THE LANCET
Global Health

Supplementary appendix 6

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

A five-country cost-effectiveness analysis of the AMBITION-cm single, high-dose liposomal amphotericin regimen for HIV-associated cryptococcal meningitis in sub-Saharan Africa

SUPPLEMENTARY MATERIAL

Table of Contents

The Ambition Study Group

In addition to the named authors, the following were members of the Ambition Study Group:

Botswana Harvard AIDS Institute Partnership / Princess Marina Hospital, Gaborone, Botswana – J Goodall, K Lechiile, N Mawoko, T Mbangiwa, J Milburn, R Mmipi, P Ponatshego, I Rulaganyang, K Seatla, K Siamisang, N Tlhako and K Tsholo.

University of Cape Town / Mitchells Plain Hospital / Khayelitsha District Hospital, Cape Town, South Africa – S April, A Bekiswa, L Boloko, H Bookholane, T Crede, L Davids, R Goliath, S Hlungulu, R Hoffman, H Kyepa, N Masina, D Maughan, T Mnguni, S Moosa, T Morar, M Mpalali, J Naude, I Oliphant, A Singh, S Sayed, L Sebesho, M Shey and L Swanepoel.

Malawi-Liverpool-Wellcome Trust Clinical Research Programme / Queen Elizabeth Central Hospital, Blantyre, Malawi – M Chasweka, W Chimang'anga, T Chimphambano, E Gondwe, H Mzinganjira, A Kadzilimbile, S Kateta, E Kossam, C Kukacha, B Lipenga, J Ndaferankhande, M Ndalama, R Shah, A Singini, K Stott and A Zambasa.

UNC Project, Kamuzu Central Hospital, Lilongwe, Malawi – T Banda, T Chikaonda, G Chitulo, L Chiwoko, N Chome, M Gwin, T Kachitosi, B Kamanga, M Kazembe, E Kumwenda, M Kumwenda, C Maya, W Mhango, C Mphande, L Msumba, T Munthali, D Ngoma, S Nicholas, L Simwinga, A Stambuli, G Tegha and J Zambezi.

Infectious Diseases Institute / Kiruddu General Hospital, Kampala, Uganda – C Ahimbisibwe, A Akampurira, A Alice, F Cresswell, J Gakuru, E Kagimu, J Kasibante, D Kiiza, J Kisembo, R Kwizera, F Kugonza, E Laker, T Luggya, A Lule, A Musubire, R Muyise, O Namujju, J Ndyetukira, L Nsangi, M Okirwoth, J Rhein, M K Rutakingirwa, A Sadiq, K Ssebambulidde, K Tadeo, A Tukundane and D Williams.

Infectious Diseases Institute / Mbarara Regional Referral Hospital, Mbarara, Uganda – L Atwine, P Buzaare, M Collins, N Emily, C Inyakuwa, S Kariisa, J Mwesigye, S Niwamanya, A Rodgers, J Rukundo, I Rwomushana, M Ssemusu and G Stead.

University of Zimbabwe / Parirenyatwa General Hospital, Harare, Zimbabwe – K Boyd, S Gondo, P Kufa, E Makaha, C Moyo, T Mtisi, S Mudzingwa, C Mutata, T Mwarumba and T Zinyandu.

Institut Pasteur, Paris, France – A Alanio, F Dromer, O Lortholary and A Sturny-Leclere.

London School of Hygiene and Tropical Medicine, London, UK – P Griffin and S Hafeez.

St George's University, London, UK – A Loyse.

Liverpool School of Tropical Medicine, Liverpool UK – E van Widenfelt.

Table S1: Trial blood monitoring schedule and proposed real-world monitoring for each treatment regimen.

	DAY 1	DAY 3	DAY 5	DAY 7	DAY 10	DAY 12	DAY 14	DAY 28
All trial participants								
Creatinine, Urea, Potassium and Sodium	X	X	X	X	X	X	X	X
Full Blood Count	X			X			X	X
ALT	X			X			X	X
AmBisome arm								
Creatinine, Urea, Potassium and Sodium	X	X						
Full Blood Count	X			X				
ALT	X			X				
Control arm								
Creatinine, Urea, Potassium and Sodium	X	X		X	X			
Full Blood Count	X			X			X	
ALT	X						X	

ALT denotes alanine aminotransferase

Table S2: Mean (+SD) empirical resource use per participant by trial arm over the 10-week trial period for all AMBITION-cm participant.

