Is simple care, better care?

Moving to a simplified regimen for cryptococcal meningitis, the AmbiOne study

MSF scientific Days, May 2026

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DOCTORS WITHOUT BORDERS

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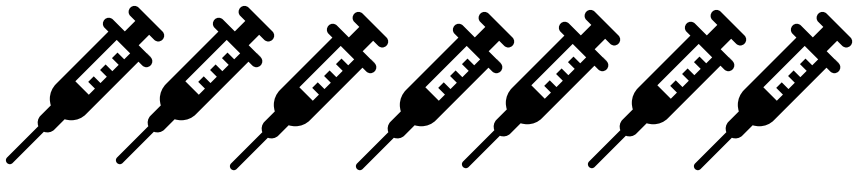
Background: Advanced HIV disease still a problem

Advanced HIV disease responsible for **630,000 deaths annually**

Cryptococcal meningitis: 2nd largest contributor to AIDS-related deaths after tuberculosis

Standard of care previously was a **minimum of 7 days** intravenous antifungal treatment



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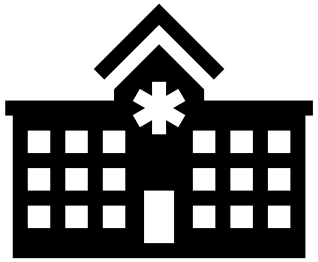
Bridging the gap between research and reality



Routine care programmes in Africa using different CM treatments

Settings: routine care

2 week mortality: 25- 40%

10 week mortality: 44 – 74%

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2: Jarvis JN, et al Ambition Study Group. Single-Dose Liposomal Amphotericin B Treatment for Cryptococcal Meningitis. N Engl J Med. 2022 Mar

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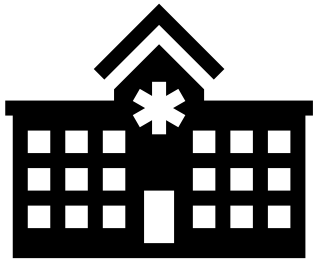

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10-week mortality: 25% (CI: 21-29%)

Single dose regimen

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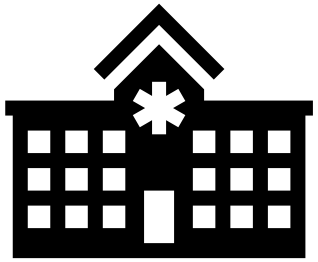

