



# The economics of cryptococcal meningitis packages of care

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**HIV LEARNING NETWORK**  
The CQUIN Project for Differentiated Service Delivery

# Outline

Why health economics in AHD packages of care?

Evidence to support decision-making: examples

Gaps in economic evidence



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# Why health economics?

- Scarce resources
- Policy question: **does this intervention work?**
- Economic question: **is it worth it?**
- Health economics defines what is **“work”** and **“worth”**



# Health services costing

- Resource use measured in all patients at individual level in all arms, e.g., bed days, CM-specific treatment, general treatment, laboratory tests, etc.
- Health care unit costs estimated empirically
- Overhead and other hospital expenditure data were aggregated and attributed proportionally to patients in all trial arms

# Example I: REMSTART

Clinical Infectious Diseases

MAJOR ARTICLE



## Cryptococcal Meningitis Screening and Community-based Early Adherence Support in People With Advanced Human Immunodeficiency Virus Infection Starting Antiretroviral Therapy in Tanzania and Zambia: A Cost-effectiveness Analysis

Godfather Dickson Kimaro,<sup>1,2</sup> Lorna Guinness,<sup>3</sup> Tinevimbo Shiri,<sup>4</sup> Sokoine Kivuyo,<sup>1</sup> Duncan Chanda,<sup>5</sup> Christian Bottomley,<sup>2</sup> Tao Chen,<sup>4</sup> Amos Kahwa,<sup>1</sup> Neil Hawkins,<sup>3</sup> Peter Mwaba,<sup>6</sup> Sayoki Godfrey Mfinanga,<sup>1,4</sup> Thomas S. Harrison,<sup>7</sup> Shabbar Jaffar,<sup>4</sup> and Louis W. Niessen<sup>4,8</sup>

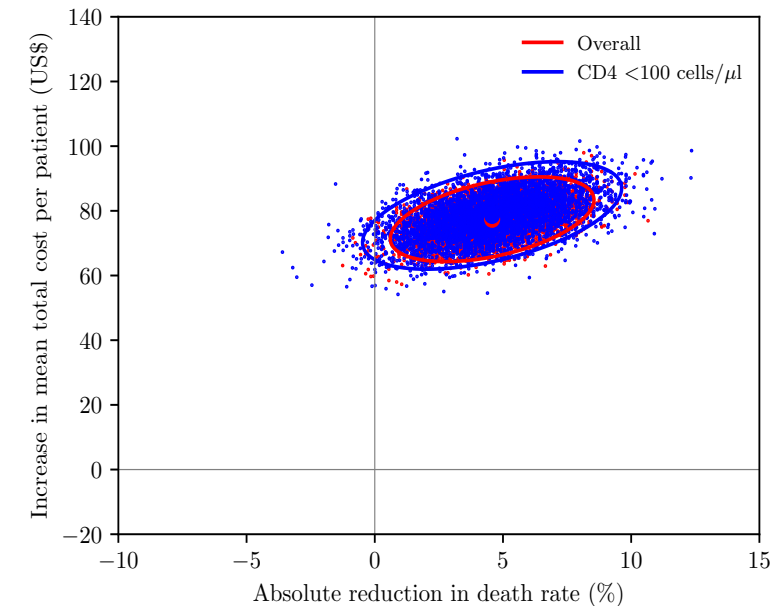
The primary economic outcome was health service care cost per life-year saved

