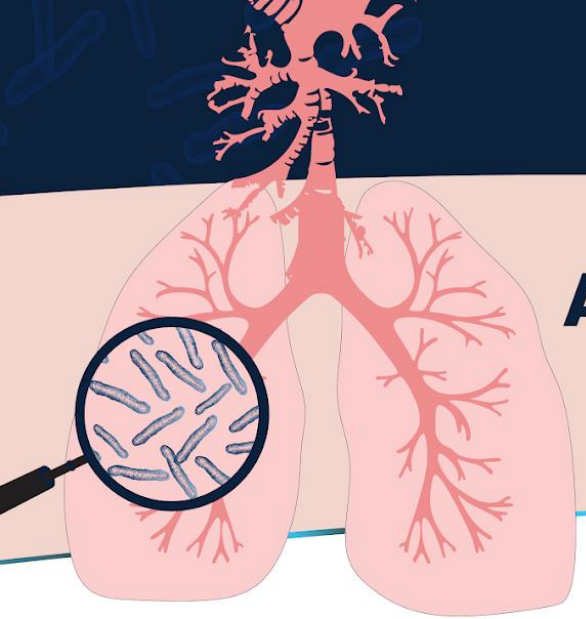


Accelerating progress to end TB

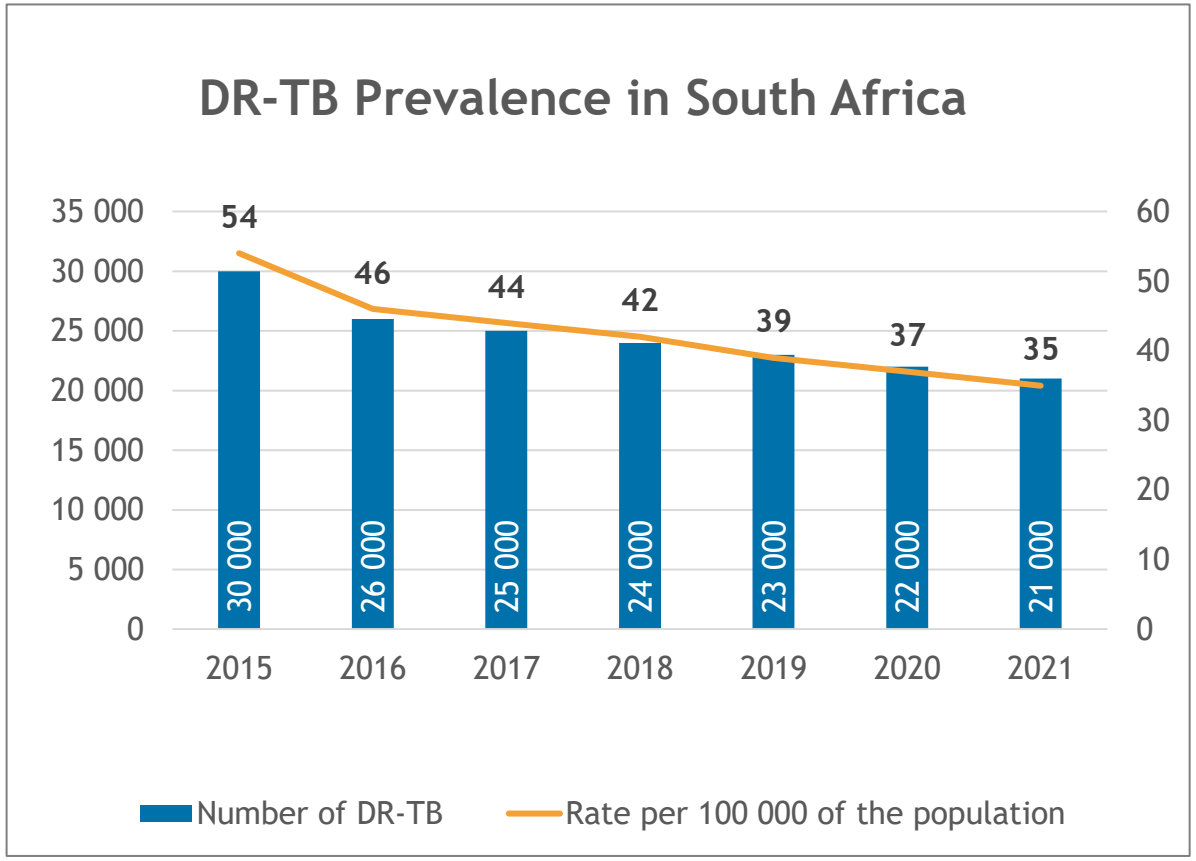
8th SA TB Conference
04 - 07June 2024
Durban ICC