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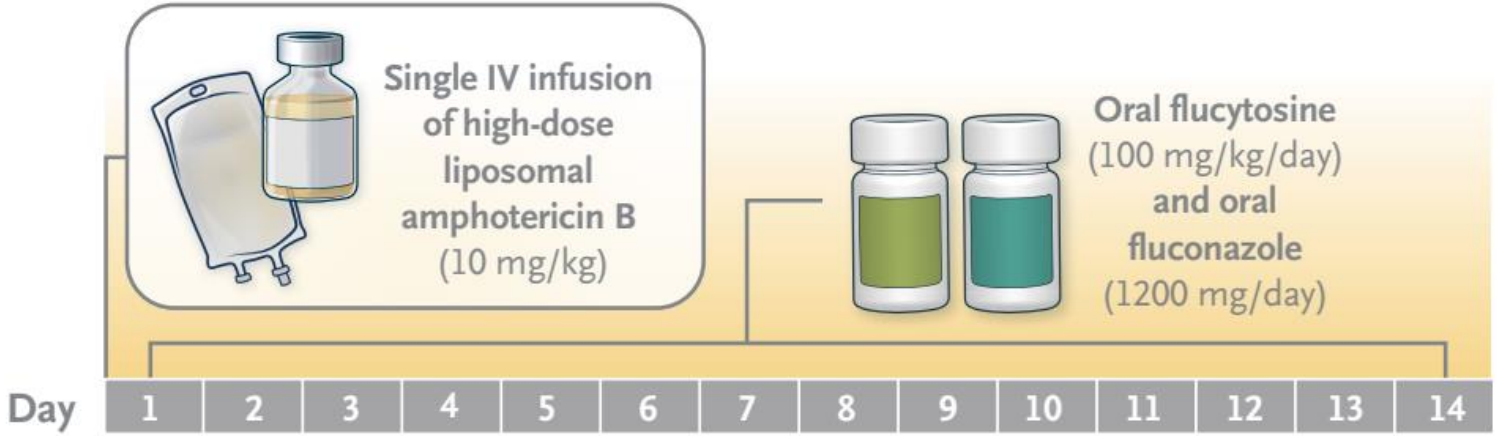
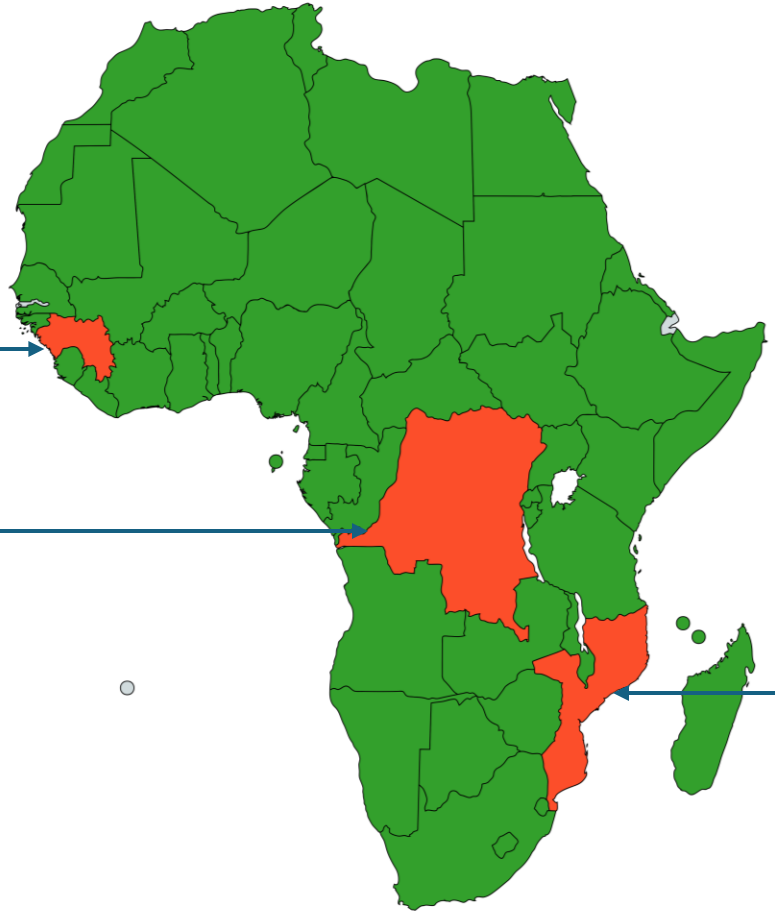
Study rationale and design

- **Evidence gap**: Real world evidence about implementation barriers of single dose regimen in low resource settings.
- **Design**: Mixed methods implementation study of single dose regimen as per 2022 WHO guidelines
- **Eligibility:** Adults (≥ 18yo) in inpatient care living with HIV and microbiologically confirmed cryptococcal meningitis that consented for inclusion.



Study sites: MSF supported HIV units

USFR, Conakry, Guinea



CHK, Kinshasa, DRC

BCH, Beira, Mozambique

2023-2026

This study was approved by the Médecins Sans Frontières Ethics Review Board under the AmbiOne protocol, on 17 October 2023 along with local ethical review boards in the respective countries.

Endpoints

Primary Outcomes (aligned with previous RCT outcomes)

- Mortality at 2- & 10-weeks from start of induction therapy for Cryptococcal Meningitis

Secondary outcomes

- Adherence to optimised care package (Intracranial pressure management, toxicity surveillance, time to diagnosis and treatment)
- Proportion of deaths after hospital discharge
- Length of hospital stay among patients that survived to discharge
- Frequency of adverse events (Serious Adverse Events grade III vs IV)

Baseline characteristics

Table 1. Baseline characteristics of participants enrolled in the AmbiOne implementation study

Characteristic (N = 177)	Result
Age (years, median [IQR])	40 [32–47]
Weight* (kg, median [IQR])	50 [43–58]
Sex, % female (n/N)	49% (86/177)
CD4 count^ (cells/μL, median [IQR])	49 [32–125]
ART experienced, % (n/N)	63% (110/175)
GCS < 15 on admission, % (n/N)	41% (73/177)
Urine TB LAM positive^^, % (n/N)	46% (53/115)
Raised opening pressure at baseline (>25cm by manometer or >19 cmH_2O if adjusted for IV infusion lines as measurement tool), %	48% (73/151)
Haemoglobin (g/dL, median [IQR])	10.3 [8.2–11.5]