Cost component	Unit price(\$)	Unit of measurement	Intervention (n=1001)	Standard care (N=998)
<b>Outpatients visits</b>				
Initial visits	8.93	Visit	Mean (STD) 1.05(0.36)	Mean (STD) 1.04(0.37)
ART eligibility assessment visit	7.99	Visit	1.16(0.44)	1.10(0.33)
Six-monthly clinic review visit	8.92	Visit	0.81(0.77)	0.79(0.81)
Routine follow-up visit	7.62	Visit	3.89(2.77)	3.56(2.81)
Home visit <sup>b</sup>	19.51	Visit	3.06(1.43)	0.01(0.18)
<b>Laboratory</b>				
CD4 count test	20.86	Test	1.55(0.62)	1.51(0.62)
Liver function (ALT) test	1.16	Test	1.27(0.59)	1.19(0.56)
Creatinine test	0.41	Test	0.89(0.44)	0.87(0.44)
Haemoglobin (Hb) test	1.15	Test	1.46(0.73)	1.35(0.68)
Syphilis (VDRL) test	1.13	Test	0.03(0.18)	0.03(0.17)
Pregnancy test	2.50	Test	0.14(0.47)	0.13(0.44)
Xpert test	25.23	Test	0.96(0.61)	0.82(0.46)
CrAg test	5.24	Test	0.98(0.13)	0.01(0.08)
CSF test	21.55	Test	0.01(0.09)	0.00(0.00)
Chest X-ray	2.70	X-ray	0.05(0.21)	0.04(0.19)
<b>Medication</b>				
Days on antiretroviral therapy	0.56	Day	260.47(137.23)	250.27(140.70)
Days on co-trimoxazole treatment	0.02	Day	263.22(136.00)	254.82(139.76)
10-week fluconazole course <sup>c</sup>	6.35	Course	0.07(0.37)	0.00(0.00)
<b>Hospitalisation</b>				
Overnight hospital stay	35.00	Day	0.18(1.17)	0.22(1.55)

# REMSTART: Cost-effectiveness analyses

	Life expectancy (years) <sup>a</sup> , 95% CI	Standard care arm				Intervention arm				Incremental comparison of the intervention versus standard care		
		N	Mean total cost (US\$) per person (95% CI)	All-cause mortality		N	Mean total cost (US\$) per person (95% CI)	All-cause mortality		Incremental cost (US\$) per person (95% CI)	Incremental death (%) (95% CI)	ICER (incremental cost per life years saved) (95% CI)
				Events (95% CI)	Death rate (95% CI)			Events (95% CI)	Death rate (95% CI)			
CD4 <200 cells / $\mu$ l	24.0 (22.2 – 25.8)	998	262 (254 – 269)	180 (156-203)	18.0 (15.6-20.3)	1001	339 (331-347)	134 (113-156)	13.4 (11.3-15.6)	77 (66-88)	-4.6 (-7.8, -1.3)	70 (43, 211)
CD4<100 cells / $\mu$ l	18.7 (17.2 – 20.3)	707	262 (253 – 271)	144 (123-165)	20.2 (17.4-23.3)	724	341 (331-350)	114 (94-134)	15.7 (13.0-18.5)	79 (65-92)	-4.5 (-8.6, -0.6)	91 (49, 443)

CrAg screening plus adherence support improved survival by 24%, *i.e.*, from 18.0% to 13.4%, at an extra cost of about \$80 per patient.



# Example II: ACTA

Clinical Infectious Diseases

MAJOR ARTICLE



## Healthcare Costs and Life-years Gained From Treatments Within the Advancing Cryptococcal Meningitis Treatment for Africa (ACTA) Trial on Cryptococcal Meningitis: A Comparison of Antifungal Induction Strategies in Sub-Saharan Africa

Tao Chen,<sup>1,2</sup> Lawrence Mwenge,<sup>2,3</sup> Shabir Lakhji,<sup>3</sup> Duncan Chanda,<sup>4</sup> Peter Mwaba,<sup>5</sup> Sile F. Mollo,<sup>6</sup> Adrian Gheorghie,<sup>7</sup> Ulla K. Griffiths,<sup>7</sup> Robert S. Heyderman,<sup>8,9,10</sup> Cecilia Kanyama,<sup>11</sup> Charles Kouanfack,<sup>12,13</sup> Sayoki Mfinanga,<sup>1,14</sup> Adrienne K. Chan,<sup>15,16</sup> Elvis Temfack,<sup>17,18</sup> Sokoine Kivuyo,<sup>14</sup> Mina C. Hosseini,<sup>11,19</sup> Olivier Lortholary,<sup>18,20</sup> Angela Loyse,<sup>6</sup> Shabbar Jaffar,<sup>1,3</sup> Thomas S. Harrison,<sup>6,b</sup> and Louis W. Niessen,<sup>1,21,b</sup> for the ACTA Trial Team<sup>c</sup>