Comparison of Drug-Resistant Tuberculosis (DR-TB) Mortality File Reviews between 2020 and 2021/22 in KwaZulu Natal (KZN), South Africa

Dr Louisa Dunn

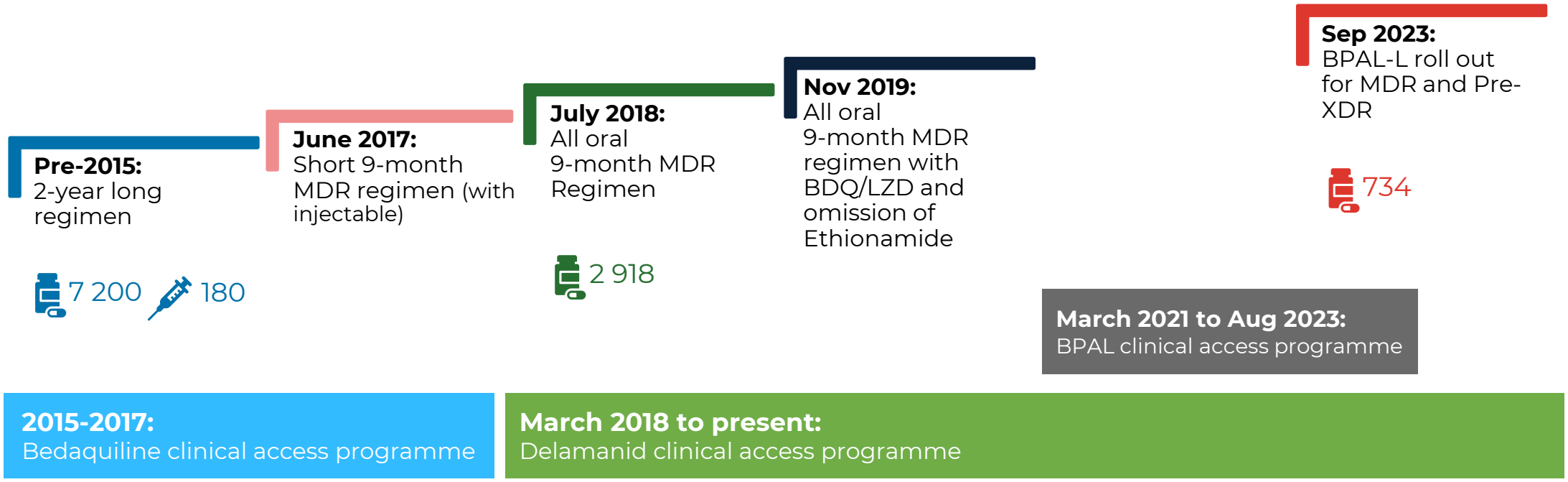
Drug Resistant TB in South Africa

- One of only **10 countries on all three WHO high burden lists for TB, TB/HIV co-infection and drug-resistant TB (DR-TB)**
- Estimated incidence: 35 per 100 000 of population per year in 2021 (21 000)
- KwaZulu-Natal (KZN) in South Africa is a DR-TB hotspot at the centre of a regional epidemic

