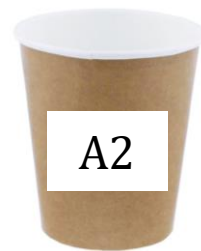
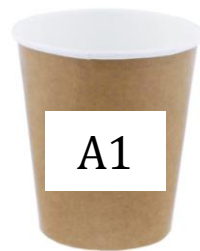
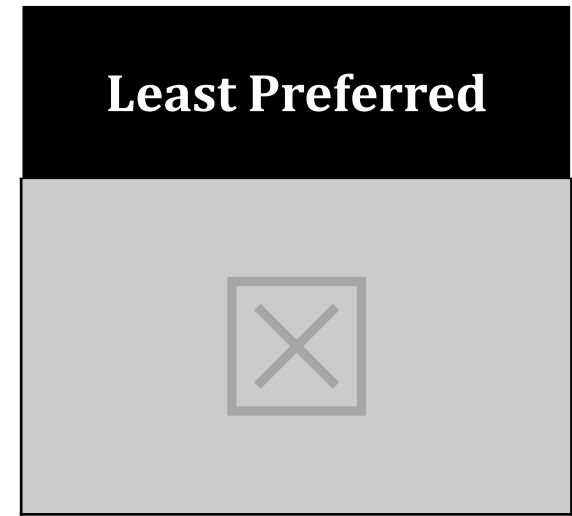
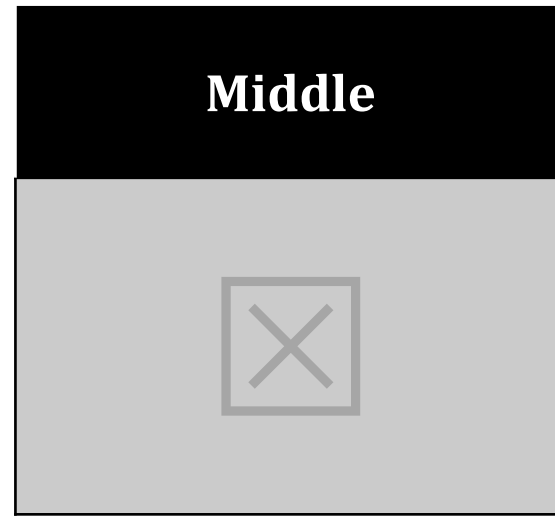
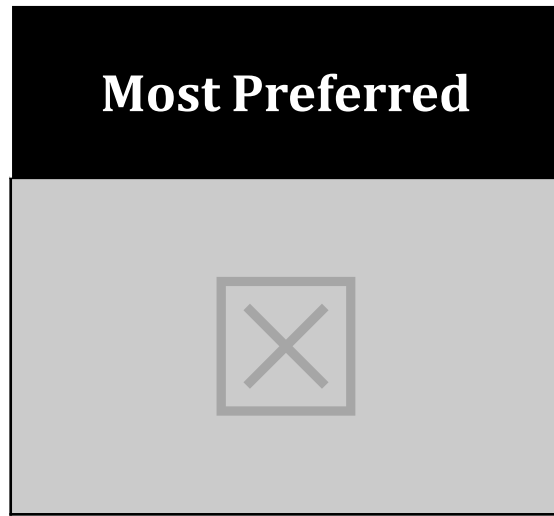


Relative (ranking) preferences

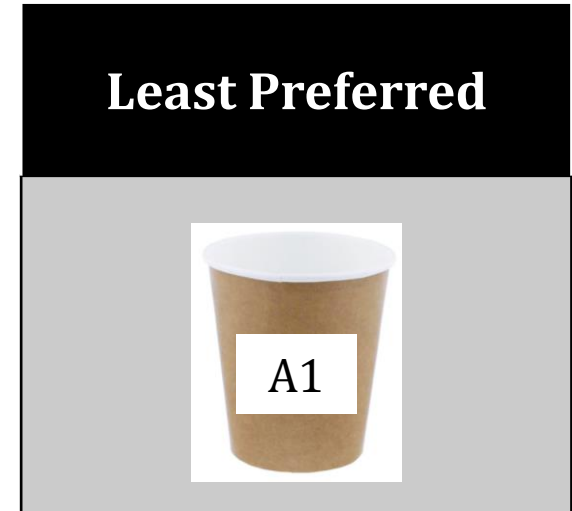
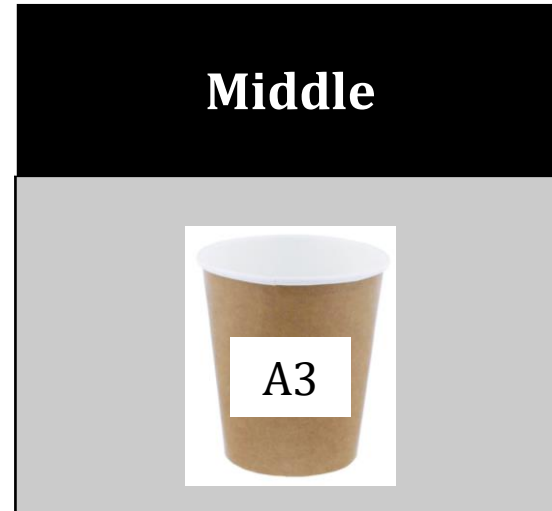
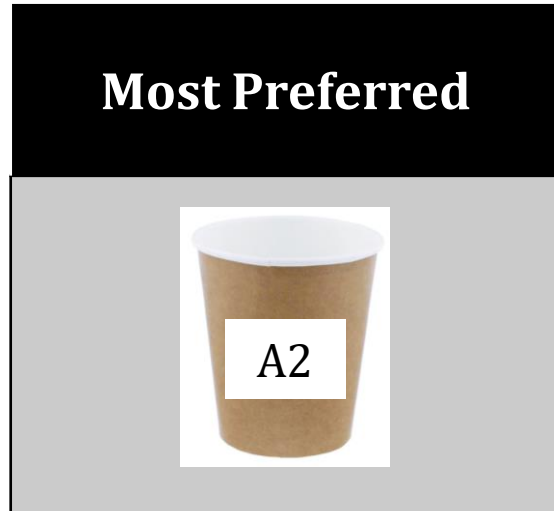


