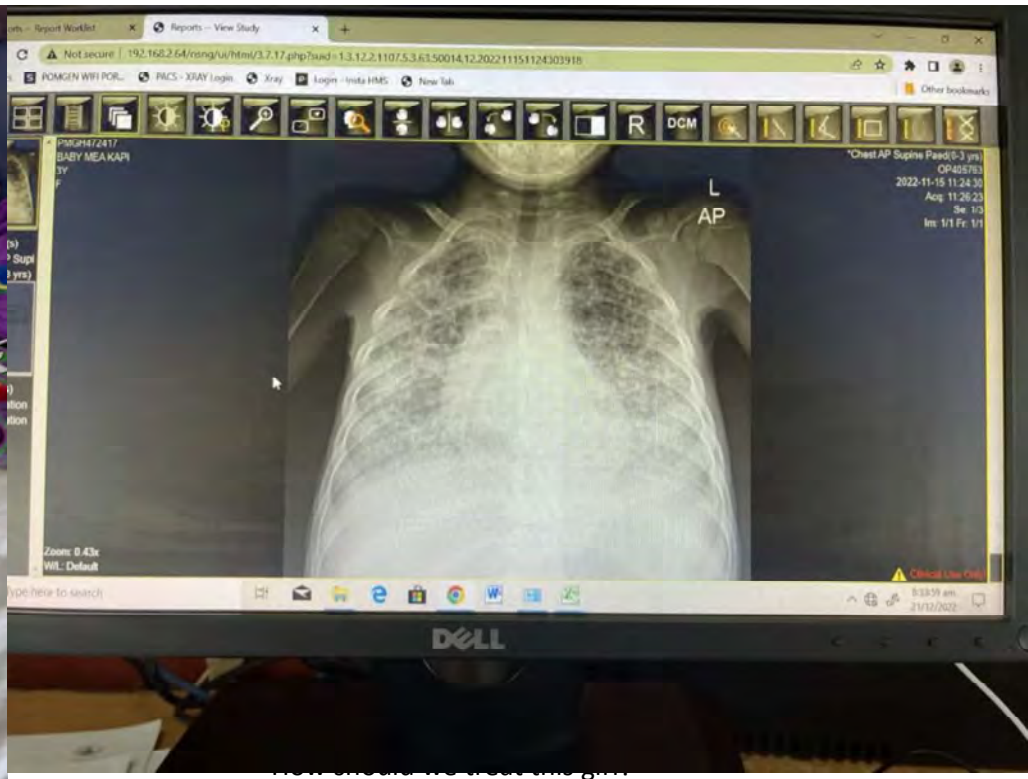
Current treatment regimens for DR-TB in children and review of recommendations for PNG

Dr Gordon Pukai SMO-
Child TB/ HIV



- Start MDR treatment immediately

Lessons learned

- Challenge when Xpert is negative and/or your ability to work up differential diagnosis is limited
  - Leads to overdiagnosis and treatment of TB when it is not TB
  - clinical and contact history critical

- These children may have “severe disease” and not be eligible for shorter regimens