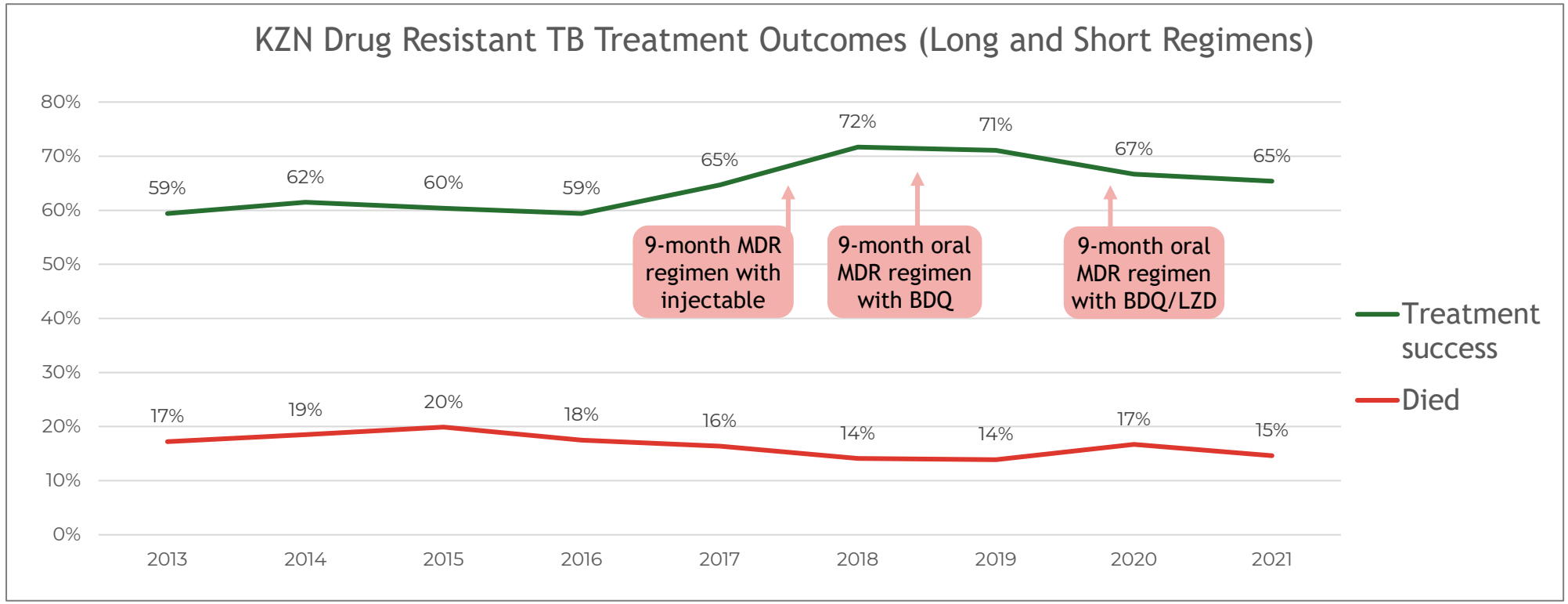


National TB Programme Response in South Africa

- TB Programme leaders prioritize advances in DR-TB treatment
- Hosted clinical trials that have shaped international WHO policy and guidelines



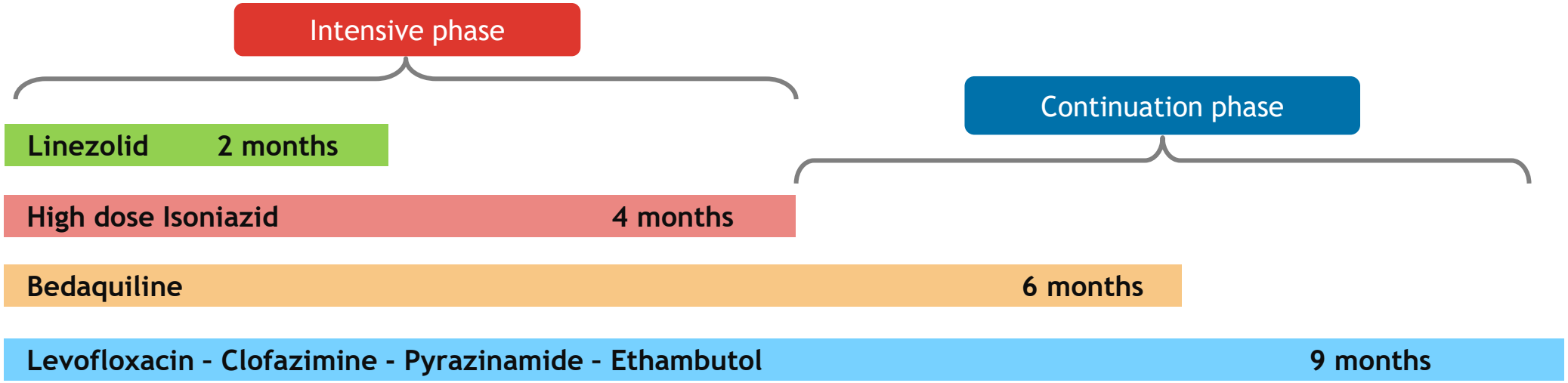
KZN Drug Resistant TB Treatment Outcomes and Evolution of National TB Programme Regimens



