

When treatment options narrow: management of bedaquiline-resistant tuberculosis in Uzbekistan

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With expanded treatment, bedaquiline resistance is rising

- In Mozambique, prevalence of bedaquiline resistance among MDR/RR-TB isolates increased from 3% in 2016 to 14% in 2021
- In South Africa, recent data shows emerging resistance is common among people with sustained culture positivity

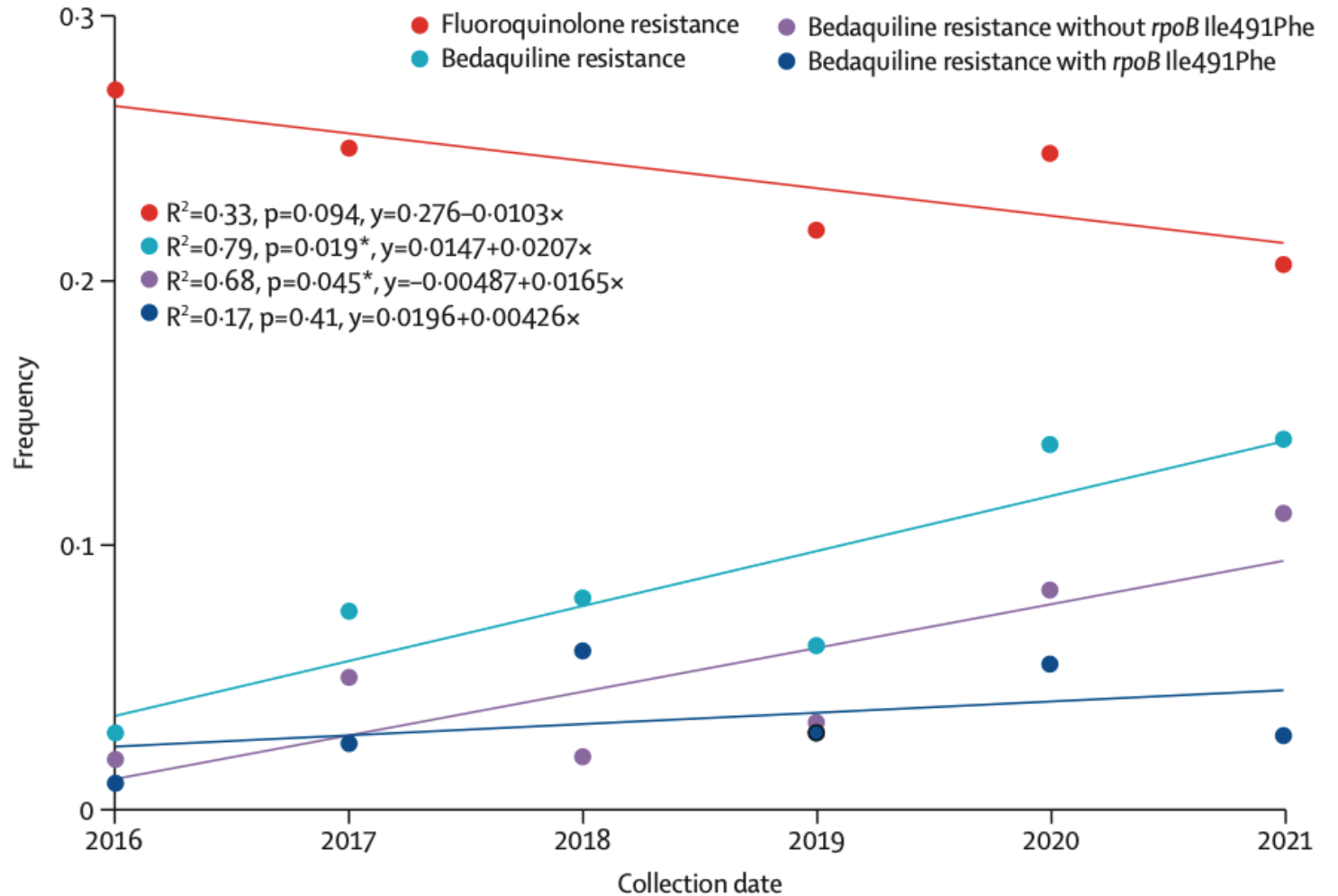


Figure: Rising prevalence of bedaquiline resistance in Mozambique



Increasing bedaquiline resistance threatens the effectiveness of short regimens for MDR/RR-TB and raises the possibility of a return to injectable-based regimens