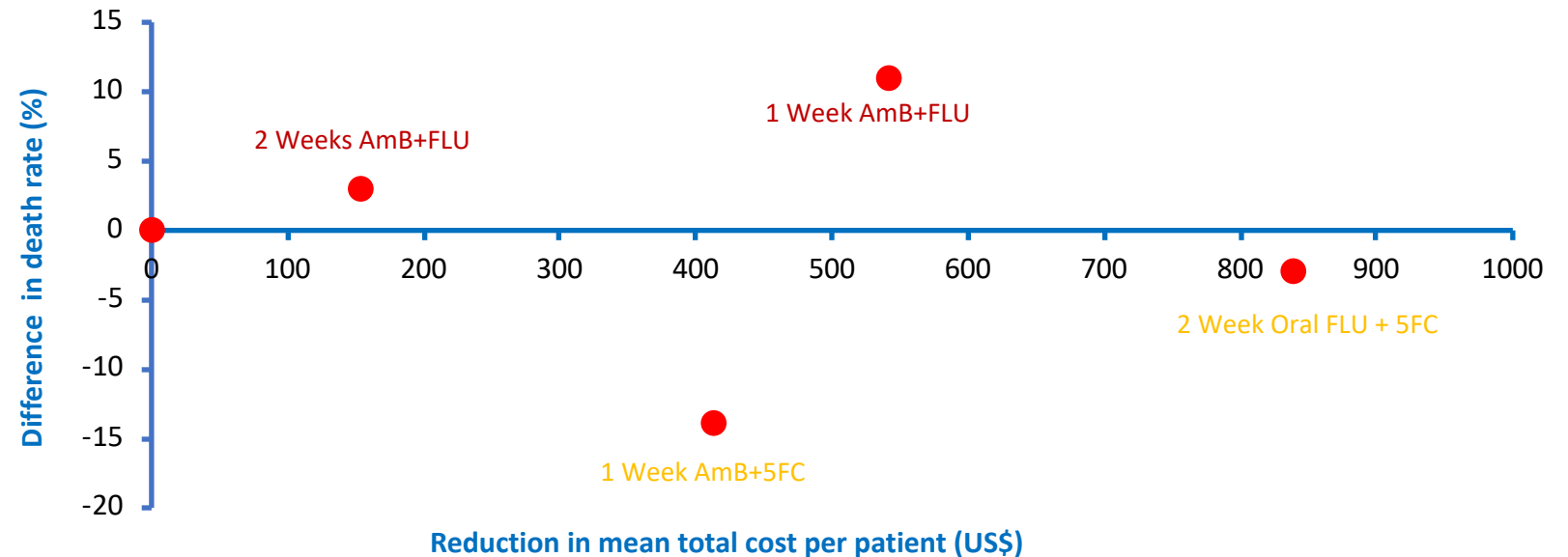
Mean (standard deviation) resource use per patient by trial arm, over 10 weeks trial period.