Resource	AmBisome (n=406)	Control (n=407)
Hospitalisation		
Hospital admission, per bed-day	12·98 (9·06)	12·93 (7·12)
Hospital readmission, per bed-day	1·77 (5·15)	1·62 (5·01)
Lumbar puncture	5·66 (5·77)	6·01 (6·50)
Blood Tests		
Chemistry	4·11 (1·70)	4·34 (2·08)
Chemistry plus ALT	4·24 (1·86)	4·18 (1·73)
Full blood count	5·10 (2·74)	5·18 (2·58)
CD4 count	0·85 (0·40)	0·85 (0·43)
HIV viral Load	0·49 (0·56)	0·50 (0·54)
Microbiology		
CSF analysis	1·52 (0·94)	1·56 (1·10)
Urine culture	0·098 (0·42)	0·093 (0·40)
Bacterial blood culture, aerobic	0·18 (0·56)	0·14 (0·50)
Sputum culture, mycobacteria	0·015 (0·12)	0·0098 (0·099)
Sputum AFB	0·030 (0·17)	0·027 (0·18)
Sputum GeneXpert	0·094 (0·32)	0·088 (0·32)
CSF GeneXpert	0·24 (0·51)	0·22 (0·49)
Radiology		
Chest x-ray	0·41 (0·66)	0·37 (0·60)
CT Head	0·14 (0·41)	0·12 (0·35)
Cryptococcal specific treatment		
Fluconazole, per 200mg	255·06 (99·77)	212·93 (91·76)

Flucytosine, per 500mg	137·02 (45·57)	69·50 (21·18)
AmB, per 50mg	0	7·74 (2·26)
L-AmB, per 50mg	11·17 (2·21)	0
Other treatment		
5% dextrose, per litre	1 (0)	6·56 (1·41)
0.9% normal saline, per litre	2 (0)	13·12 (2·83)
Intravenous potassium, per ampoule	1 (0)	6·56 (1·41)
Oral potassium, per tablet	11·71 (1·33)	33·32 (7·98)
Oral magnesium, per tablet	5·86 (0·67)	16·66 (3·99)
Blood transfusion, per unit	0·20 (0·79)	0·43 (1·02)
Thrombophlebitis treatment (oral)†	0·012 (0·11)	0·049 (0·22)
Thrombophlebitis treatment (IV)†	0·0074 (0·86)	0·020 (0·14)
Bacteraemia†	0·027 (0·16)	0·030 (0·17)

*AFB denotes acid fast bacilli; ALT alanine aminotransferase; AmB amphotericin B deoxycholate; CSF cerebrospinal fluid; CT computerised tomography; L-AmB liposomal amphotericin.

†A standard, complete course of antimicrobial treatment for the indication listed.