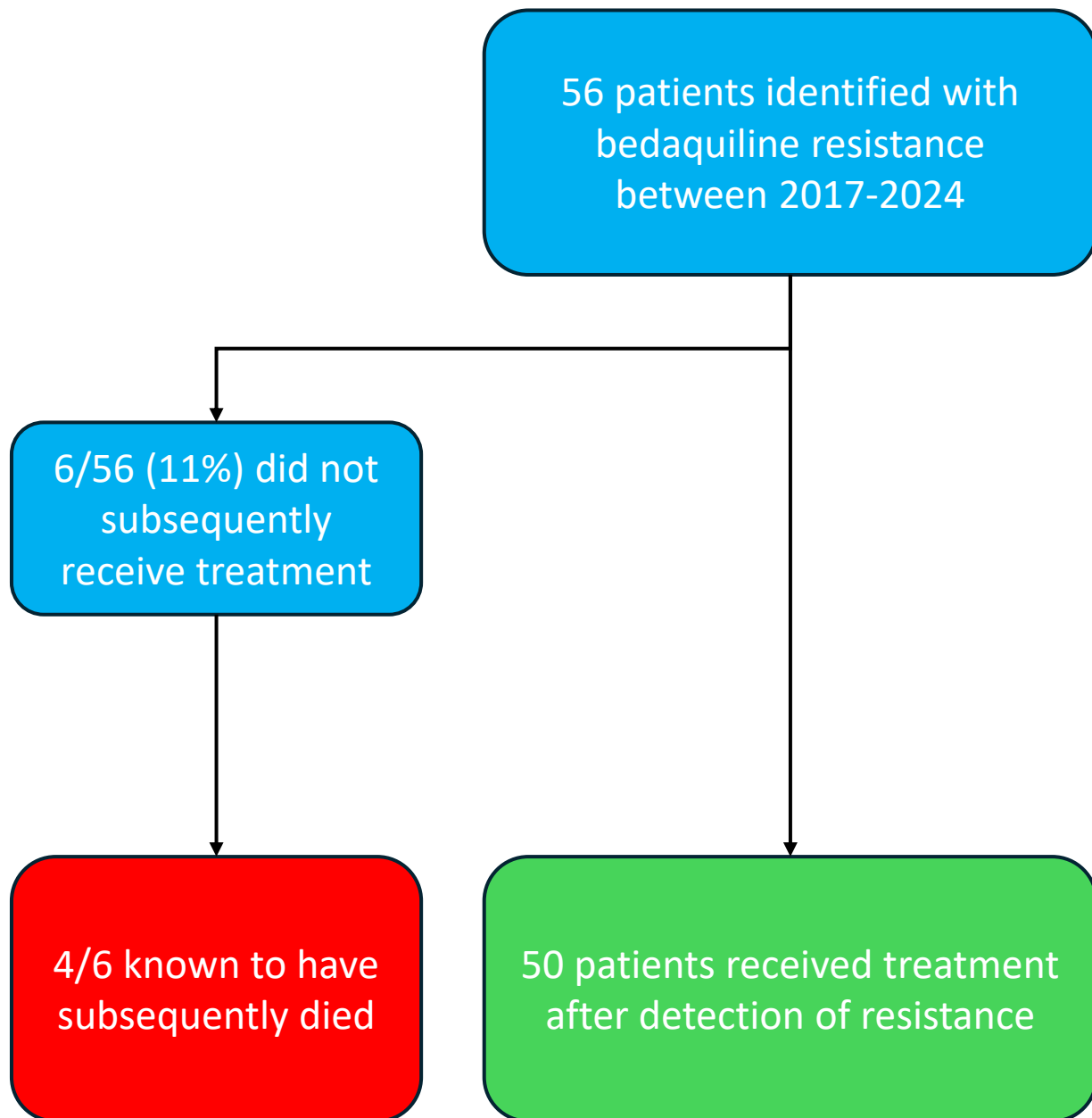
Optimal treatment of bedaquiline-resistant TB is not known

