Developing an Antimicrobial Strategy for Sepsis in Malawi

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5.4.1 Study population

In total, 425 participants were recuited to the study between 19th February 2017 and 2nd October 2018; 225 participants with sepsis (arm 1), 100 inpatients without antimicrobial exposure at baseline (arm 2) and 100 community members (arm 3). Flow of participants through the study is shown in Figure 5.1. It was often challenging to collect stool samples from participants but 87% (1416/1631) eligible patient-visits resulted in the collection of a stool sample. Drop out from the study and failure to collect stool samples were similar in arm 1 and 2 and with no apparent systematic bias, but both drop out and missing samples were less frequent in arm 3 (Figure 5.2A). There was siginifcant variation in the timing of stool sample collecion, with a distribution around the ostensible collation day (Figure 5.2B).

The baseline characetristics of the enrolled participants are shown in Table @tab:(dassim-2-demog). There were some important differences between the arms of the study: despite matching on age and sex, antimicrobial-unexposed participants were older. They were also less likely to be HIV-infected than participants with sepsis (13% [12/89] of those with known HIV status were HIV-infected versus 67% [143/213] with sepsis), and less likely to have been treated for TB. Sepsis participants were more likely to have recieved antimicroials or been hospitalised in the previous 4 weeks. In the community arm of the study, there were a high proportion of participants (60% [60/100]) with an unknown HIV status, and there were some differences in toilet facilities, water sources, cooking fuel and presence of animals at home across the three groups.
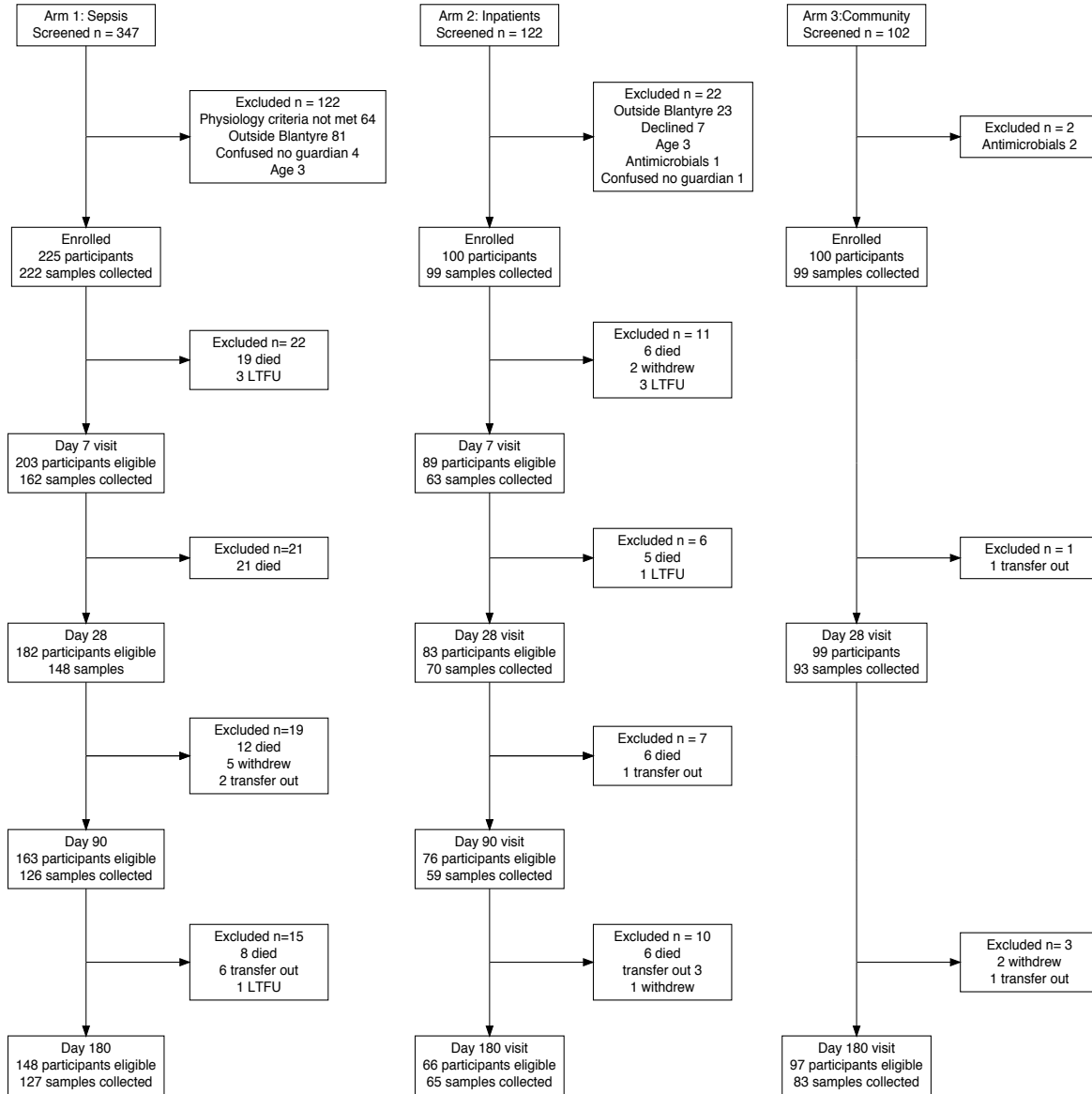
Figure 5.1: Study recruitment and follow up. At each time point *eligible participants* refers to participants who are known to be alive and have not withdrawn from the study by that time point, and *samples collected* refers to patients from whom a stool sample was sucessfully collectd for that visit.
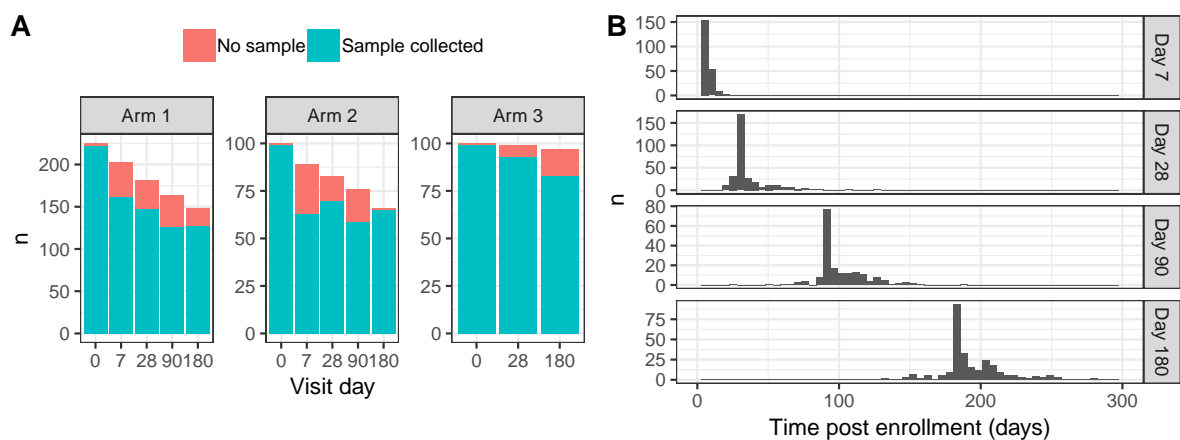
Figure 5.2: A: Missing stool samples stratified by arm and visit. Bar height at a given visit represents the number of eligible participants, coloured by successful sample collection (blue) or failure to collect a sample (red). B: Distribution of actual day of sample collection for ostensible day 7, 28, 90 and 180 samples showing considerable variation.