Figure S1: Survival to discharge from hospital and discharge data from the AMBITION-cm trial indicating the proportion of participants who survived admission and the proportion of those who survived admission and were discharged between days seven and nine.
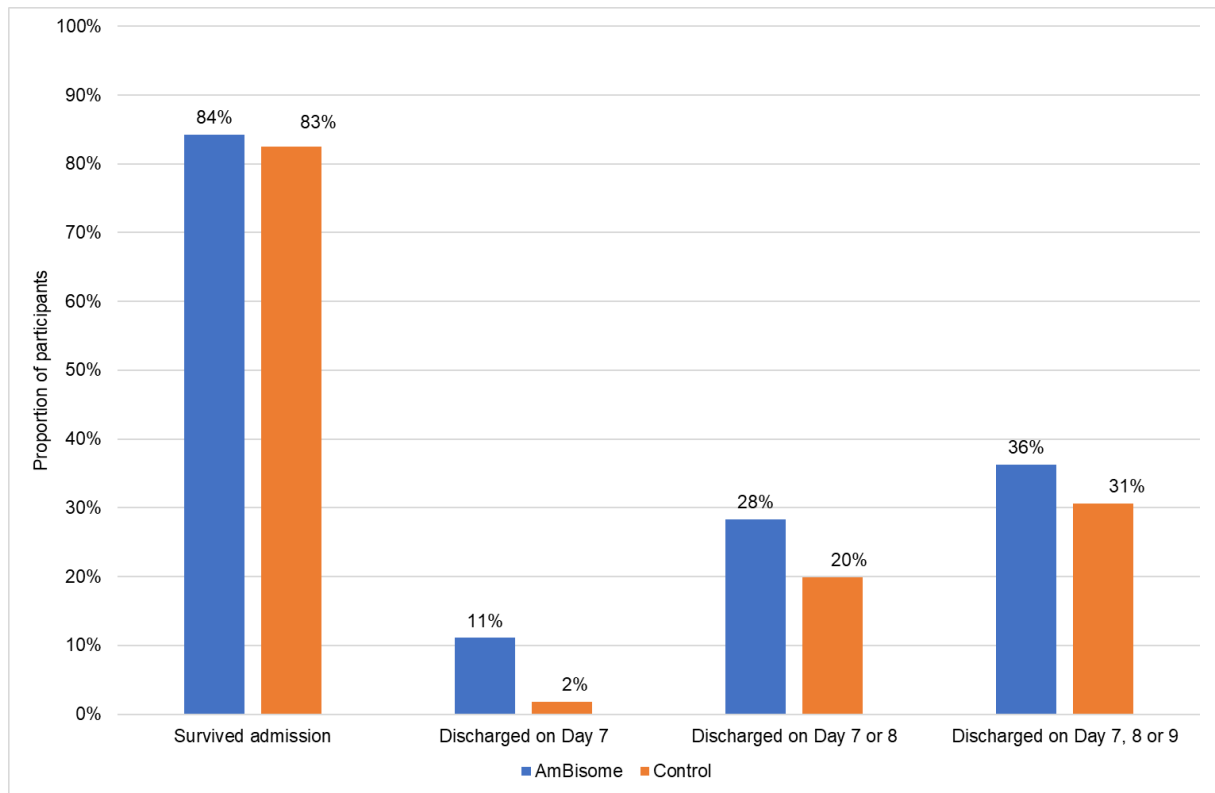
Figure S2: The proportion of the total in-trial per-participant costs attributable to different groups of resource units (US$ 2020) in the Malawi setting.
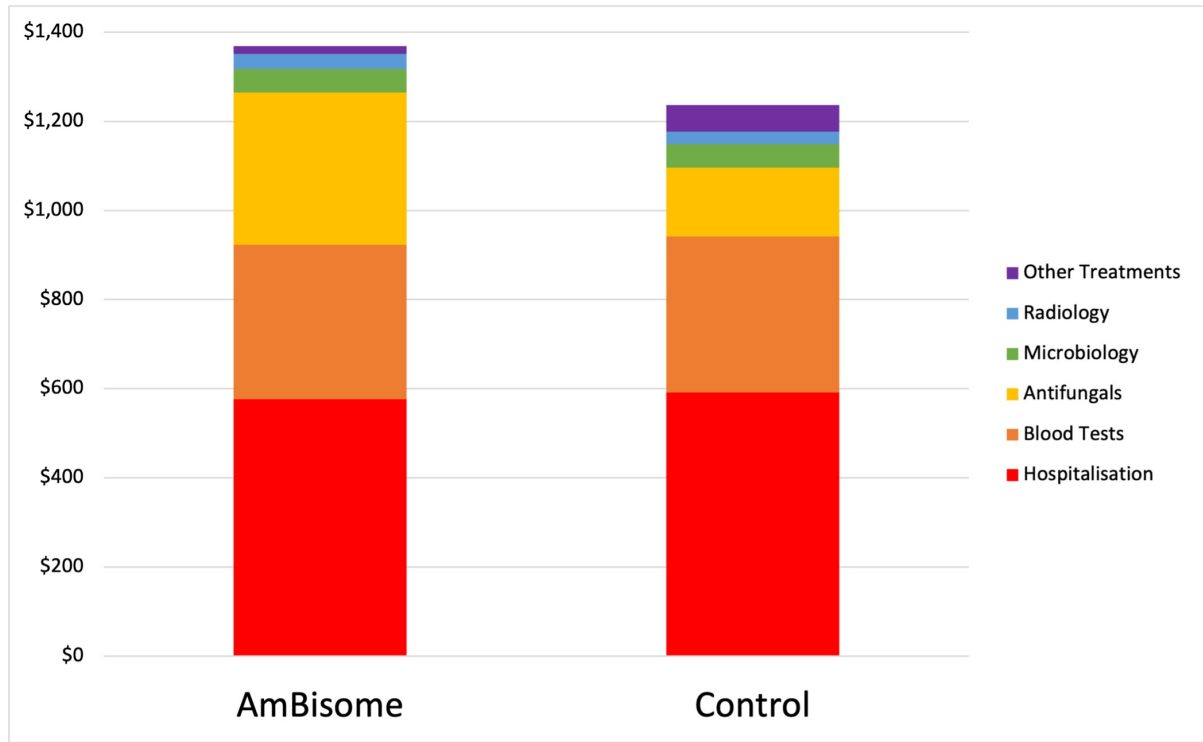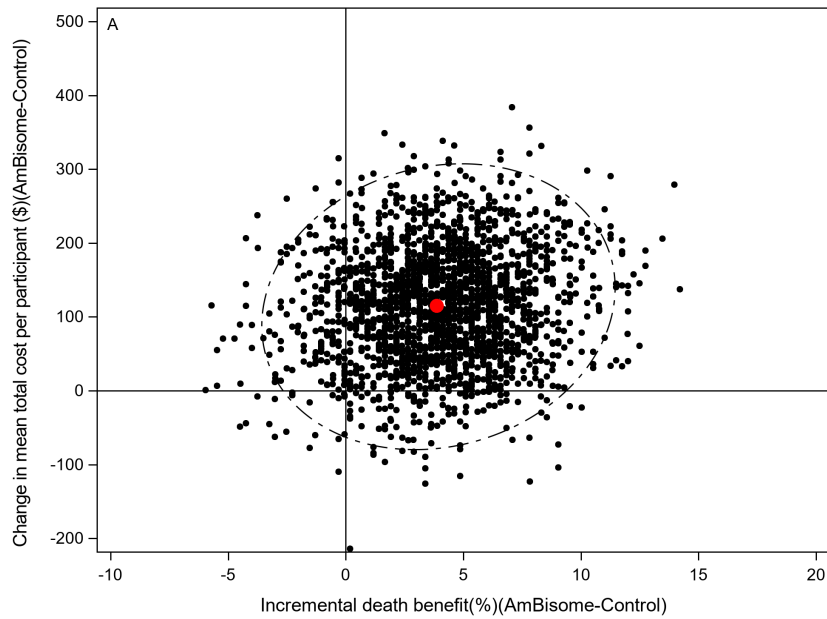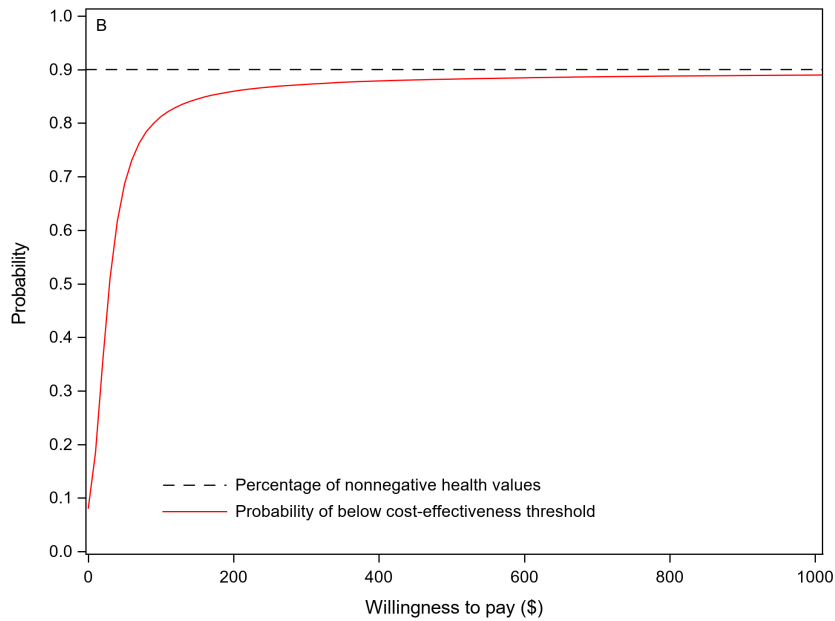
Figure S3: Health Care cost of In-Trial Resource Use for 1) Botswana, 2) South Africa, 3) Uganda and 4) Zimbabwe. A) A cost-effectiveness plane presenting the incremental costs and death benefit (%) in the AmBisome arm after 10,000 bootstrap iterations (2,000 selected at random are shown) with the red dot denoting the mean and the ellipse showing 95% confidence intervals of the simulation and B) Cost-effectiveness acceptability curve of the AmBisome arm against the control. The red line denotes the cumulative probability of AmBisome being more cost effective than the control treatment at a particular willingness to pay (WTP). The dashed line denotes the cumulative probability of negative health benefits.