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Primary outcomes: 2- & 10-week mortality

2-week mortality:

22.0%

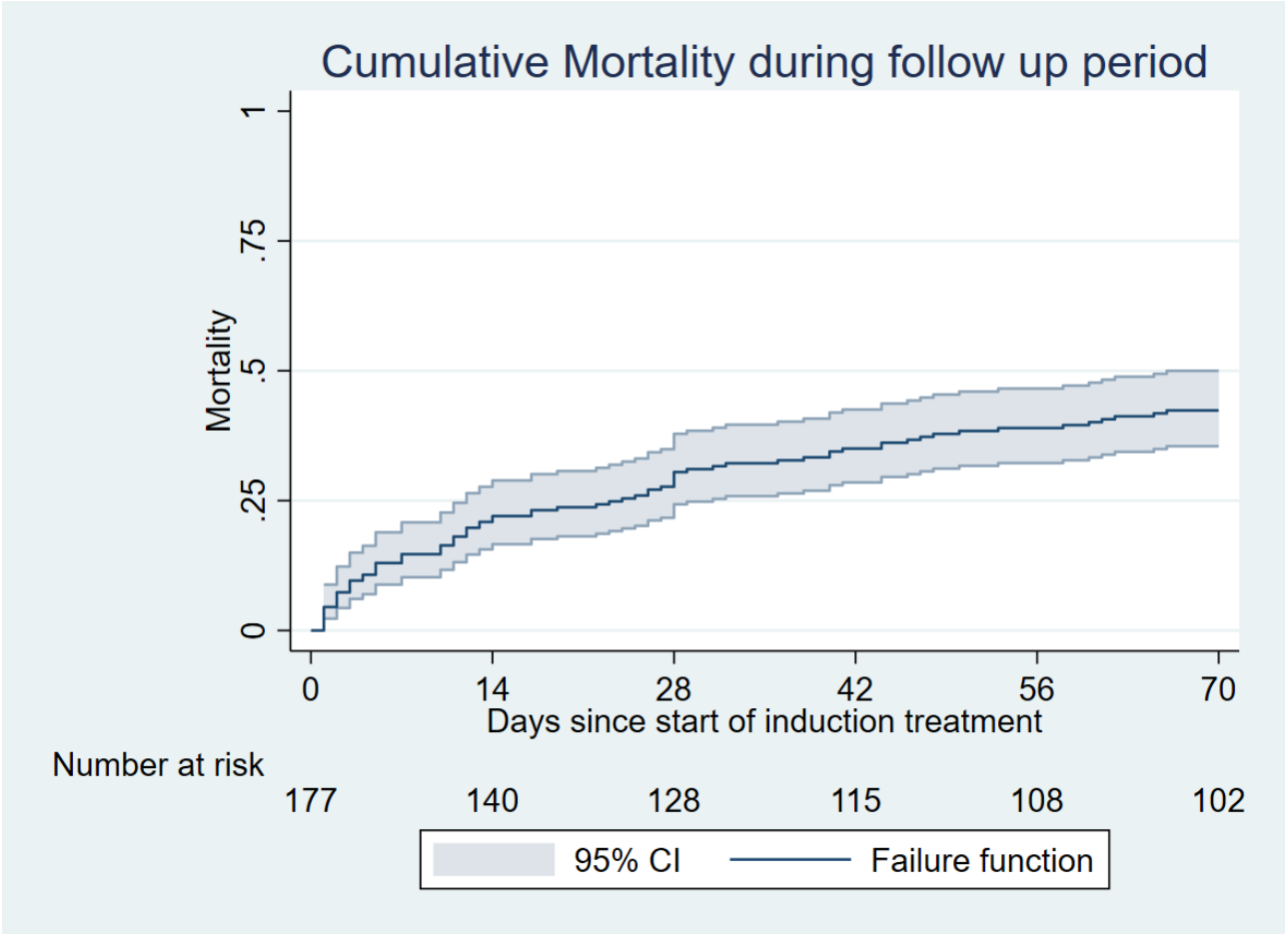
(95% CI, 16.6-28.9)

10-week mortality

42.4%

(95% CI, 35.5-50.0)

Lost to follow up <1% (1/177) – censored at last contact.