Methods

- Retrospective cohort study of all patients with bedaquiline-resistant TB in Karakalpakstan, Jan 2017 – Dec 2024
- Review of clinical and laboratory records
 - Baseline drug resistance profiles
 - Treatment regimens
 - Sputum culture results
- Outcomes
 - Sustained sputum culture conversion (SCC)
 - TB-free survival (alive, had completed treatment or in care, and had SCC) at 12, 18, and 24 months



Results



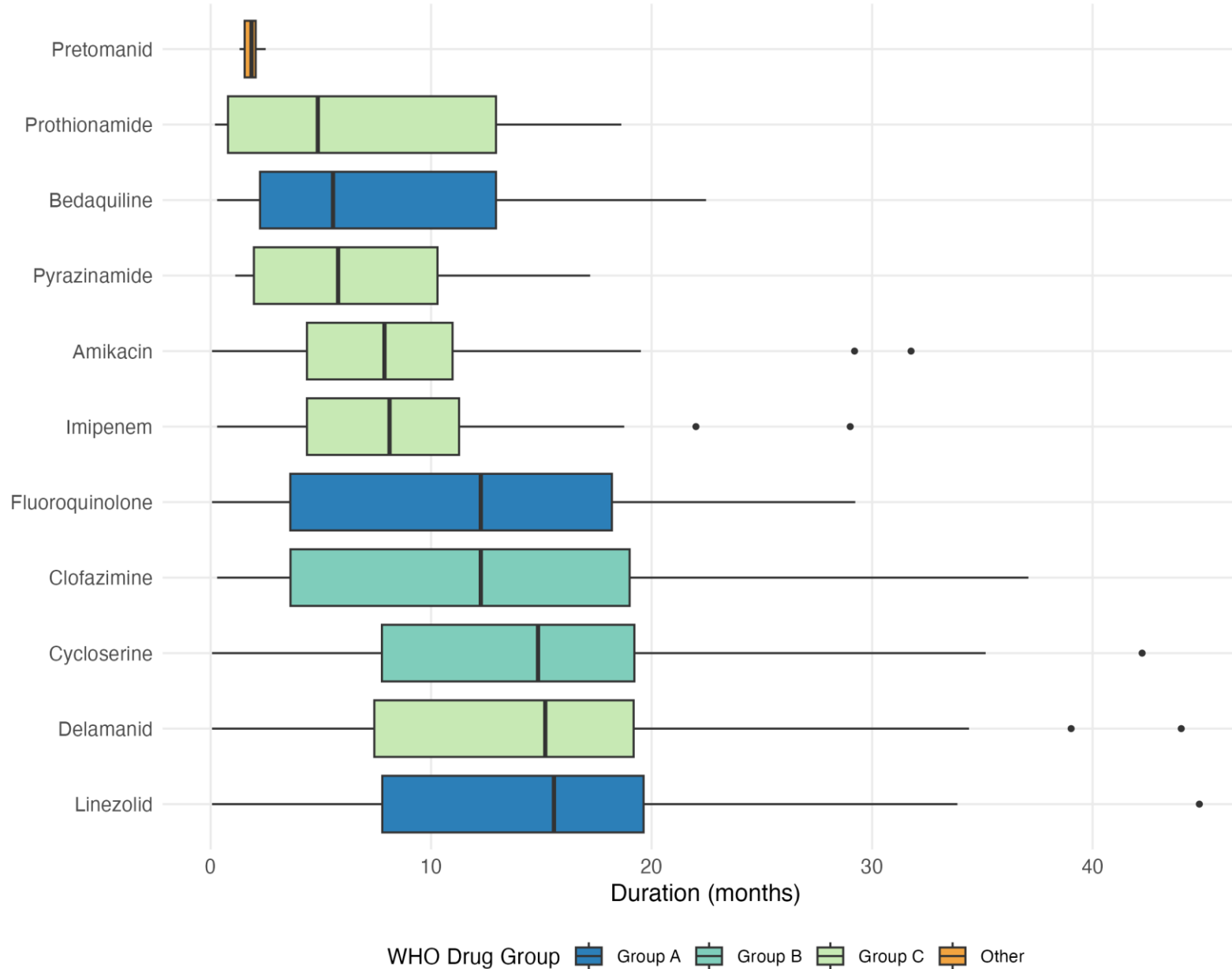
Characteristic	People with BDQ resistance starting treatment (n=50)
Age in years (median; IQR)	41 (27-52)
Male sex	64%
BMI (median; IQR)	17.9 (15.6-20.8)
Underweight (BMI<18.5kg/m ²)	58%