1A.

1B

2A.

9
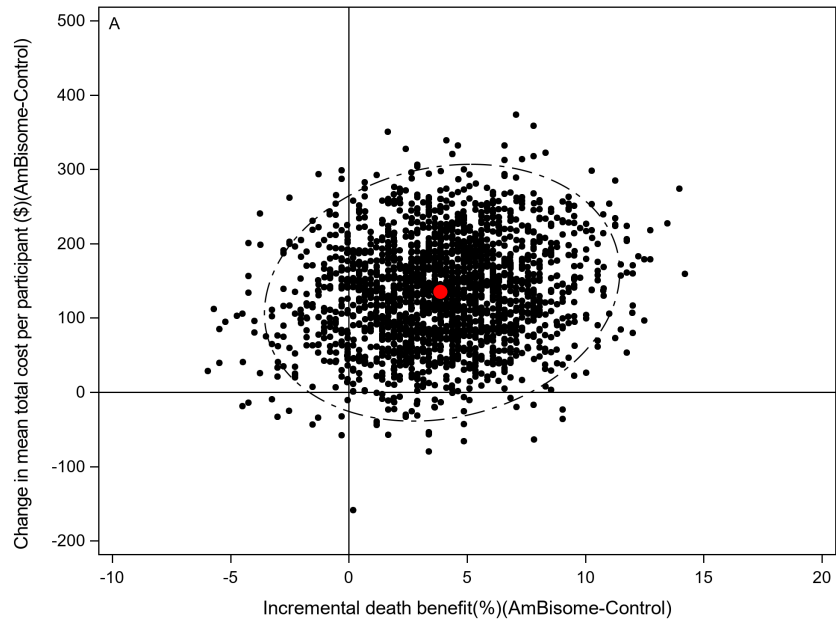
2B
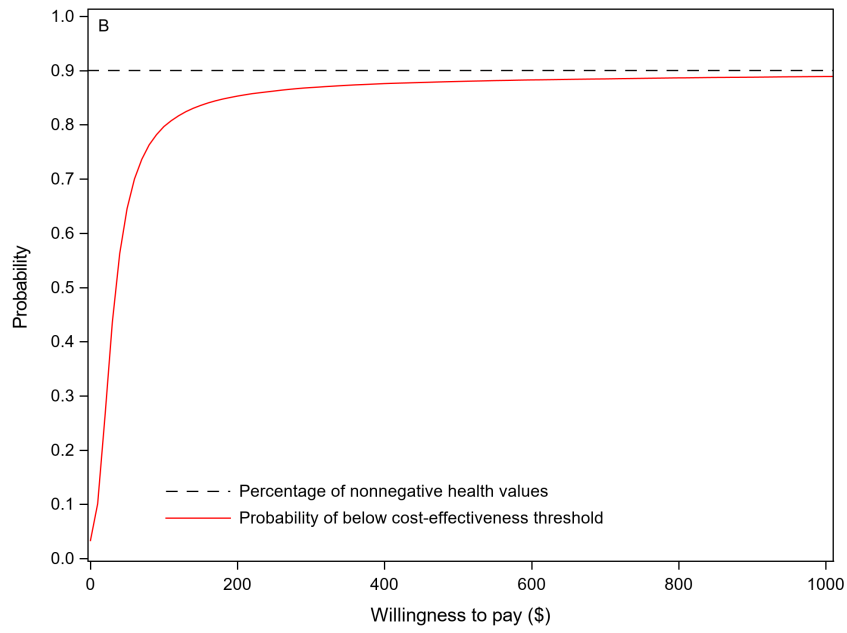
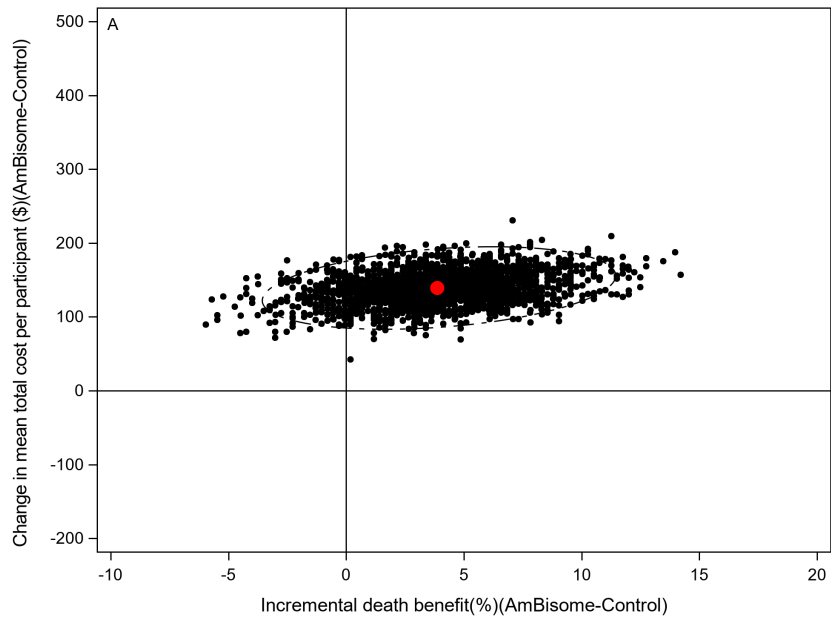