Service use item	Service use item	2 weeks oral FLU and 5FC	1 week AmB+FLU	1 week AmB+5FC	2 weeks AmB+FLU	2 weeks AmB+5FC
<b>Hospitalization</b>	Days	17.33(15.29)	17.14(18.04)	17.99(15.06)	16.09(12.27)	19.31(18.31)
<b>Re-hospitalization</b>	Days	2.02(5.23)	2.14(6.31)	0.88(2.72)	1.77(5.48)	1.38(4.10)
<b>CM-specific treatment</b>						
<b>Trial drug</b>						
Fluconazole (FLU)	Tablet (200 mg)	187.96(123.83)	147.18(130.65)	161.50(148.25)	170.68(125.26)	120.37(159.31)
Flucytosine (5FC)	Tablet (500mg)	131(56)	0.00(0.00)	74(23)	0.00(0.00)	131(59)
Amphotericin B (AmB)	Vial (50mg)	0.00(0.00)	6.50(2.60)	7.35(2.12)	12.71(5.53)	13.07(5.94)
<b>Other intervention</b>						
Potassium	days	0.00(0.00)	6.05(2.20)	6.72(1.43)	11.71(4.41)	11.83(4.62)
Magnesium	days	0.00(0.00)	6.05(2.20)	6.72(1.43)	11.71(4.41)	11.83(4.62)
<b>Blood transfusion</b>	Units	0.12(0.52)	0.23(0.66)	0.15(0.57)	0.31(0.73)	0.37(0.86)
<b>Lumber puncture</b>	times	3.13(1.84)	2.62(1.07)	3.26(1.39)	2.93(1.59)	2.98(1.44)
<b>Bio-chemistry</b>						
Total Bilirubin	times	1.69(2.95)	1.57(2.77)	1.74(2.99)	1.44(2.79)	1.63(2.94)
CRP	times	0.06(0.31)	0.09(0.39)	0.04(0.21)	0.11(0.42)	0.10(0.41)
ALT	times	3.48(2.09)	3.04(1.73)	3.69(2.00)	3.66(2.32)	3.40(1.99)
Magnesium (Mg)	times	0.19(0.73)	0.20(0.75)	0.20(0.67)	0.16(0.66)	0.22(0.81)
Potassium (K)	times	7.00(3.15)	6.23(3.21)	7.22(2.35)	7.07(3.12)	6.83(3.21)
Sodium (Na)	times	7.02(3.09)	6.25(3.21)	7.27(2.41)	7.12(3.14)	6.90(3.23)
Urea	times	6.99(3.12)	6.22(3.14)	7.19(2.44)	7.04(3.07)	6.79(3.12)
Creatinine	times	7.15(3.17)	6.32(3.32)	7.39(2.45)	7.18(3.12)	6.98(3.29)
Proteinuria	times	7.64(3.48)	6.82(3.80)	7.82(2.71)	7.87(3.63)	7.47(3.65)
<b>Full Blood Count</b>	times	4.62(2.39)	4.26(2.62)	4.68(1.96)	4.69(2.41)	4.63(2.60)
<b>CD4 Count</b>	times	0.97(0.37)	1.01(0.37)	0.93(0.29)	0.97(0.45)	0.98(0.30)
<b>Microbiology *</b>						
CSF - negative	times	0.64(0.88)	0.77(0.99)	1.27(1.04)	0.75(0.84)	1.34(1.21)
CSF - positive	times	2.44(1.88)	1.83(1.14)	1.95(1.39)	2.17(1.63)	1.56(1.02)

# ACTA: Cost-effectiveness analyses

ACTA treatment arms	Total cost per patient and death rate (%) per arm		Incremental comparison of 1 week of AmB+5FC versus 2 weeks of FLU+5FC		
	Mean total costs	Deaths (%)	Incremental costs per patient	Incremental death rate (%)	Incremental costs per life year saved
2 week Oral FLU+5FC	1442 (1336 -1565)	35(28-41)	Reference	Reference	Reference
1 week AmB+FLU	1763 (1567 -1979)	49(39-58)	-	-	-
1 week AmB+5FC	1861 (1724 -2033)	24(16-31)	419 (236, 619)	11 (0.6, 21)	208 (91, 1210)
2 weeks AmB+FLU	2125 (1946 -2313)	41(32-49)	-	-	-
<b>2 week AmB + 5FC</b>	2285 (2070 -2525)	38(29-46)	-	-	-

Reduction in cost per patient and change in deaths in 4 arms relative to that in the gold standard of 2 weeks AmB+5FC