Previous TB treatment	80%
Previous BDQ exposure	68%
Previous BDQ sensitivity result	44%

Phenotypic drug resistance	People with BDQ resistance starting treatment (n=50)
Fluroquinolone	70%
Clofazamine	32%
Amikacin	14%
Linezolid	6%

Median duration of treatment after BDQ resistance=18 months (IQR: 8.9-22)

Median duration of each drug per patient who received it:



Bedaquiline (84%)

5.6 months (IQR: 2.2-13)

Imipenem (66%)

8.1 months (IQR: 4.4-11)

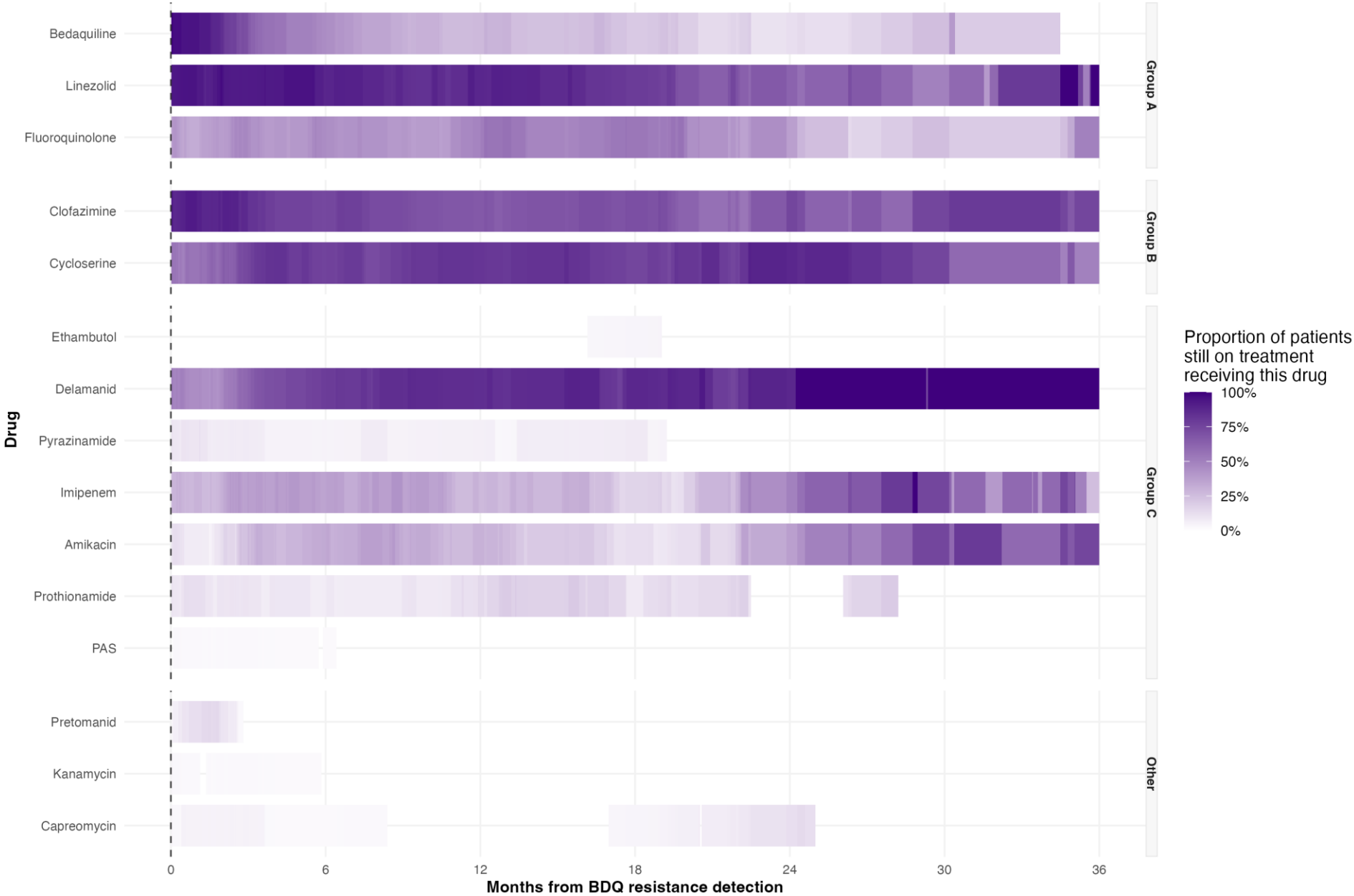
Amikacin (50%)