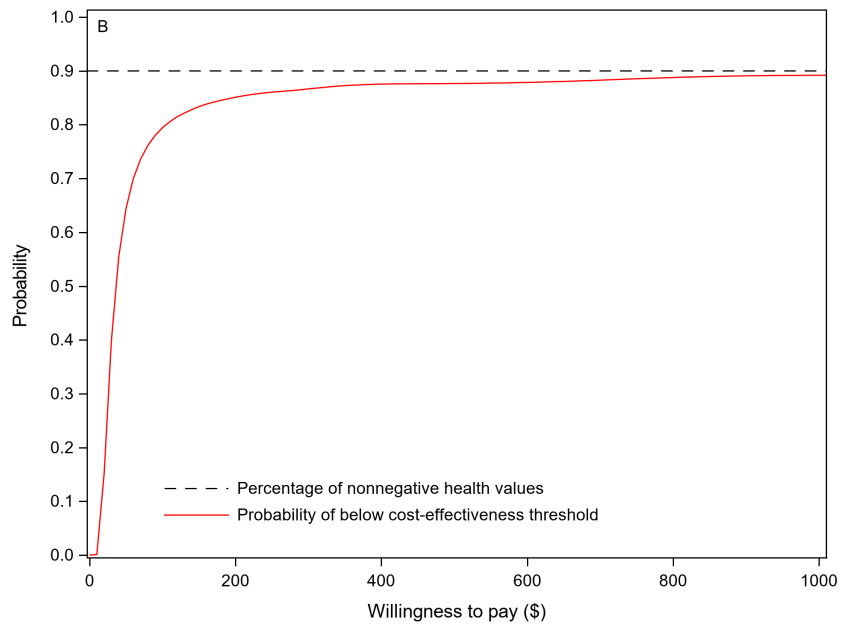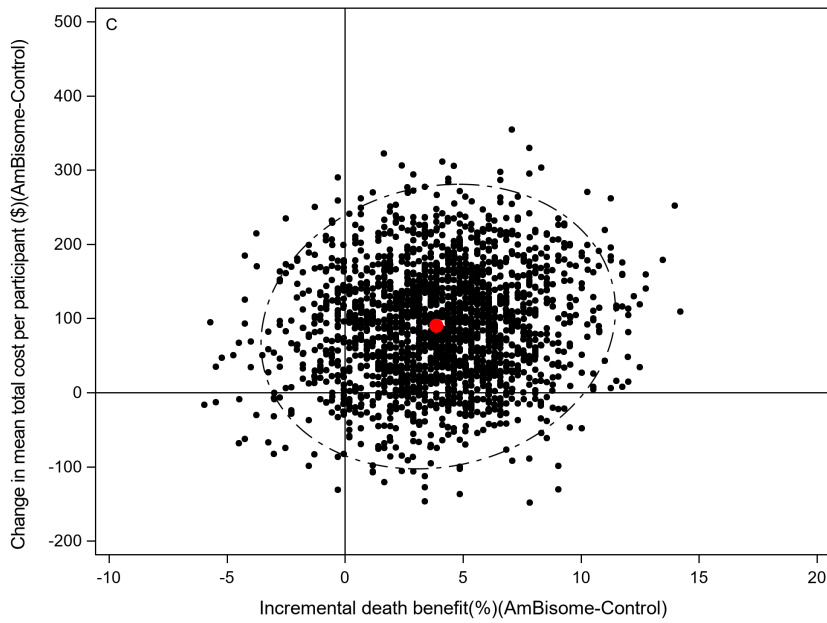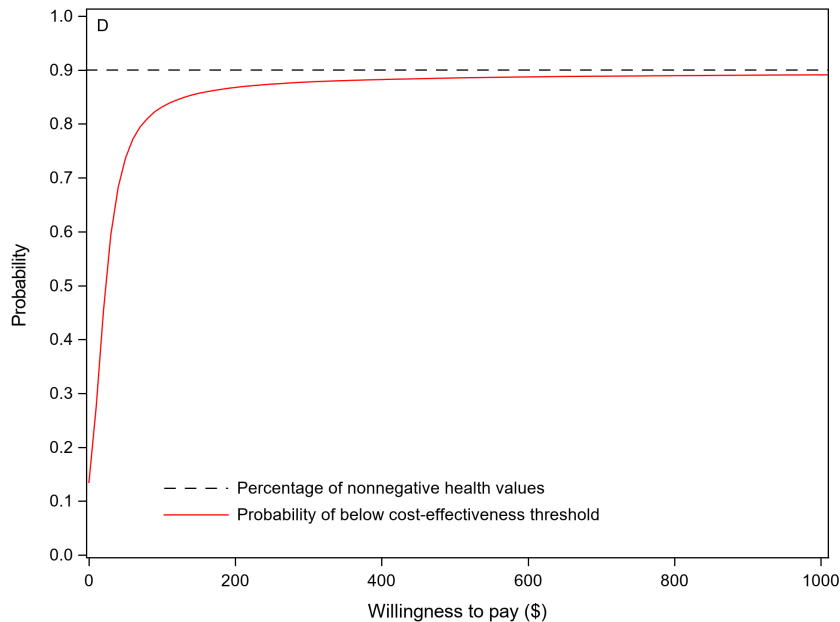
3A.
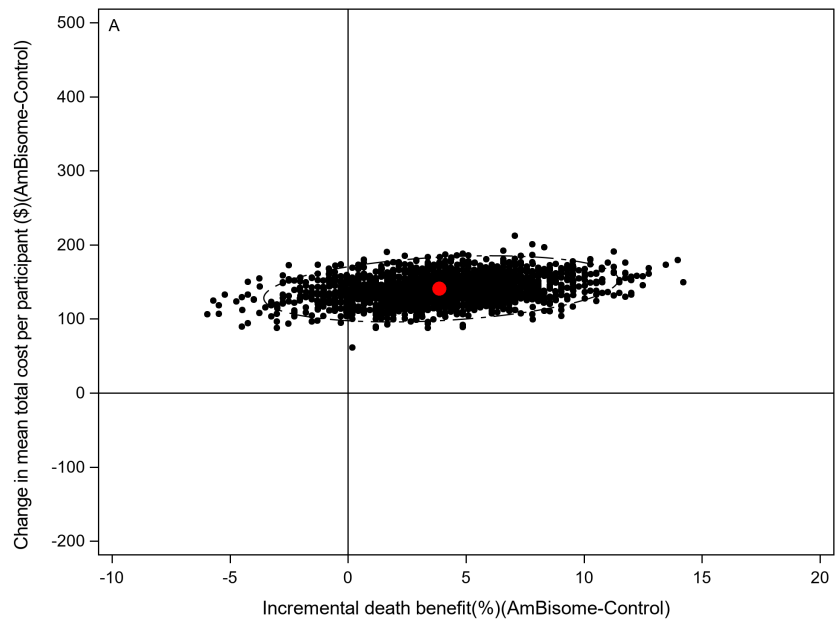
3B.