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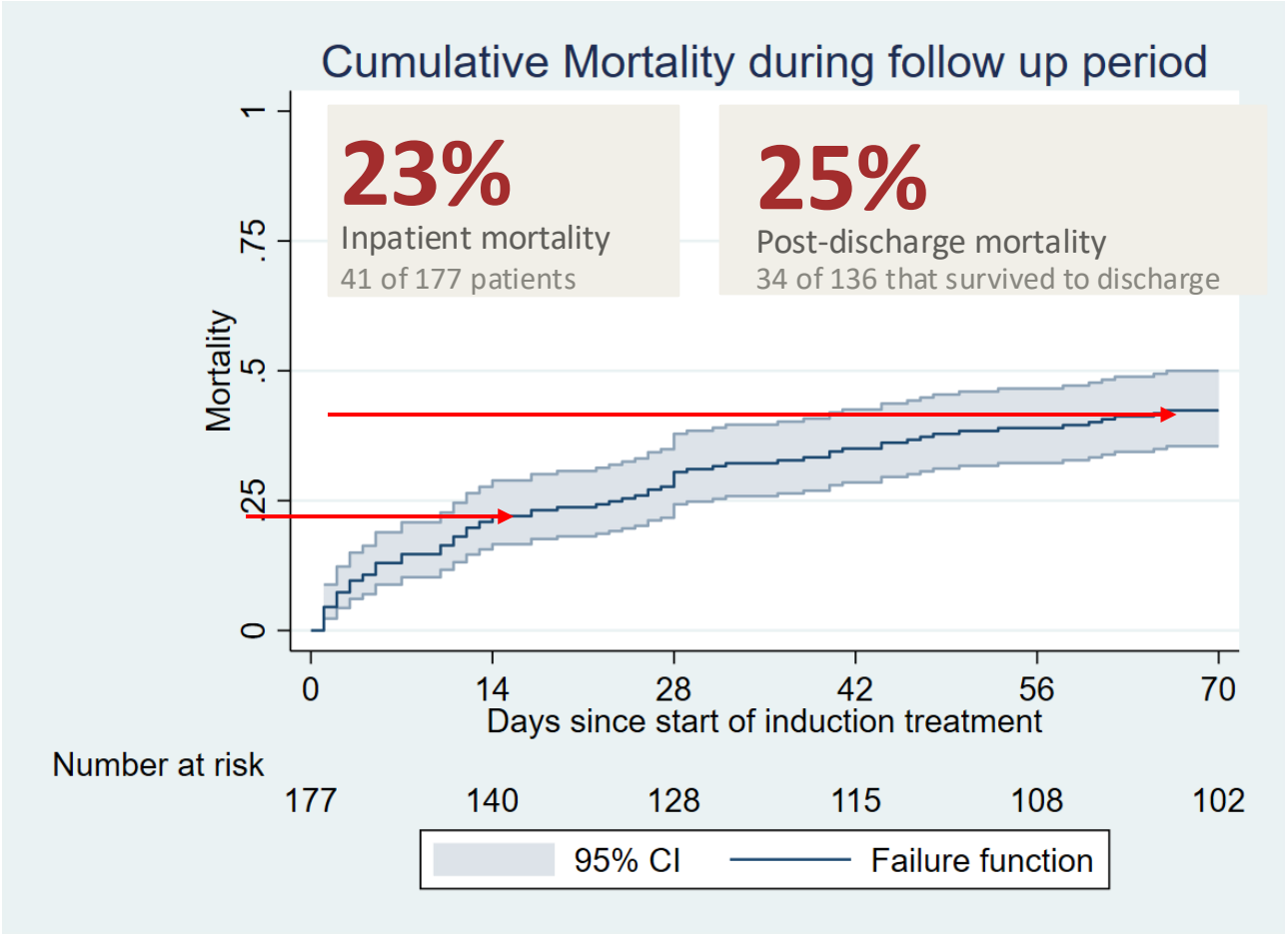
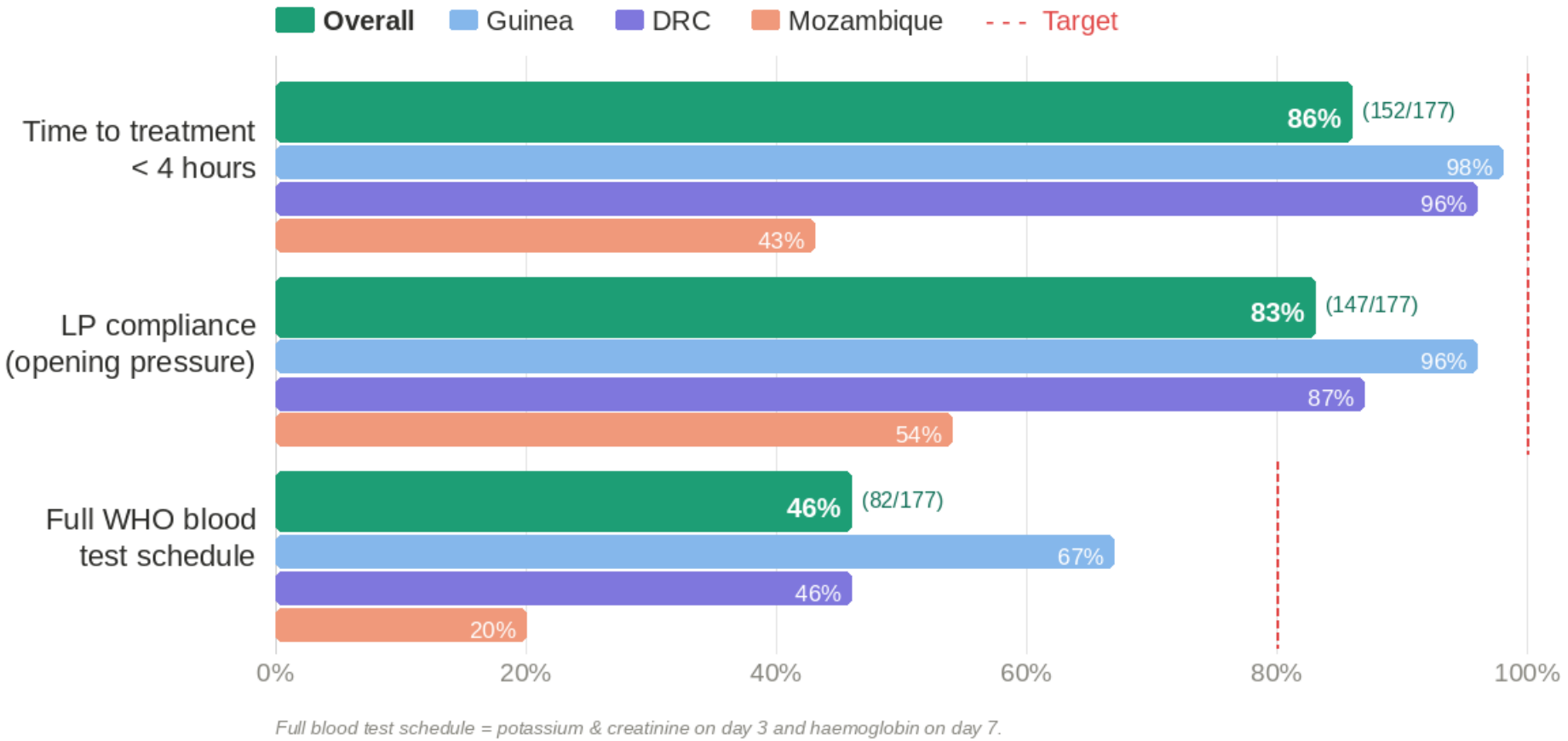