7.9 months (IQR: 4.4-11)

Linezolid (96%)

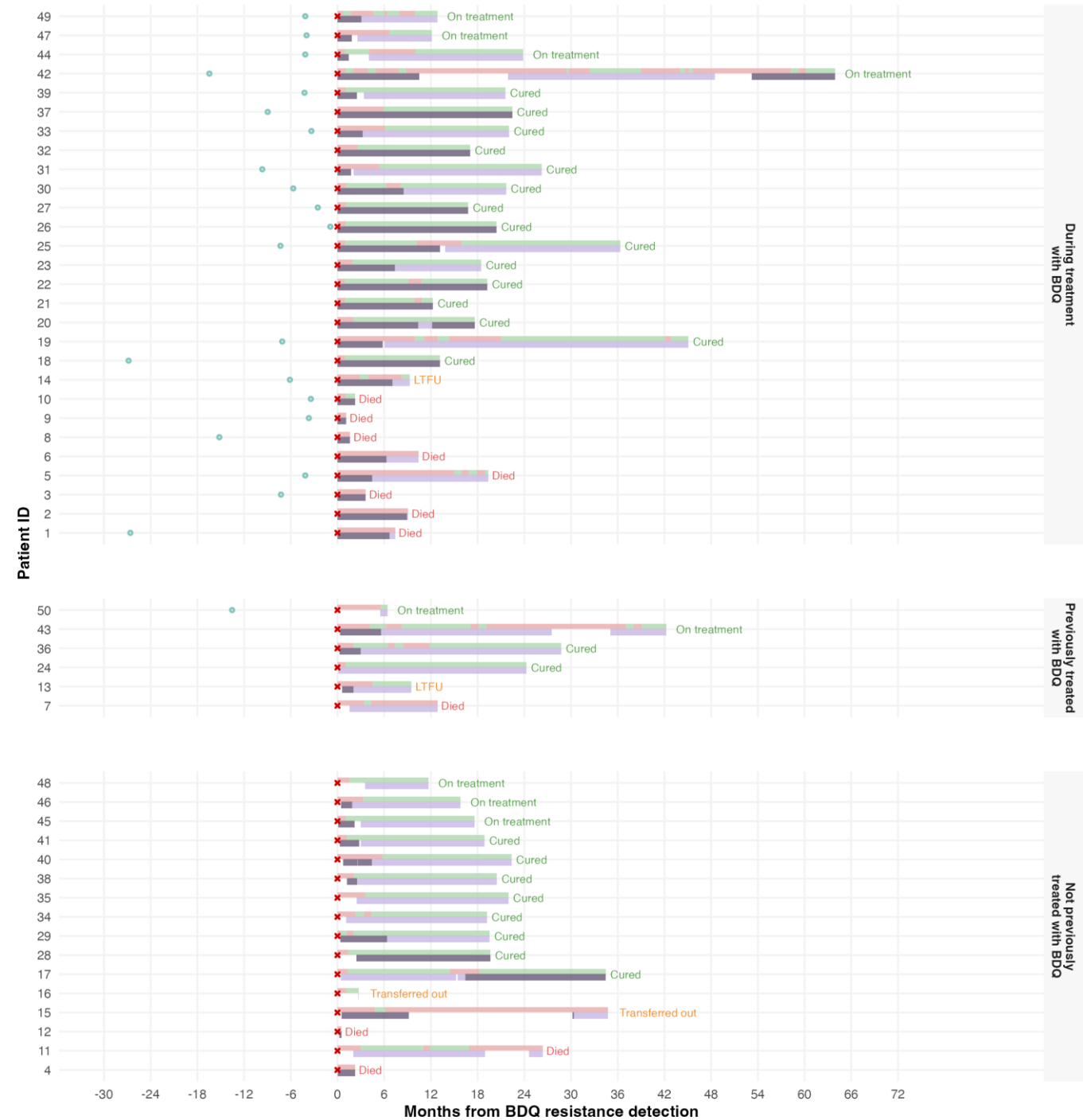
16 months (7.8-20)

