

Cost-effectiveness of AmBisome® for asymptomatic cryptococcal infection in Uganda and South Africa

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Background:

Cryptococcal meningitis

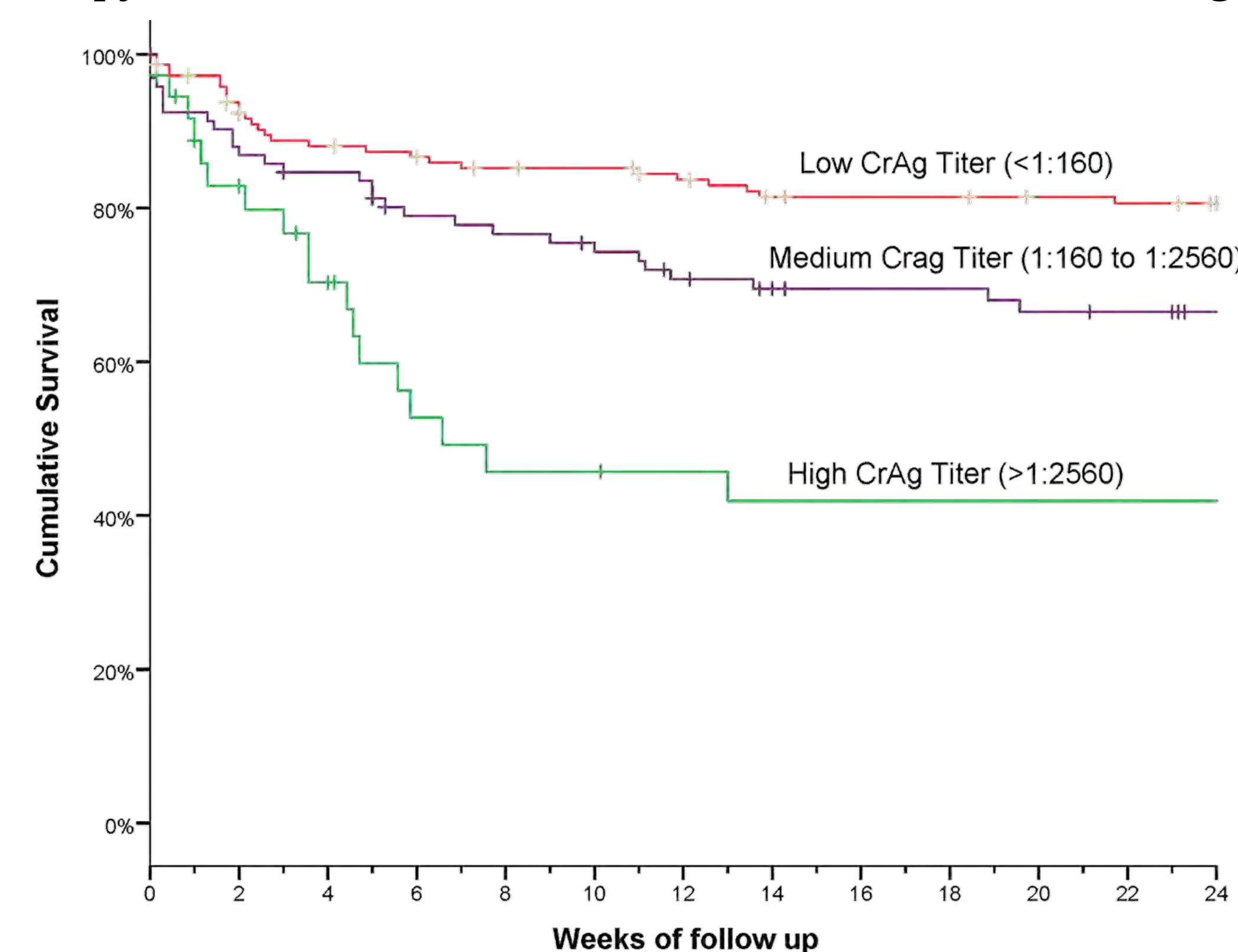
- Causes 15% of AIDS-related deaths in sub-Saharan Africa.
- Mortality from meningitis remains high at 50 to 70% in sub-Saharan Africa.

Cryptococcal antigen (CrAg) can be detected in the blood weeks before onset of meningitis

- CrAg is an independent predictor of meningitis and death.

WHO Recommendations for preemptive treatment of asymptomatic CrAg+ persons:

- Fluconazole 800mg daily x 2 weeks, then 400mg daily x 8 weeks, then 200mg to 6 mo.
- Preemptive therapy results in ~75% survival with risk of death increasing by CrAg titer



AmBisome®

Single dose AmBisome® (10mg/kg) with fluconazole is being prospectively evaluated for treatment of cryptococcal meningitis, and for asymptomatic cryptococcal infection

Discounted no-profit price for cryptococcosis therapy in 116 low and middle income countries (LMICs) is now significantly reduced at \$16.25 per vial (Sept 12 2018 Gilead UNITAID agreement).