Despite improved treatment success rates, high mortality rates have still been observed

2019 Short and Long Regimens

Short regimen (9-11 months):



Long regimen (18 months):

Core drugs: Bedaquiline, Linezolid, Levofloxacin, Clofazimine, Terizidone

- Basic Long Regimen
- Fluoroquinolone-Resistance Long Regimen
- CNS Disease Long Regimen
- Rescue Long Regimen

Objectives

USAID TB LON programme

- Supported 4 Districts in KwaZulu-Natal Province

Objectives

1. Determine individual risk factors and characteristics associated with DR-TB mortality
2. Describe the DR-TB treatment journey of people who died on treatment
3. Conduct clinical audit to determine quality of care
4. Make recommendations on targeting interventions based on the findings

Methods

- **Retrospective mortality file review** across four districts in KwaZulu-Natal
- **DR-TB mortality audit tool** developed to assess:
    - **Individual demographics, characteristics and risk factors**
    - TB Diagnosis
    - HIV history
    - **Treatment journey** including regimen choice, response to treatment and adverse events
    - Clinical audit
    - Mortality assessment including time to death, place of death and causality
- **Two cohorts:**
    - **2020 Cohort People** who were notified between January – June 2020, and had a died DR-TB outcome (N=30)
    - **2021/22 Cohort People** who were notified between April 2021 and March 2022, and had a died DR-TB outcome (N=58)
- **Descriptive statistics**