Secondary outcomes: Implementation fidelity



Full blood test schedule = potassium & creatinine on day 3 and haemoglobin on day 7.

Key implementation lessons

- Co-location of LP kits, CrAg tests, and L-AmB in the emergency room reduced time to treatment.
- Laboratory monitoring challenging to achieve despite implementation focus.

Secondary outcomes:

Length of stay

37%

Discharged within 7 days

50 of 136 patients

Key observation

More than a third of survivors were discharged within 7 days, a benefit of the single dose regimen. Earlier discharge was associated with better outcomes (HR 0.25, p = 0.005, mitigated by clinical state)

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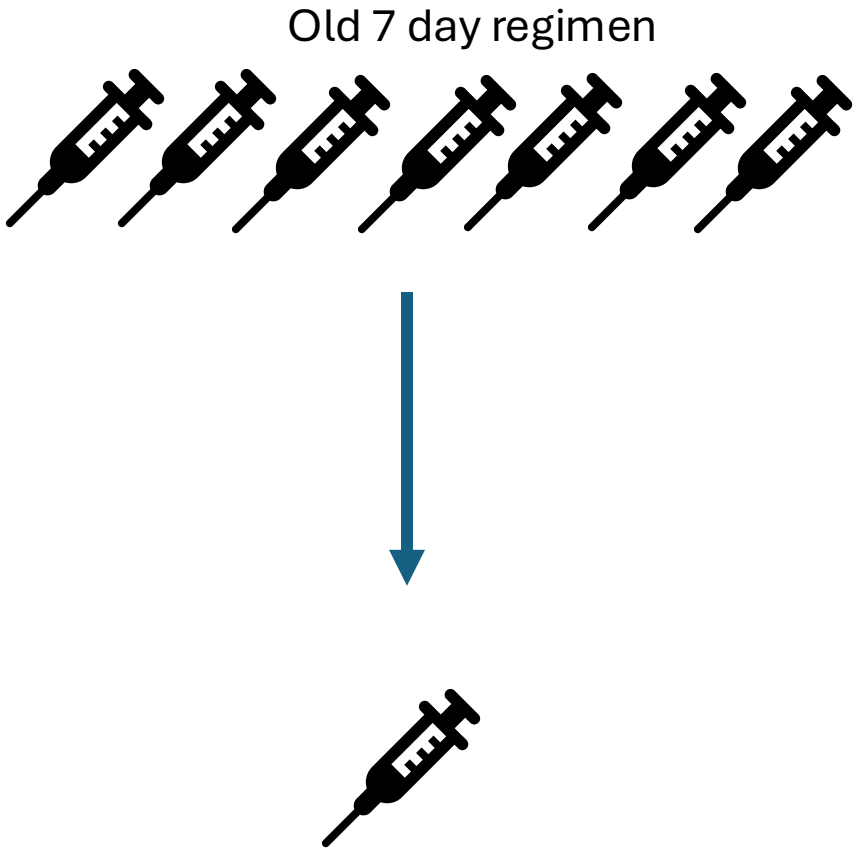
Qualitative work: high acceptability for a simpler regimen

High acceptability - a regimen more compatible with resource limited healthcare systems

- Nurses: Marked **reduction in burden of IV administration** work
- Doctors: Perceived **reductions in length of stay and laboratory monitoring requirements**.
- **Initial adoption hesitancy**: simplified seen as inferior by some HCWs.



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Qualitative work: challenges

System level challenges in cryptococcal care: "the system is full of trap doors"

- Late referral from other services.
- Performance of lumbar puncture a significant barrier in non-specialist centres.
- Cost to participants is a significant barrier to post discharge care.

"Sometimes the family has to decide if they want to pay for a readmission or for a funeral"

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Total pill burden for 50kg patient in first 10 weeks of CM treatment	
Pill	Total
Flucytosine	140
Fluconazole	308
Rifafour (RHZE)	280
Pyridoxine	70
Cotrimoxazole	308
Folic Acid	42
TLD (1 tablet)	42
DTG boost	42
	1190

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Conclusions and discussion

Single-dose L-AmB was **feasible** to implement outside of controlled research settings with **acceptable early outcomes.**

Substantial mortality between weeks 2 and 10, largely post-discharge, indicates that regimen simplification must be paired with strengthened follow-up.

Limited capacity for laboratory monitoring and shorter length of stay underscored the operational advantage of simplified regimens

Summary

- What is your main question?
  - What were the outcomes and implementation barriers of single L-AmB for CM.
- What did you find?
  - Gap remains in survival between research outcomes and real-world routine settings.
  - The early post discharge period is a key focus for interventions.
- Why is it important?
  - Need for implementation focus on care quality to close the gap between outcomes in research settings and routine care.
  - Lower toxicity and shorter length of stay bring health system and individual benefits

Acknowledgements

Merci beaucoup, obrigado, matondi

- **Participants**
- Study teams and collaborators
- Ministry of Health partners
- Regulatory authorities
- Academic partners

Jonathan Falconer*[1,2] , Cedric Mafu[3], Romao Sabuni[4], Oulare Ibrahima[5], Barry Ibrahima[5], Montserrat Barrios[4], Naftal Joao[4], Gisele Mucinya[3], Alain Tshimungu[3], Freddy Mangana[1], Sako Fode Bangaly[5], Destin Nyalenge[3], Adelard Shyaka[5], Petros Isaakidis,[1] Antonio Flores[1], Rosie Burton[1], Tom Ellman[1],, David Lawrence[6], Nelesh P. Govender[2], Joseph Jarvis[6], Esther Casas[1]

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