SOME DATA FROM PMGH

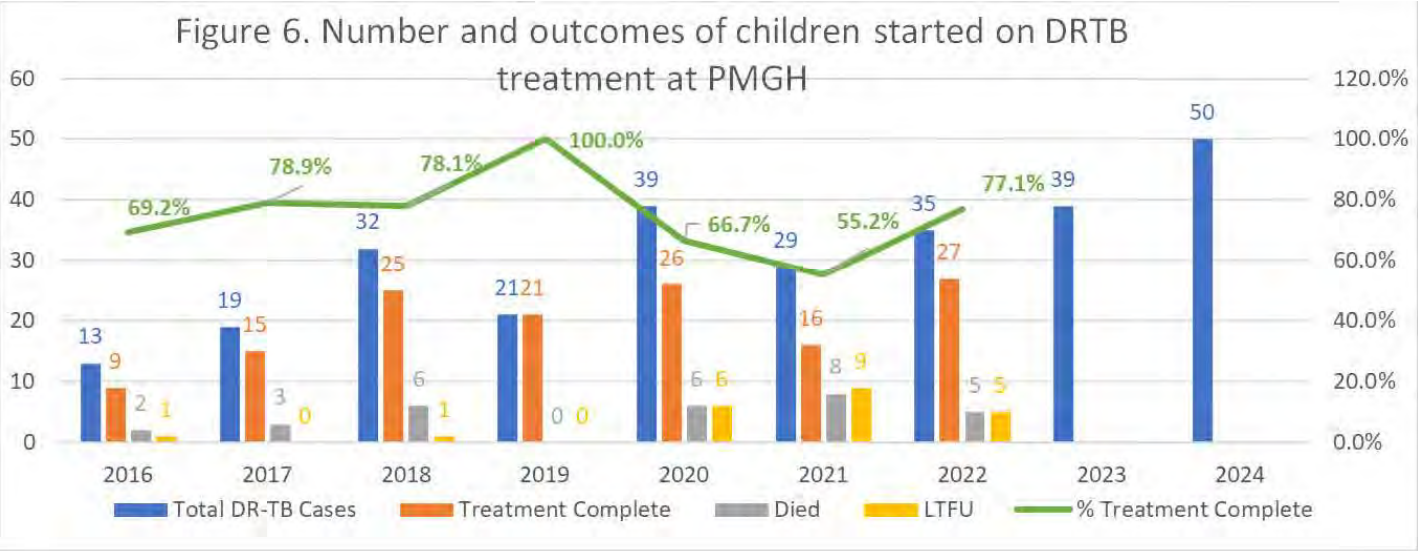


Figure 6. Number and outcomes of children started on DRTB treatment at PMGH
60
50
40
30
20
10
0
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
0.0%
69.2%
78.9%
78.1%
100.0%
66.7%
55.2%
77.1%
13
9
2
1
19
15
3
0
32
25
6
1
21
21
0
0
39
26
6
6
29
16
8
9
35
27
5
5
39
50
2016
2017
2018
2019
2020
2021
2022
2023
2024
Total DR-TB Cases
Treatment Complete
Died
LTFU
% Treatment Complete