4A.

4B

Figure S4: Health cost of Potential Real-life Resource Use for 1) Botswana, 2) South Africa, 3) Uganda and 4) Zimbabwe. A) A cost-effectiveness plane presenting the incremental costs and death benefit (%) in the AmBisome arm after 10,000 bootstrap iterations (2,000 selected at random are shown) with the red dot denoting the mean and the ellipse showing 95% confidence intervals of the simulation and B) Cost-effectiveness acceptability curve of the AmBisome arm against the control. The red line denotes the cumulative probability of AmBisome being more cost effective than the control treatment at a particular willingness to pay (WTP). The dashed line denotes the cumulative probability of positive health benefits.
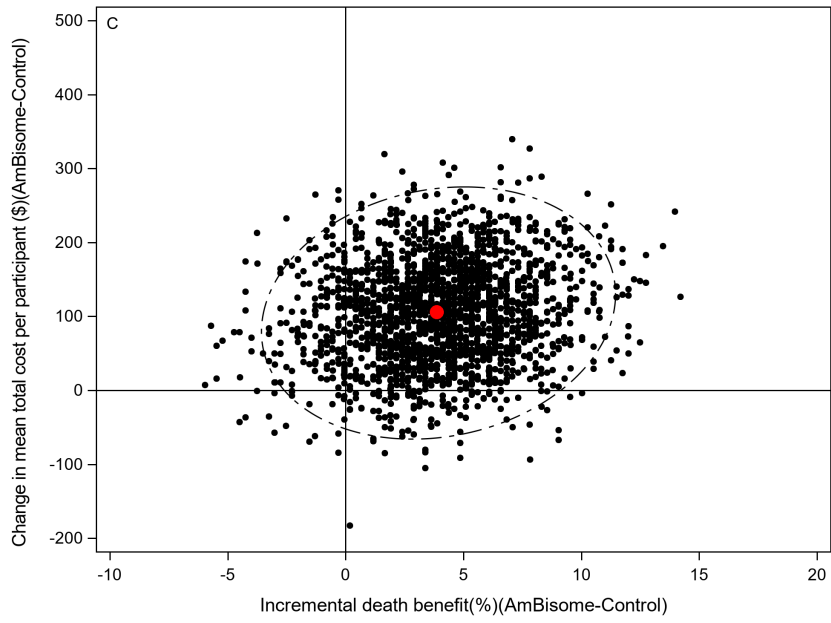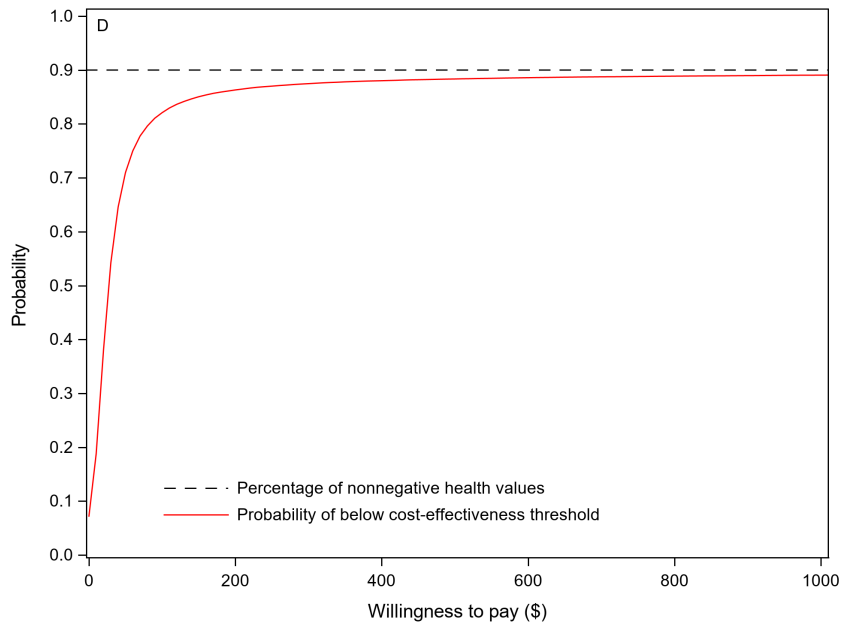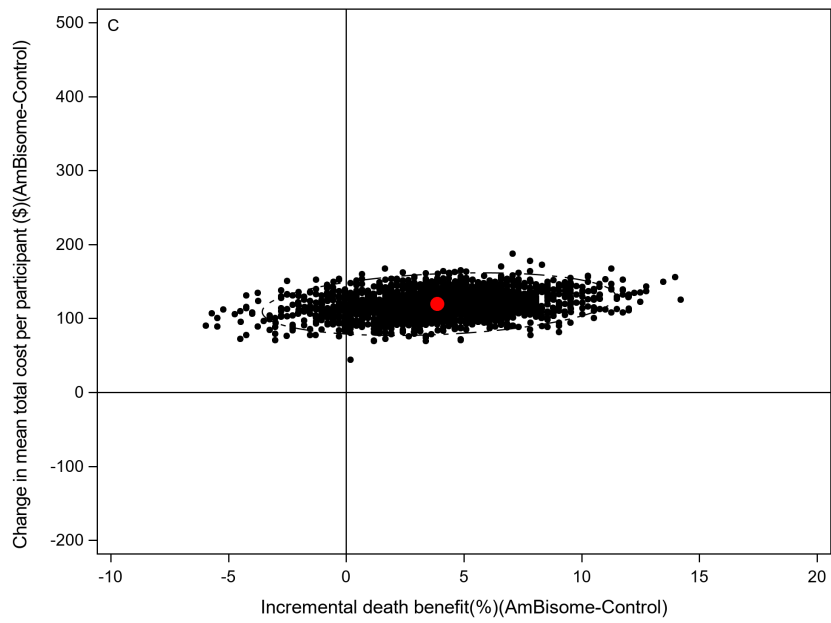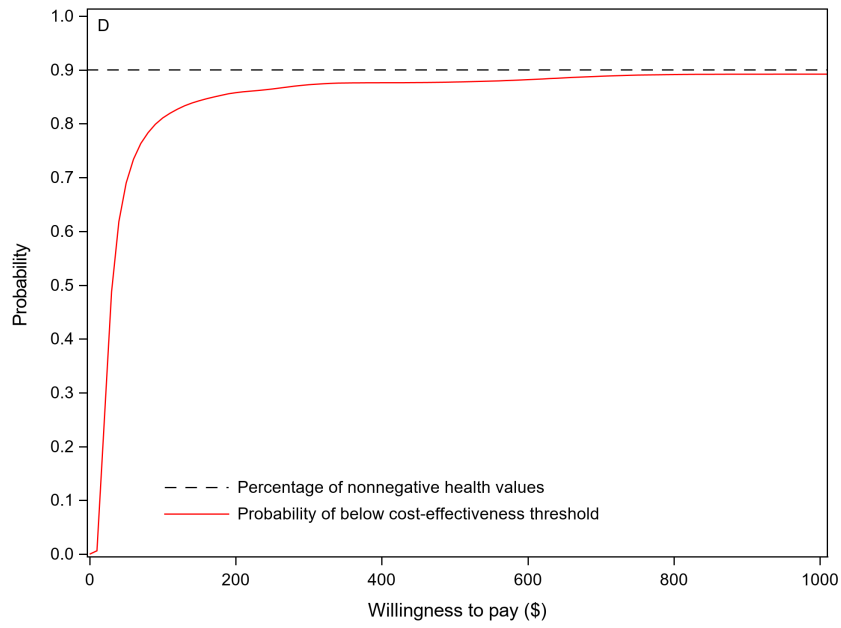
1A.

1B

2A.

2B

3A.

3B

4A.

4B