Management required prolonged therapy, often with injectable agents

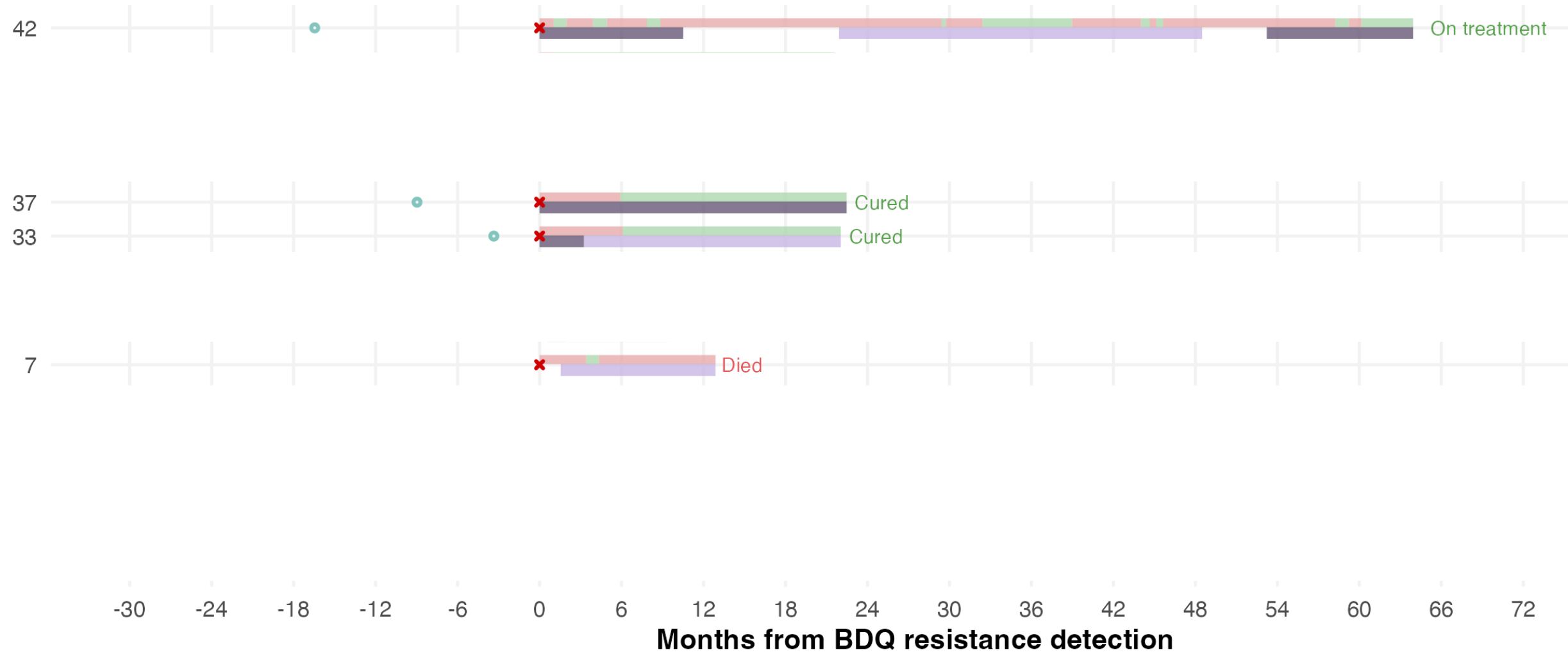


There was substantial heterogeneity in individual patient management and outcomes