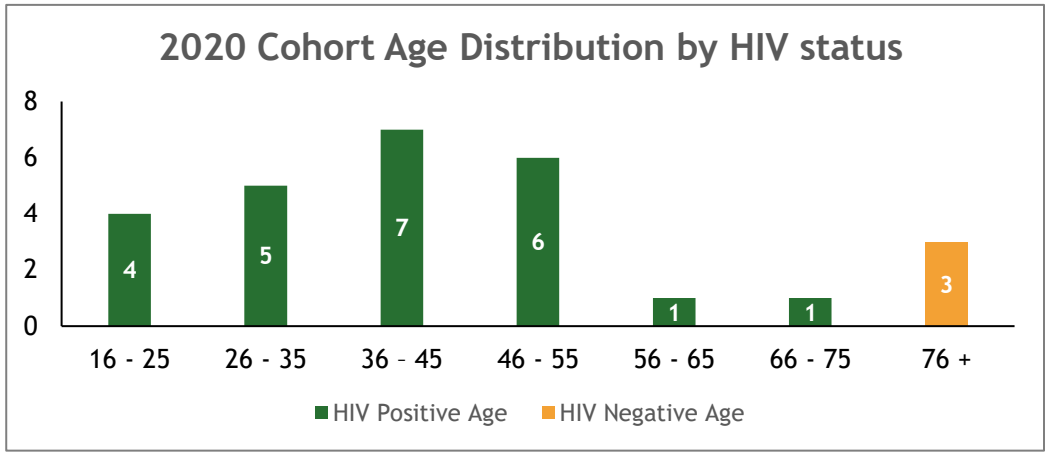
Severe Adverse Events

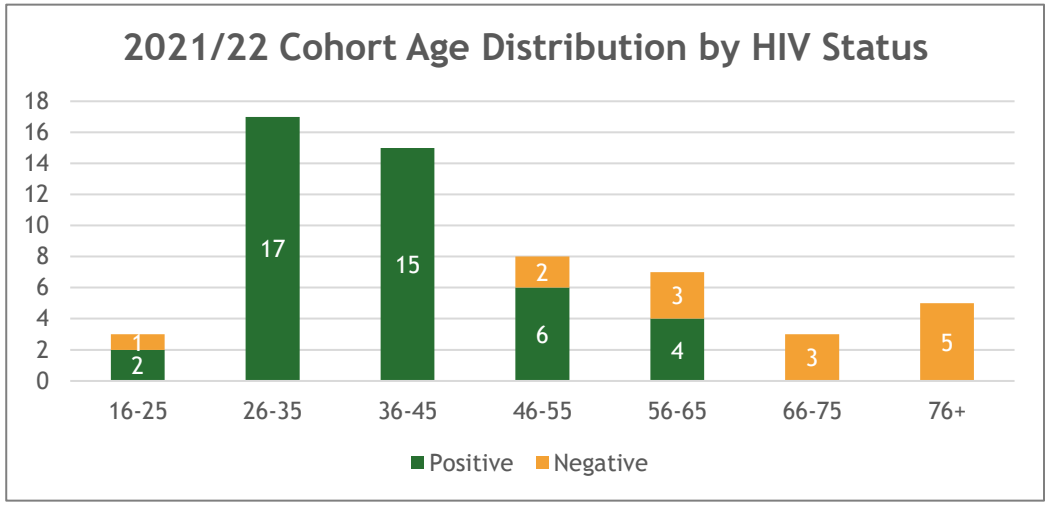
- **Adverse Events (AEs)** were identified through review of:
  - Doctor progress notes
  - Nursing notes
  - Laboratory results
  - ECGs
- AEs graded using a **standardised grading scale**
- **Severe Adverse Events (SAEs)**
  - Grade 3 or higher
  - Adverse events resulting in temporary or permanent suspension of a drug
  - Serious adverse event

Common SAE criteria
Prolonged QTcf (> 500ms)
Hepatitis (ALT >200 or Bilirubin >3 X ULN)
Myelosuppression (Hb <8.0 or platelets < 50, or Neut < 1.0)
Peripheral Neuropathy (Severe, limiting self-care ADLs)
Optic Neuropathy (Decrease in VA >6/12 or > 3 lines from baseline)
Acute Kidney Injury (Creat > 3 X increase from baseline or 354 microm/L)
Nausea and Vomiting (Persistent, minimal intake 48 hours, OR IV fluids)
Depression (Severe, PHQ-9 20-27, suicidal ideation with intent)
Seizures (New onset, multiple despite medical intervention)
Skin Disorder (Severe, Steven Johnson reaction, Toxic epidermal necrolysis)