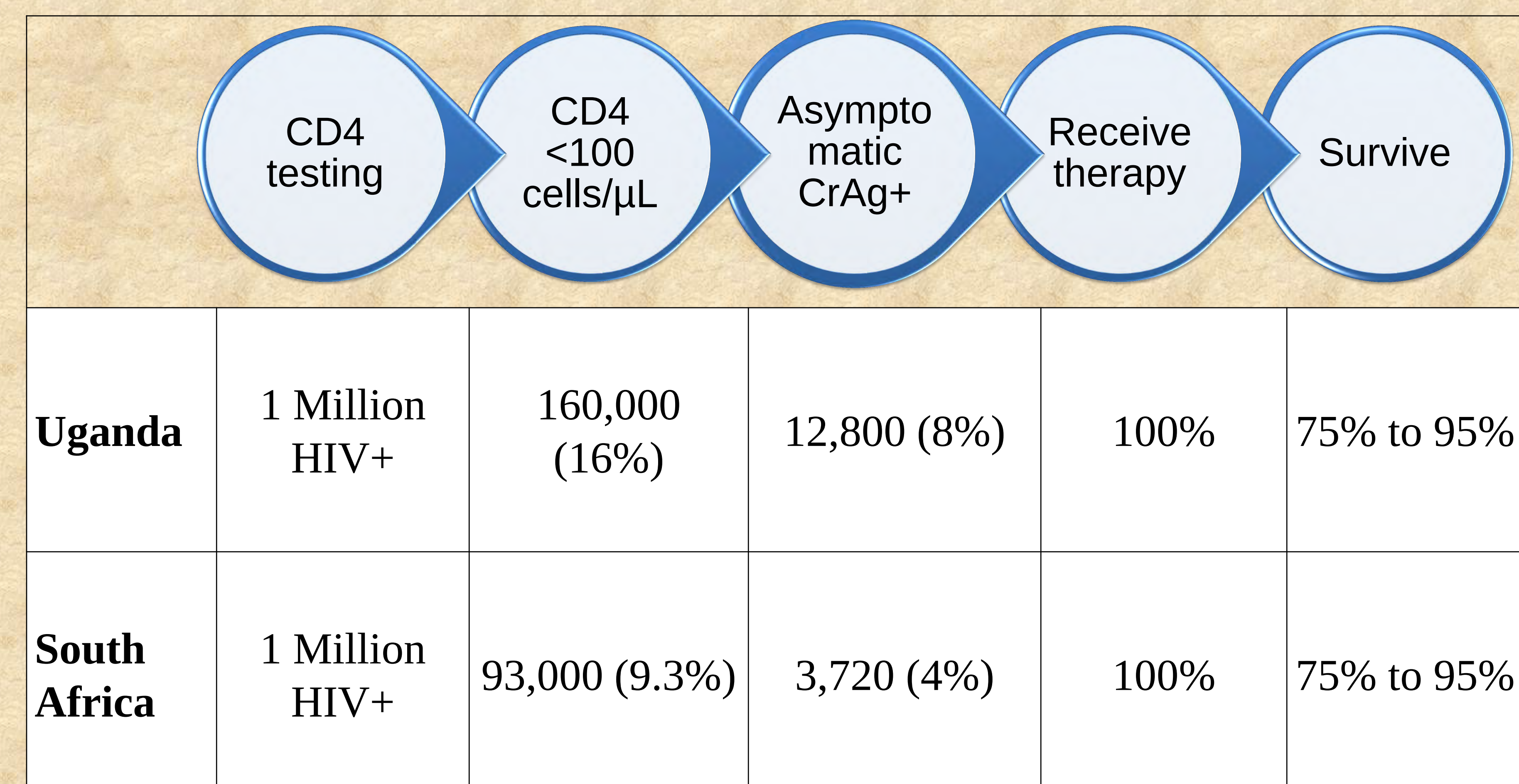
Objective: We sought to explore the threshold efficacy and cost of AmBisome® + fluconazole that would improve on current standard of care fluconazole therapy in Uganda (low income) and South Africa (middle income).