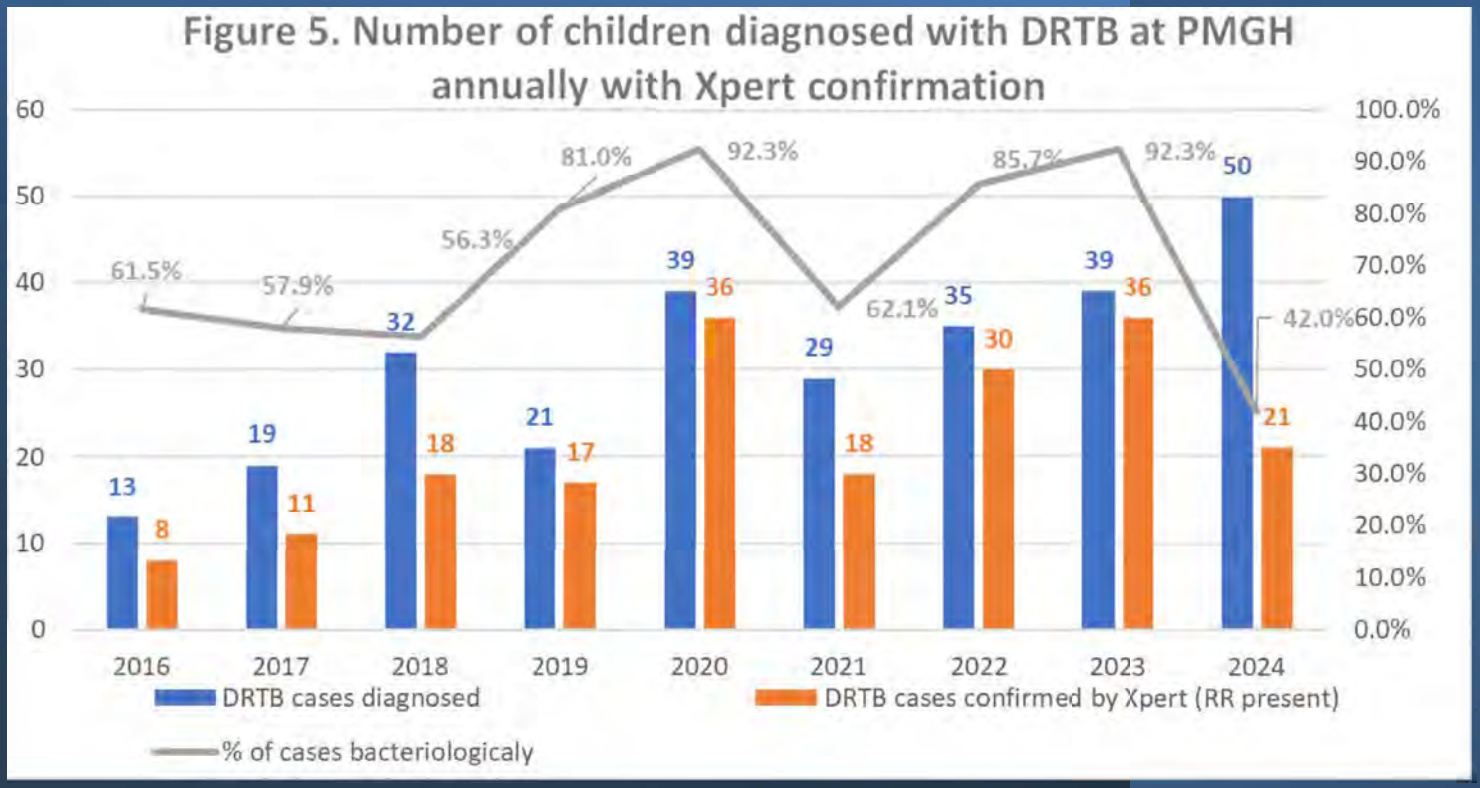


Figure 5. Number of children diagnosed with DRTB at PMGH annually with Xpert confirmation
60
50
40
30
20
10
0
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
61.5%
57.9%
56.3%
81.0%
92.3%
62.1%
85.7%
92.3%
42.0%
13
8
19
11
32
18
21
17
39
36
29
18
35
30
39
36
50
21
2016
2017
2018
2019
2020
2021
2022
2023
2024
DRTB cases diagnosed
DRTB cases confirmed by Xpert (RR present)
% of cases bacteriologicaly

DISCUSSIONS ABOUT MDR TREATMENT IN CHILDREN IN PNG

PNG MDR treatment guideline overview

- 2014 – 2016: long regimens with injections 18-24 months
  - Km, Lzd, Lfx, Cfz, Cs, Eth, Pza
- 2017: short course an option for some, but still with injections
  - Km, Lfx, HD-INH, Cfz, Eth, PZA, Eto for 9 months
  - Otherwise, stick to longer 18-24 month regimens
- 2019: injection free longer regimen for 18 months
  - Sentinel 2019: Bdq/Dlm, Lzd, Lfx, CFZ
- 2024: shorter all-oral 9-12 month regimen
  - Sentinel 2022: Bdq, Lzd, Lfx, Cfz, Cs

How PNG updated Paediatric MDR guidelines

- Consultation with outside paediatric experts including WHO Geneva
- Meetings with paediatricians who work in remote part of PNG to understand their challenges
  - Particularly changing the regimens during treatment?
  - How to deal with severe and non-severe disease?
  - What if we don't have drugs?
  - Can we simplify regimens and not have multiple options?