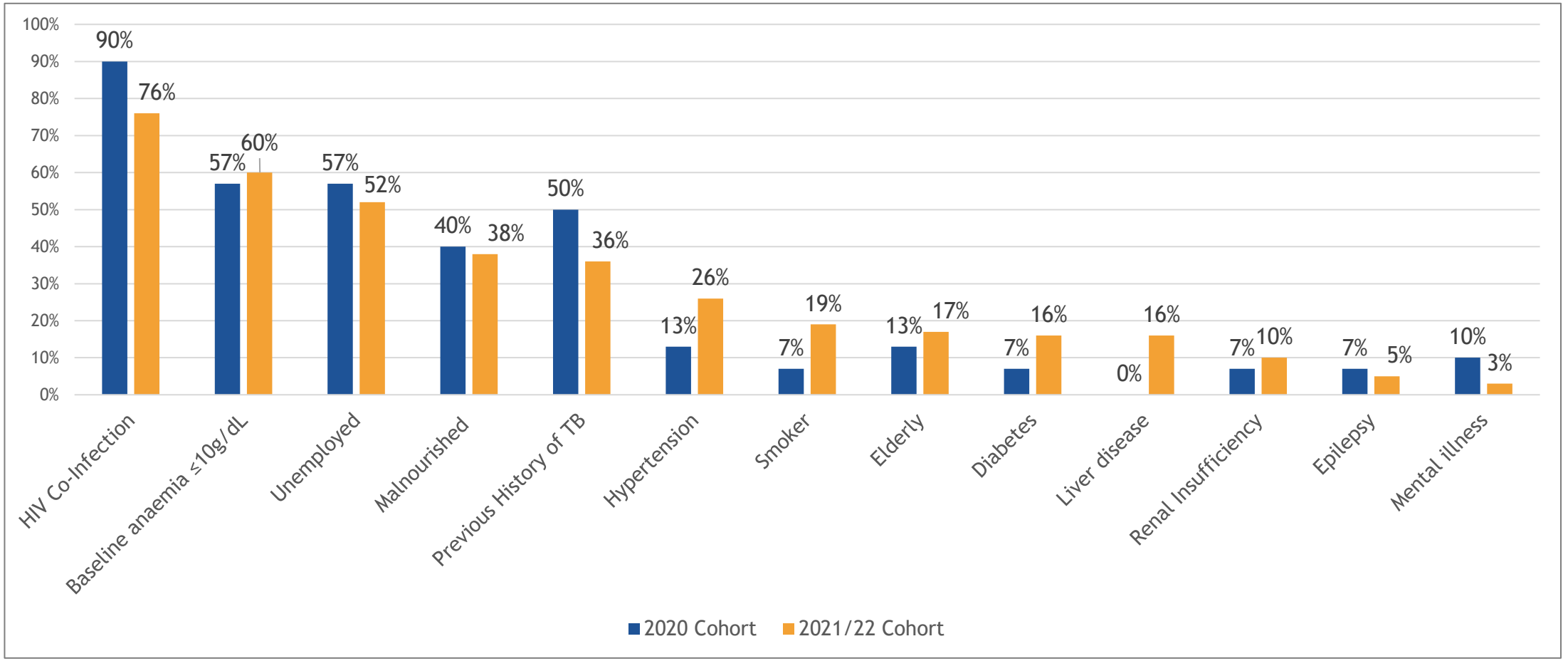
DR-TB Mortality Audit: Demographics

	2020 Cohort % (N)	2021/22 Cohort % (N)
Gender		
Male	50% (15)	41% (24)
Female	50% (15)	59% (34)
Age		
Median	40 years	40 years
HIV positive median	38 years	37 years
HIV negative median	78 years	67 years
HIV Status		
Positive	90% (27)	76% (44)
Median CD4 at DR-TB diagnosis	64	102
Median Viral Load at DR-TB diagnosis	112 500	4 897





Risk Factors



Results: Severe Adverse Events

	2020 Cohort (N = 30)
People who experienced a severe adverse event	**77% (23)**
SAEs	
Myelosuppression	40% (12)
Nausea and Vomiting	20% (6)
Hepatitis	10% (3)
Peripheral Neuropathy	7% (2)
Acute Kidney Injury	7% (2)
Optic Neuropathy	7% (2)
Skin Disorder	3% (1)
Other SAEs	13% (4)

- Hospitalisations
- Poor recording and reporting of severe adverse events
- Gaps in recognition and management of adverse events

	2021/22 Cohort (N = 58)
People who experienced a severe adverse event	**62% (36)**
SAEs	
Myelosuppression	24% (14)
Nausea and Vomiting	17% (10)
Acute Kidney Injury	9% (5)
Hepatitis	7% (4)
Peripheral Neuropathy	7% (4)
Prolonged QTcF	3% (2)
Other SAEs	36% (21)

Other SAEs: Hospitalisation with acute dyspnoea (4), developed CCF (3), severe weight loss (3), new onset seizures (2), lactic acidosis (2), acute neurological deficit (1), hypoglycaemia (1), acute abdomen (1), psychosis (2), pancreatitis (2), acutely unwell with epigastric pain (1), delirium (1), fall and head injury on ward (1) hospitalisation acutely unwell, IP file missing (1)