Methods:

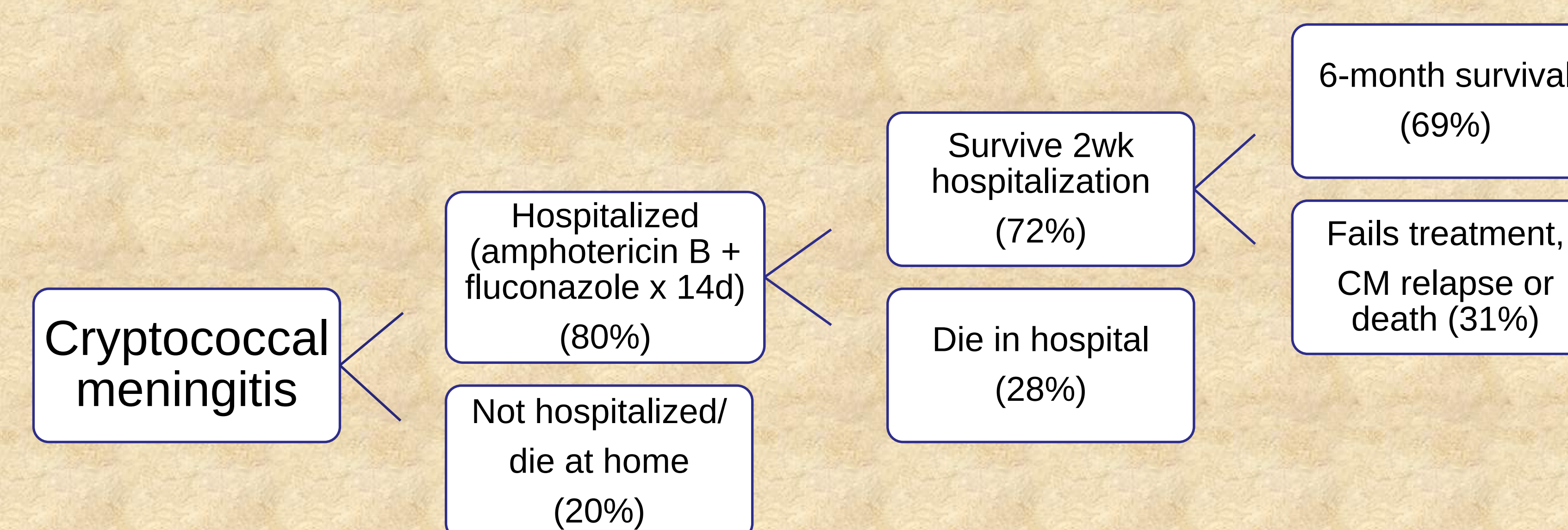
- We used a decision analytic model to evaluate CrAg screening and treatment outcomes for those in Uganda and South Africa with a CD4<100 cells/μL with AmBisome® 10mg/kg x1 with fluconazole preemptive treatment.
- We estimated costs for CrAg screening, preemptive therapy, hospitalization, and maintenance therapy with AmBisome® + fluconazole, compared to fluconazole alone.
- Parameter assumptions were taken from large prospective CrAg screening studies in Uganda and clinical trials from sub-Saharan Africa.
- CrAg+ persons could be: a) asymptomatic and eligible for preemptive treatment; or b) symptomatic with meningitis and hospitalized.
- Hospitalized patients with meningitis were treated with Amphotericin B deoxycholate + fluconazole x 14 days
- We varied parameters for LMICs CrAg prevalence and hospitalization costs

Methods:

Model: Cascade of screening and treatment



Model: Cryptococcal meningitis assumptions



Input Costs

CrAg Screening		Meningitis treatment	
	Costs (USD)		Costs (USD)
CrAg test cost	\$3.41	Hospital stay x 14 days	\$139.18
Fluconazole 200mg tablet	\$0.14	Amphotericin B deoxycholate 50mg x 14d	\$165.94
AmBisome® 50mg vial	\$16.25	Lab testing	\$89.18
Preemptive AmBisome® (10mg/kg x1) + fluconazole course	\$201.56	Personnel	\$93.03
		Lumbar punctures x 3	\$27.88
		Hospital supplies	\$47.69
		Total hospitalization (Uganda)	\$562.90
		Total hospitalization (South Africa)	\$2940