# Example III: Oral 5FC+FLU

Clinical Infectious Diseases

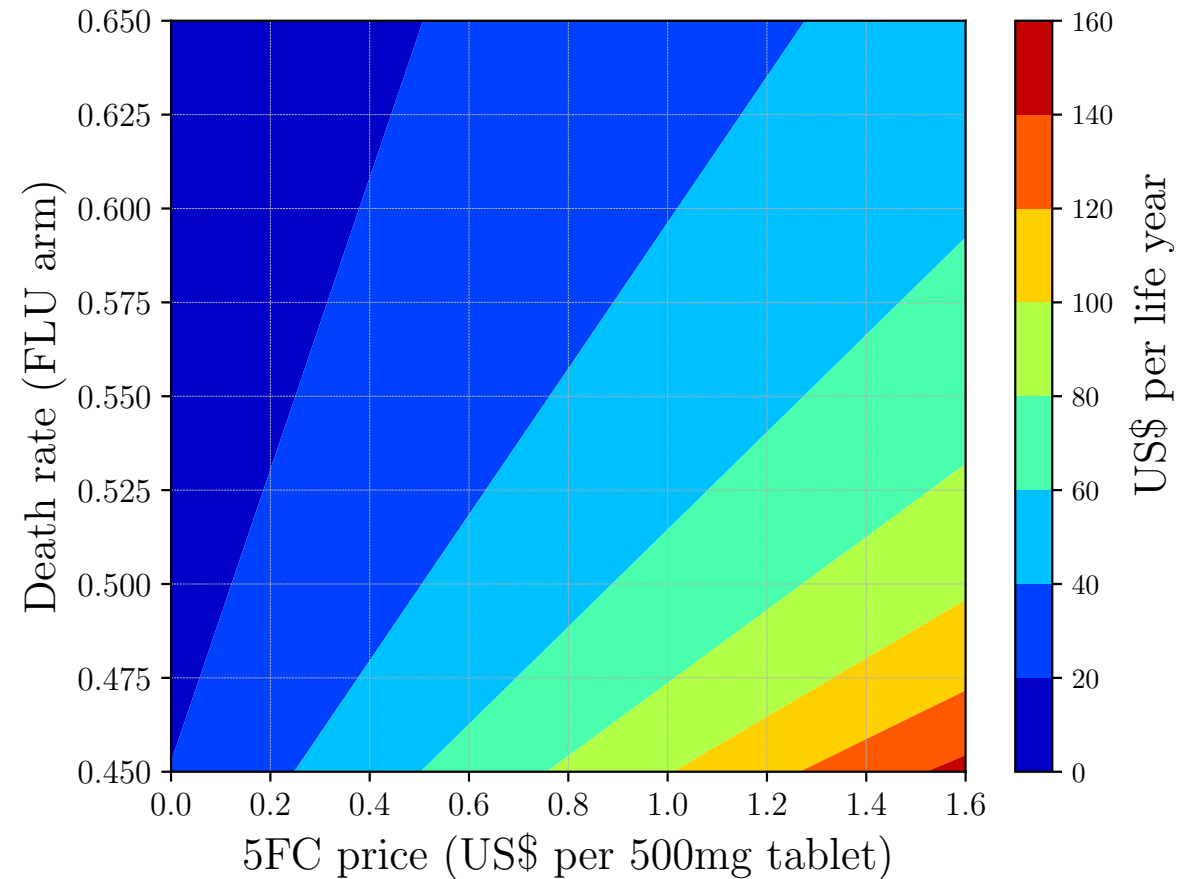
MAJOR ARTICLE



## Addition of Flucytosine to Fluconazole for the Treatment of Cryptococcal Meningitis in Africa: A Multicountry Cost-effectiveness Analysis

Tinevimbo Shiri,<sup>1a</sup> Angela Loyse,<sup>2a</sup> Lawrence Mwenge,<sup>3</sup> Tao Chen,<sup>1</sup> Shabir Lakhi,<sup>4</sup> Duncan Chanda,<sup>4,5</sup> Peter Mwaba,<sup>6</sup> Sile F Molloy,<sup>2</sup> Robert S. Heyderman,<sup>7,8,9</sup> Cecilia Kanyama,<sup>10</sup> Mina C. Hosseinipour,<sup>10,11</sup> Charles Kouanfack,<sup>12,13</sup> Elvis Temfack,<sup>14,15</sup> Sayoki Mfinanga,<sup>1,16</sup> Sokoine Kivuyo,<sup>16</sup> Adrienne K. Chan,<sup>17,18</sup> Joseph N. Jarvis,<sup>19,20</sup> Olivier Lortholary,<sup>15,21</sup> Shabbar Jaffar,<sup>1</sup> Louis W Niessen,<sup>1,22</sup> and Thomas S Harrison<sup>20</sup>

Total costs per patient and death rate (%)			Incremental comparison of 2 weeks of oral FLU + 5FC versus oral FLU monotherapy		
Treatment	Total costs (\$)	Deaths (%)	Incremental costs/patient (\$)	Incremental death (%)	ICER/life year saved
FLU alone	628(557-709)	54(43-64)	reference	reference	
FLU + 5FC	847(776-929)	35(29-42)	219(110-329)	19(6-30)	65(28-208)



# Gaps in economic evidence

- Costs to patients, families and society in general, including health care financing
- Long term consequences unknown
- Implementation
- Quality of life