I'll now go back to 2019 to show how we evolved

All oral MDR regiment for kids of all ages

- Bdq [6] – Lzd – Lfx – Cfz x 18/12 for all forms of TB

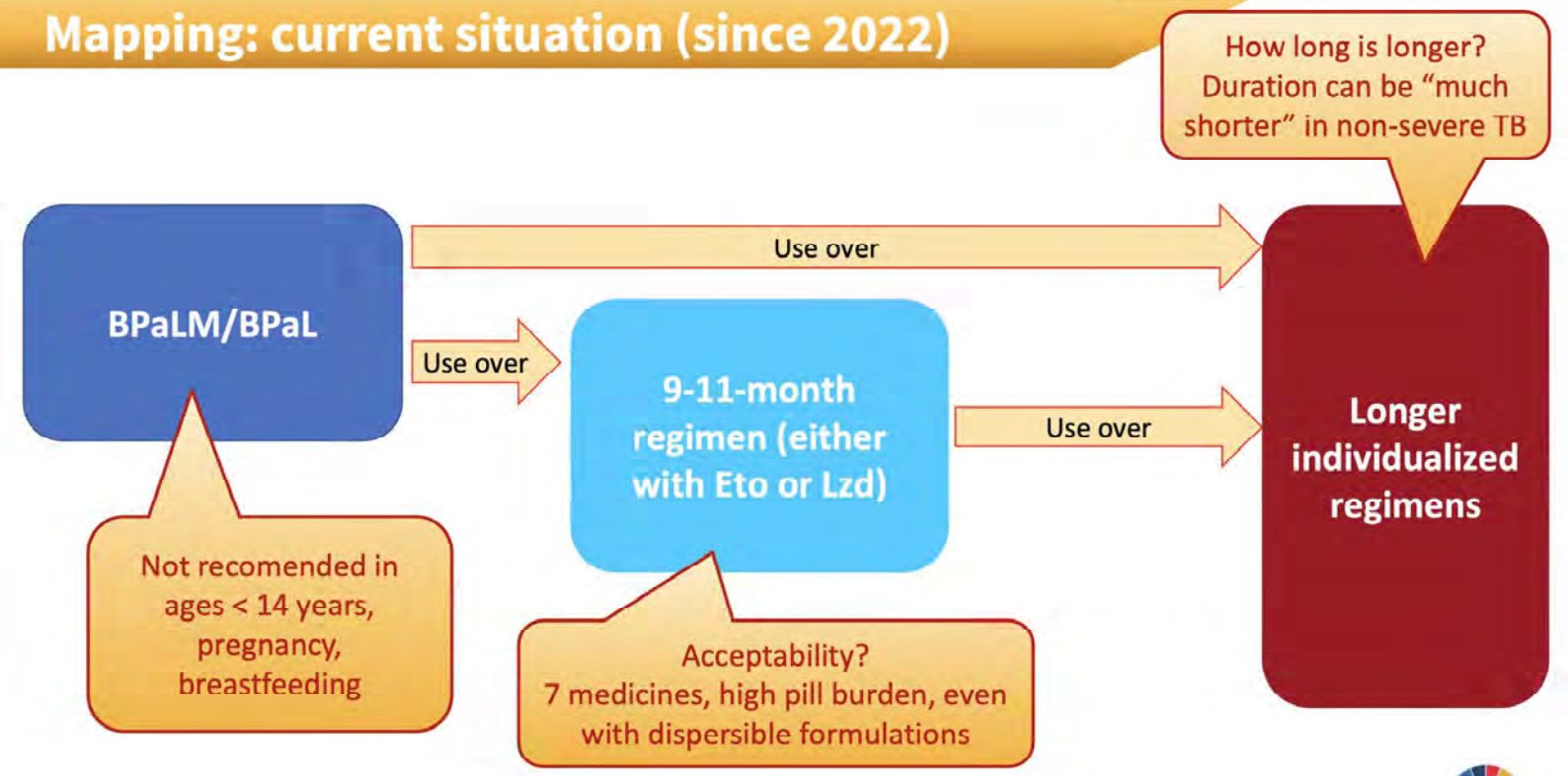
Intensive phase: BDQ-LZD-LFX-CFZ x 6/12

Remember BDQ has a 5-6 month half life

Continuation phase: LZD-LFX-CFZ x 12/12

Management of Multidrug-Resistant Tuberculosis in Children:
A FIELD GUIDE 2019

Mapping: current situation (since 2022)



World Health Organization

SLIDES CREDIT DR. SABINE VERKUIJL WHO

END TB

PNG MDR treatment guideline overview

- BPaL/M introduction is good but only for adults
- The WHO 9-month regimen was challenging for PNG
  - Due to resistance profile in PNG
  - High pill burden
  - May not be appropriate for severely malnourished children, meaning potentially 3 different regimens based on
    - Regimen for non-severe disease (ie 9 month WHO)
    - Regimen for severe disease
    - Regimen for CNS/Diss/Osteo

BMC Infectious Diseases

RESEARCH Open Access

Evolution and spread of a highly drug resistant strain of *Mycobacterium tuberculosis* in Papua New Guinea

Arnold Bairomugisa[1], Evelyn Lavu[2,3], Sushil Pandey[1], Suman Majumdar[4,5], Jennifer Banamu[6], Chris Coulter[1], Ben Marais[4], Lachlan Coin[1], Stephen M. Graham[4,5] and Philipp du Cros[4*]