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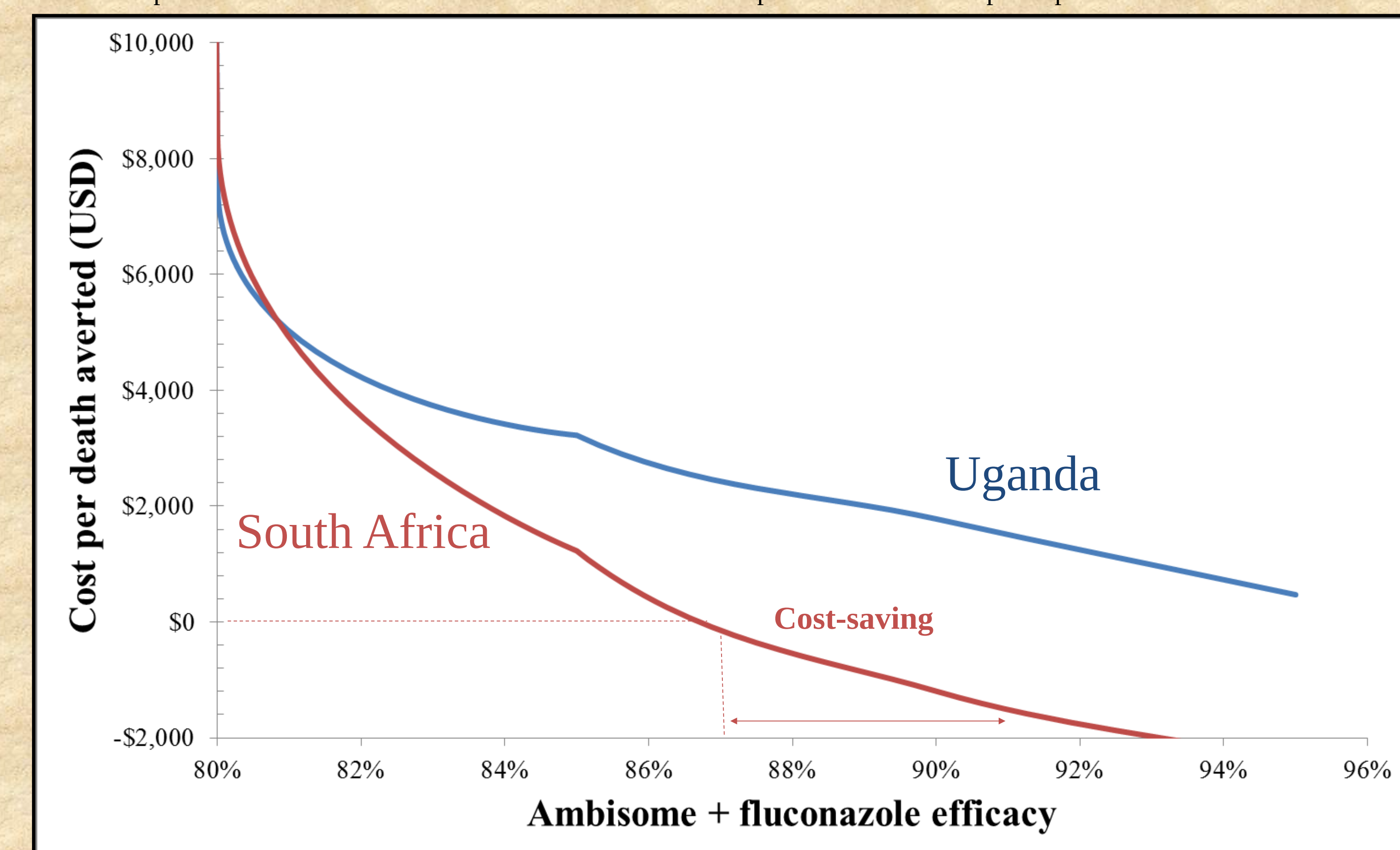
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Results: Cost to avert one death by AmBisome® price and efficacy

Uganda

AmBisome® Price	AmBisome® + fluconazole efficacy	Cost per death averted*	Ugandan Interpretation
\$16.25	75%	\$>2,000,000	
\$16.25	80%	\$7552	
\$16.25	85%	\$3218	
\$16.25	90%	\$1778	Cost-effective
\$16.25	95%	\$470	Cost-effective

* Cost per death averted with AmBisome® + fluconazole compared to fluconazole preemptive treatment alone



South Africa

AmBisome® Price	AmBisome® + fluconazole efficacy	Cost per death averted*	South African Interpretation
\$16.25	75%	\$>1,000,000	
\$16.25	80%	\$8407	Cost-effective
\$16.25	85%	\$1222	Cost-effective
\$16.25	90%	\$-1195	Cost saving
\$16.25	95%	\$-2400	Cost saving

Discussion:

- Single dose AmBisome® for asymptomatic Cryptococcal infection given at 10mg/kg once in conjunction with fluconazole has the potential to save lives and costs, if proven effective.
- At the discounted price of \$16.25 per vial, AmBisome® + fluconazole would be cost-saving in South Africa if >87% effective, and cost-effective if ≥80% effective
- At the discounted price of \$16.25 per vial, AmBisome® + fluconazole would be cost-effective at ≥90% efficacy in Uganda
- Studies on the efficacy of single dose AmBisome® for asymptomatic cryptococcal antigenemia are needed