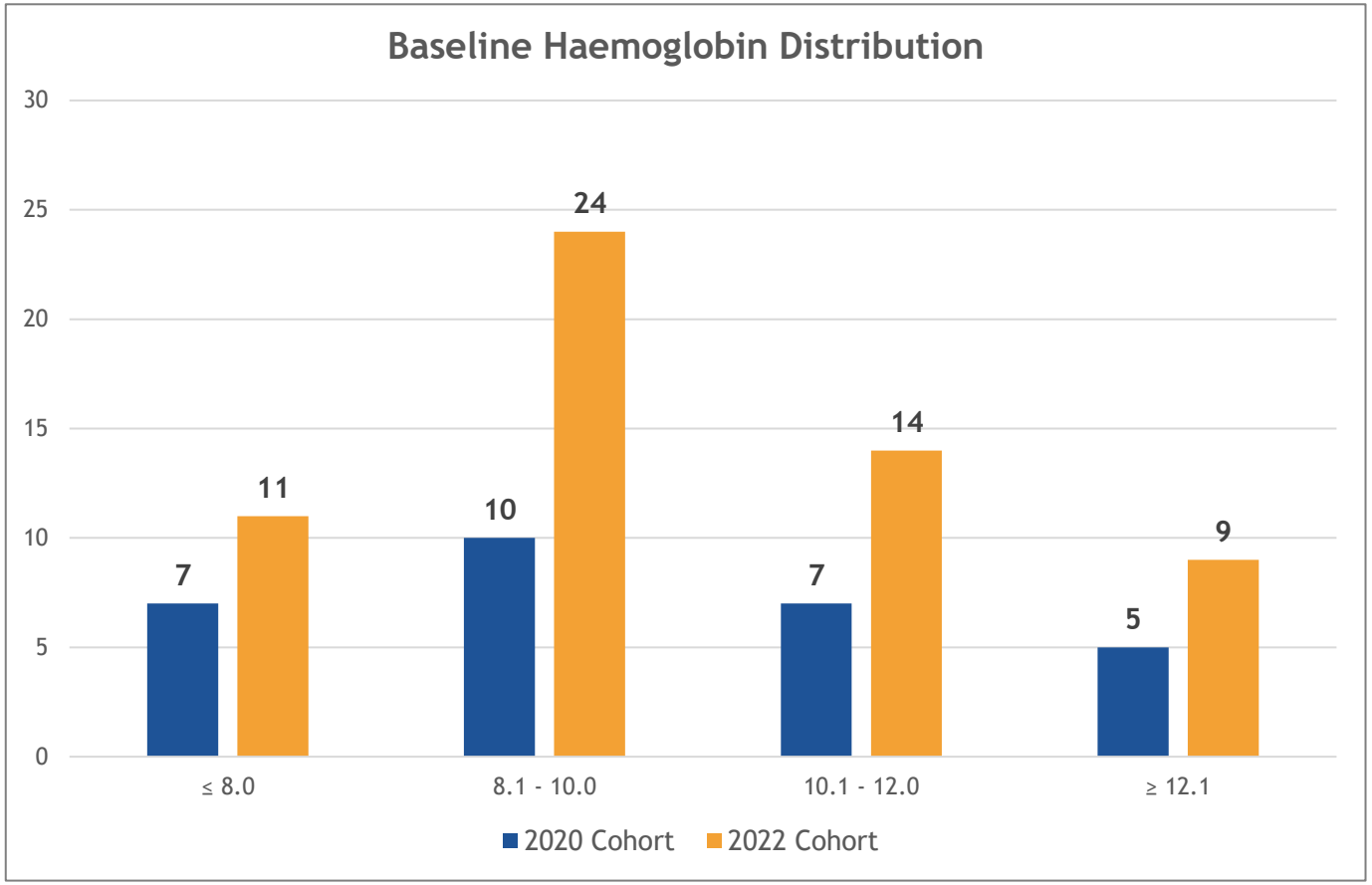
Baseline Haemoglobin at DR-TB Treatment Initiation

2020 Cohort:

- Haemoglobin < 10g/dL in 57% (17/30)
- Haemoglobin < 8g/dL in 23% (7/30)