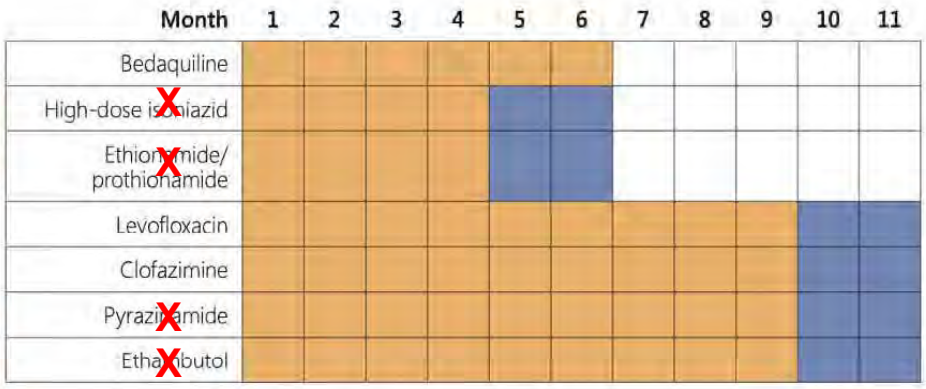
Resistance risk with INH and Eto

PZA resistance

Eth resistance

WHO 9-month all-oral regimen

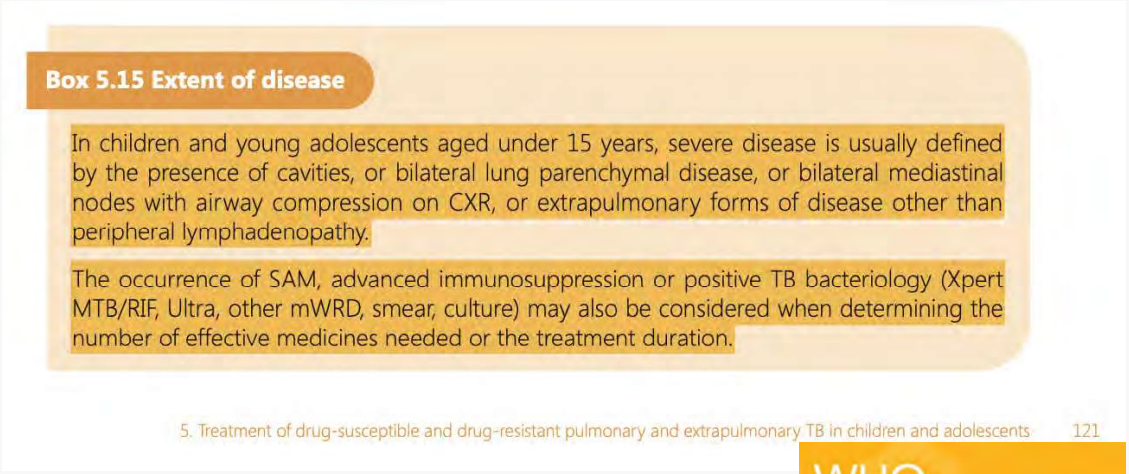
Figure 5.2. TB medicines and duration of treatment for the standardized all-oral bedaquiline-containing shorter regimen



Orange = standardized MDR/RR-TB treatment course.

Blue = added months if still smear-/culture-positive after 4 months of treatment.

Additional considerations

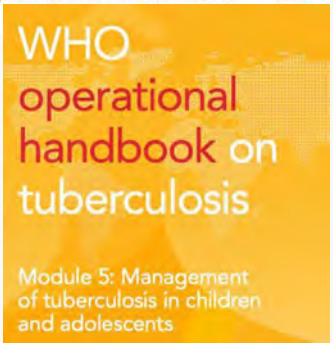


Box 5.15 Extent of disease

In children and young adolescents aged under 15 years, severe disease is usually defined by the presence of cavities, or bilateral lung parenchymal disease, or bilateral mediastinal nodes with airway compression on CXR, or extrapulmonary forms of disease other than peripheral lymphadenopathy.

The occurrence of SAM, advanced immunosuppression or positive TB bacteriology (Xpert MTB/RIF, Ultra, other mWRD, smear, culture) may also be considered when determining the number of effective medicines needed or the treatment duration.

5. Treatment of drug-susceptible and drug-resistant pulmonary and extrapulmonary TB in children and adolescents 121



- PNG TB-HIV co-infection rate is ~8% - shows that kids are sick
- Malnutrition rates based off Dr. Landi study ~45%
  - This means up to 50% of our kids cannot get on the WHO shorter regimen