<https://blogs.sun.ac.za/dttc/benefit-kids-formulation-development/>

Relative (ranking) preferences








Relative (ranking) preferences



Relative (ranking) preferences

1. "I liked the way that tasted!"
2. "That smelled good!"
3. "The after-taste was really nice!"
4. "That taste made me feel good!"
5. "Overall, that tasted great!"

				
Strongly agree	Agree	Neutral	Disagree	Strongly disagree

Findings – Macleods moxifloxacin

	Rank Sum	Mean Rank (SD)	Friedman's F (p-value)
Overall, which Macleods moxifloxacin formulation did the child prefer to take? (N=96)			
A1 (Novel blend 1)	180	1.88 (0.81)	
A2 (Existing blend)	231	2.41 (0.69)	
A3 (Novel blend 2)	165	1.72 (0.79)	24.937 (<0.001)*

Findings – Macleods moxifloxacin

	A1 (Novel blend 1) (n=97)	A2 (Existing blend) (n=97)	A3 (Novel blend 2) (n=97)
I like the way that tasted!			
Strongly agree (%)	31 (32.0)	23 (23.7)	42 (43.3)
Agree (%)	23 (23.7)	16 (16.5)	15 (15.5)
Neutral (%)	14 (14.4)	12 (12.4)	11 (11.3)
Disagree (%)	10 (10.3)	22 (22.7)	16 (16.5)
Strongly disagree (%)	19 (19.6)	24 (24.7)	13 (13.4)

Findings – Microlabs moxifloxacin

	Rank Sum	Mean Rank (SD)	Friedman's F (p-value)
Overall, which Microlabs moxifloxacin formulation did the child prefer to take? (N=94)			
B1 (Existing blend)	224	2.38 (0.79)	
B2 (Novel blend 2)	165	1.76 (0.79)	
B3 (Novel blend 1)	175	1.86 (0.74)	21.213 (<0.001)±

Findings – Microlabs moxifloxacin

	B1 (Existing blend) (n=97)	B2 (Novel blend 2) (n=97)	B3 (Novel blend 1) (n=97)
I like the way that tasted!			
Strongly agree (%)	11 (11.3)	19 (19.6)	20 (20.6)
Agree (%)	9 (9.3)	16 (16.5)	11 (11.3)
Neutral (%)	7 (7.2)	23 (23.7)	17 (17.5)
Disagree (%)	26 (26.8)	14 (14.4)	19 (19.6)
Strongly disagree (%)	44 (45.4)	25 (25.8)	30 (30.9)

Findings – Macleods linezolid

	Rank Sum*	Mean Rank** (SD)	Friedman's F (p-value)
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Overall, which Macleods linezolid formulation did the child prefer to take? (N=95)

C1 (Novel blend 2)	190	2.00 (0.86)	
C2 (Novel blend 1)	186	1.96 (0.81)	
C3 (Existing blend)	194	2.04 (0.78)	0.337 (0.884)

Findings – Microlabs linezolid

	Rank Sum*	Mean Rank** (SD)	Friedman's F (p-value)
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Overall, which Microlabs linezolid formulation did the child prefer to take? (N=95)

D1 (Novel blend 1)	195	2.05 (0.78)	
D2 (Novel blend 2)	187	1.97 (0.86)	
D3 (Existing blend)	188	1.98 (0.82)	0.400 (0.819)

Lessons

- Very rapid data collection and analysis timelines possible (~8 weeks of field work!).
- REC oversight – not a trial; socio-behavioural science and observational.
- We recommended that the manufacturers change the formulation blend that they would have taken forward for market.
- Even data from the youngest children (5-6-year-olds) was coherent, believable, and different to that of older children.
- Children and their caregivers were broadly enthusiastic about participation.