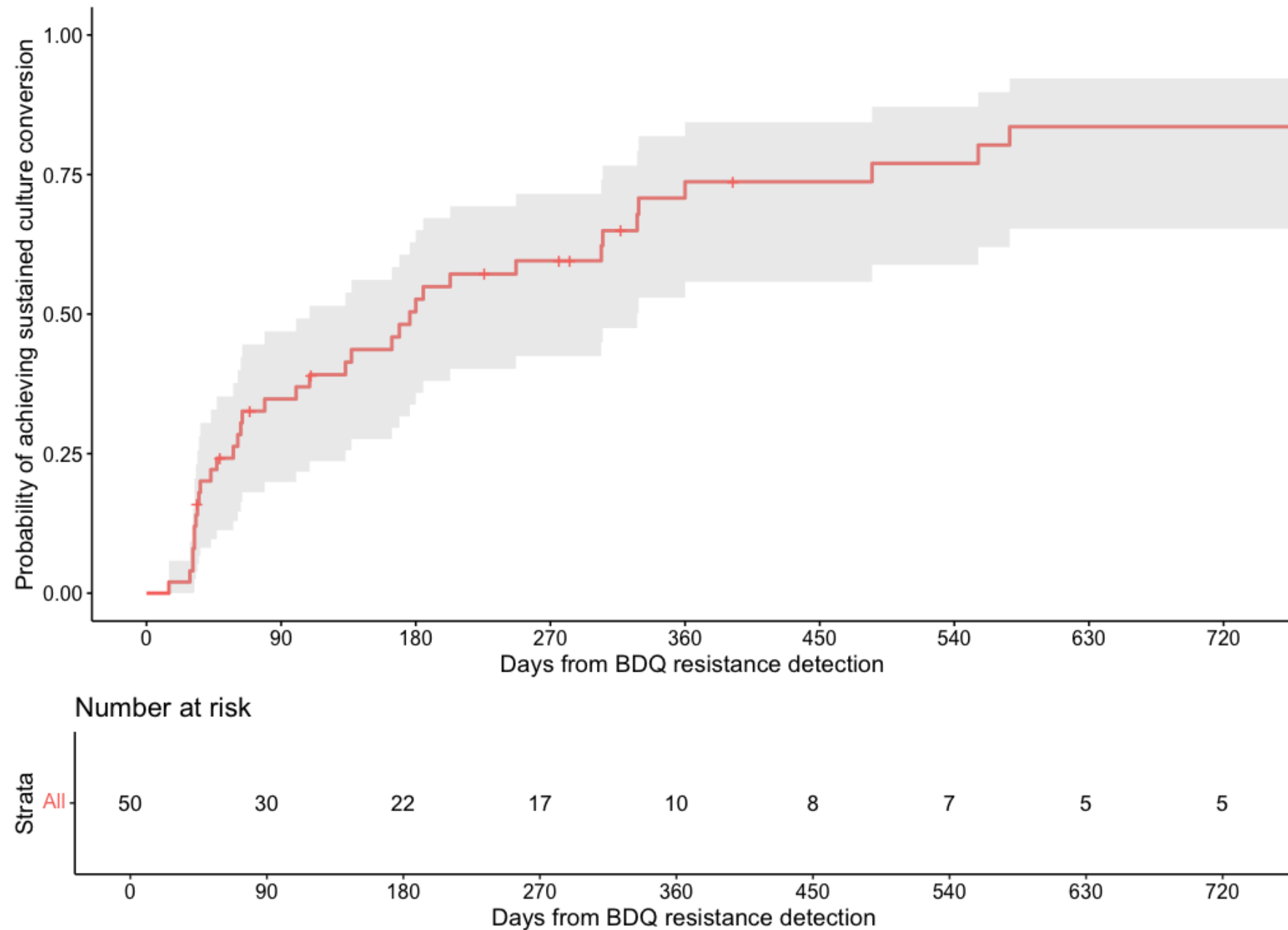
These profiles include all known treatment episodes