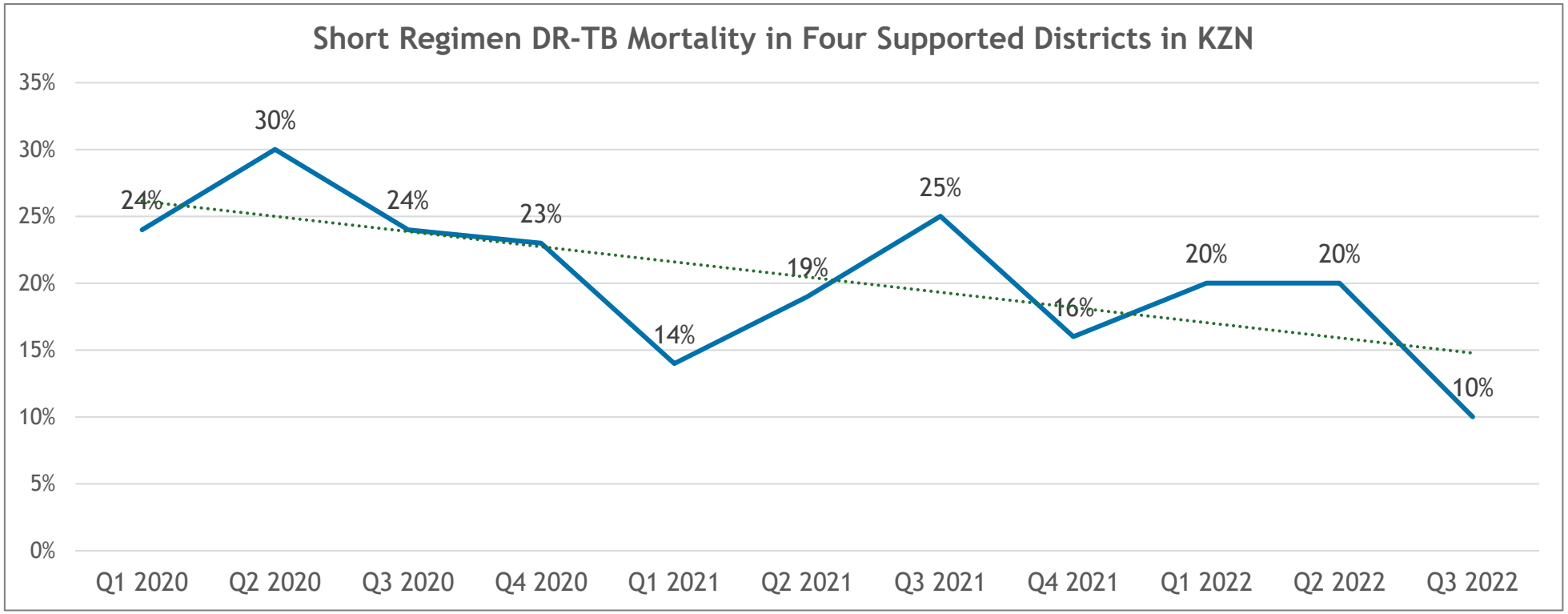
2021/22 Cohort:

- Haemoglobin < 10g/dL in 60% (35/58)
- Haemoglobin < 8g/dL in 19% (11/58)



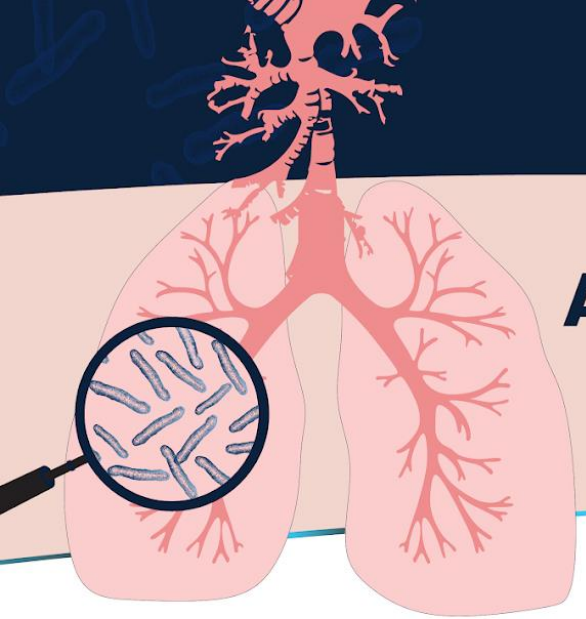
Mortality Rates Over the Period Studied

- Over the duration of the period of study and implementation, short course DR-TB regimen mortality rates are declining in the four districts in KZN



Conclusion

- Introduction of new and repurposed drugs and shortened regimens has improved treatment success rates
- Mortality rates have remained too high
- High incidence of SAEs in patients who died after DR-TB notification in both 2020 and 2021/22 mortality file reviews
- Most frequently observed SAEs have been consistent
- Rate of SAEs appears to have dropped during this period alongside overall reductions in mortality rates
  - May indicate improved competency in safely delivering current regimens
- To continue the gains made in mortality rates:
  - Ongoing in-depth mortality file reviews should be institutionalized with responsive action plans implemented
  - Continuous capacity strengthening and mentorship
  - Robust active drug safety monitoring.



Accelerating progress to end TB

8th SA TB Conference
04 - 07June 2024
Durban ICC

Acknowledgements

- KZN Department of Health
- USAID
- THINK
- SA TB Conference