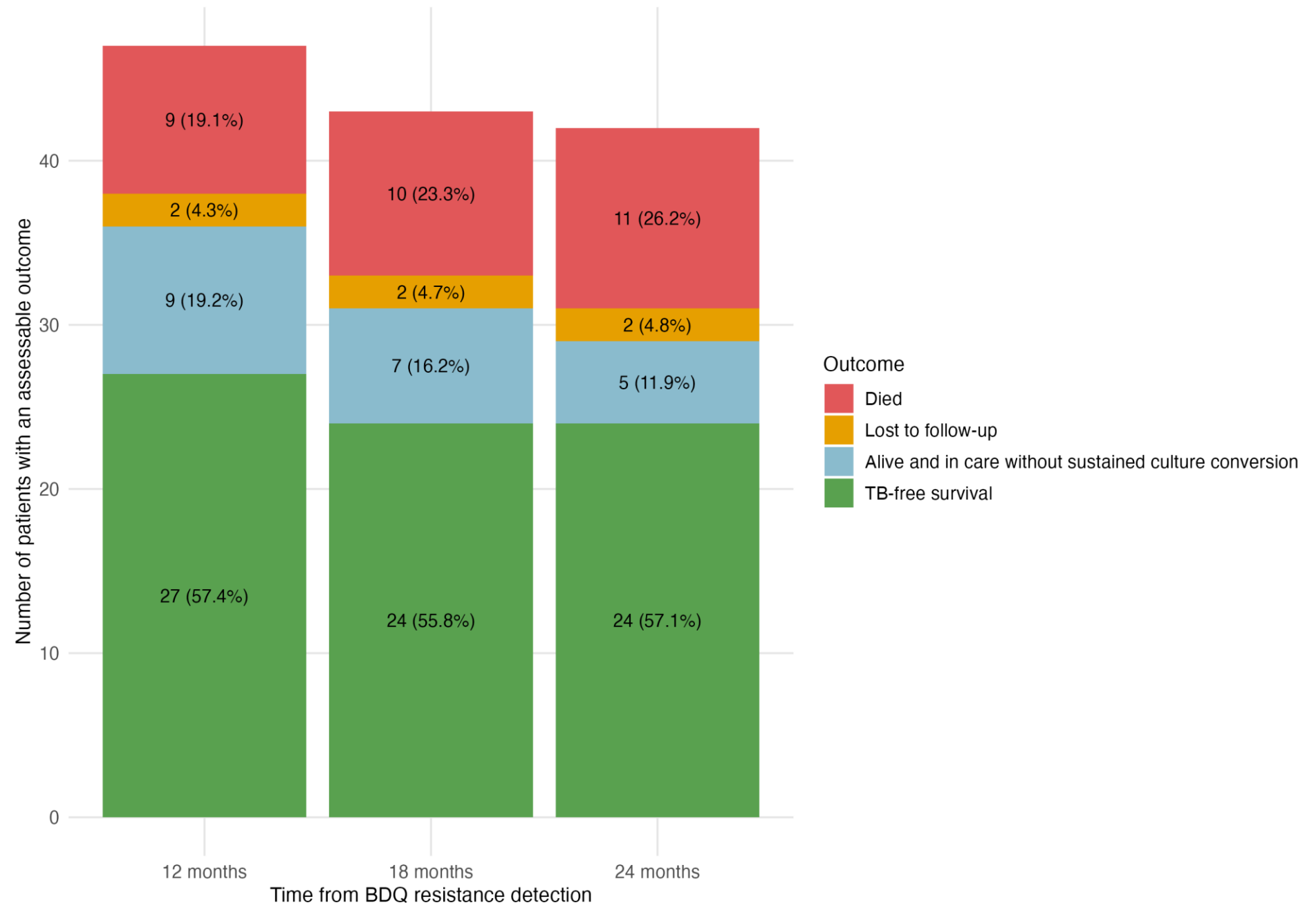
Bedaquiline...what to do....?



Median time to sustained culture conversion 176 days (IQR: 58-485)



56% (24/43) patients had TB-free survival at 18 months



To be considered assessable, patients had to have been followed up at least until the time point, or have had a definitive outcome before it

Key messages and implications

- Bedaquiline-resistant TB is a growing problem, including in people who have never received bedaquiline or any TB treatment, and in people who do not have fluoroquinolone resistance.
- Management required prolonged treatment with limited drug options, including substantial usage of injectable agents.
- Sputum culture conversion was much longer than for patients with bedaquiline-sensitive TB (~30 days), and overall outcomes were comparable to the treatment of drug-resistant TB in the pre-bedaquiline era.
- Rapid, near-patient resistance testing is needed to identify cases of resistance early and guide regimen selection
- New treatment strategies are urgently needed for bedaquiline-resistant TB