Table 5.1: Participant Characteristics

| Variable	Sepsis	Inpatient	Community	p	Total
Demographics					
Age (yr)	**35.9 (27.8-43.5)**	**40.4 (29.1-48.3)**	**32.5 (24.0-38.4)**	**<0.001**	**35.6 (26.9-43.9)**
Male sex	114/225 (51%)	51/100 (51%)	40/100 (40%)	0.533	205/425 (48%)
HIV/TB status					
HIV Reactive	**143/225 (64%)**	**12/100 (12%)**	**18/100 (18%)**	**<0.001**	**173/425 (41%)**
HIV Non Reactive	**70/225 (31%)**	**77/100 (77%)**	**22/100 (22%)**	**<0.001**	**169/425 (40%)**
HIV Unknown	**12/225 (5%)**	**11/100 (11%)**	**60/100 (60%)**	**<0.001**	**83/425 (20%)**
Ever treated for TB	**37/225 (16%)**	**5/100 (5%)**	**4/100 (4%)**	**0.002**	**46/425 (11%)**
Of those, current TB treatment	10/37 (27%)	0/5 (0%)	4/4 (100%)	0.098	14/46 (30%)
ART status*					
Current ART*	117/143 (82%)	9/12 (75%)	18/18 (100%)	0.859	144/173 (83%)
Months on ART	28.7 (3.7-72.6)	35.1 (2.9-79.8)	31.5 (13.0-79.9)	0.693	29.5 (3.8-72.8)
ART regimen: EFV/3TC/TDF	110/117 (94%)	8/9 (89%)	17/18 (94%)	1.000	135/144 (94%)
ART status					
Current CPT†	98/141 (70%)	5/12 (42%)	7/18 (39%)	0.328	110/171 (64%)
Healthcare exposure last 4wk					
Antibiotics	**60/225 (27%)**	**0/100 (0%)**	**0/100 (0%)**	**<0.001**	**60/425 (14%)**
Hospitalised	**18/225 (8%)**	**1/100 (1%)**	**0/100 (0%)**	**0.001**	**19/425 (4%)**
Tobacco/alcohol use					
Never tobacco	196/225 (87%)	93/100 (93%)	90/100 (90%)	0.929	379/425 (89%)
Ex tobacco	17/225 (8%)	6/100 (6%)	2/100 (2%)	0.180	25/425 (6%)
Current tobacco	12/225 (5%)	1/100 (1%)	8/100 (8%)	0.070	21/425 (5%)
Current alcohol	51/225 (23%)	16/100 (16%)	18/100 (18%)	0.502	85/425 (20%)
Education					
Primary incomplete or complete	97/225 (43%)	50/100 (50%)	42/100 (42%)	0.739	189/425 (44%)
Some secondary education	47/225 (21%)	18/100 (18%)	30/100 (30%)	0.238	95/425 (22%)
Secondary school complete	48/225 (21%)	16/100 (16%)	19/100 (19%)	0.677	83/425 (20%)
No formal schooling	16/225 (7%)	13/100 (13%)	4/100 (4%)	0.094	33/425 (8%)
College or higher	17/225 (8%)	3/100 (3%)	5/100 (5%)	0.346	25/425 (6%)
Employment					
Unemployed	82/225 (36%)	34/100 (34%)	32/100 (32%)	0.866	148/425 (35%)
Self-employed	56/225 (25%)	32/100 (32%)	35/100 (35%)	0.325	123/425 (29%)
Currently employed	65/225 (29%)	26/100 (26%)	18/100 (18%)	0.269	109/425 (26%)
Student	21/225 (9%)	6/100 (6%)	15/100 (15%)	0.153	42/425 (10%)
Retired	1/225 (0%)	2/100 (2%)	0/100 (0%)	0.280	3/425 (1%)

Toilet facilities					
Pit latrine with slab +/- foot rest	**104/225 (46%)**	**25/100 (25%)**	**35/100 (35%)**	**0.039**	**164/425 (39%)**
Pit latrine with slab and cover +/- foot rest	**45/225 (20%)**	**19/100 (19%)**	**55/100 (55%)**	**<0.001**	**119/425 (28%)**
Hanging toilet/latrine	**59/225 (26%)**	**48/100 (48%)**	**9/100 (9%)**	**<0.001**	**116/425 (27%)**
Flush Toliet (any type)	14/225 (6%)	5/100 (5%)	1/100 (1%)	0.118	20/425 (5%)
No toilet	2/225 (1%)	2/100 (2%)	0/100 (0%)	0.533	4/425 (1%)
Composting toilet	1/225 (0%)	1/100 (1%)	0/100 (0%)	0.720	2/425 (0%)
Main water source					
Public tap/standpipe	**51/225 (23%)**	**8/100 (8%)**	**66/100 (66%)**	**<0.001**	**125/425 (29%)**
Piped outside dwelling	**69/225 (31%)**	**37/100 (37%)**	**9/100 (9%)**	**<0.001**	**115/425 (27%)**
Tube well/borehole	**64/225 (28%)**	**35/100 (35%)**	**15/100 (15%)**	**0.032**	**114/425 (27%)**
Piped into dwelling	30/225 (13%)	11/100 (11%)	7/100 (7%)	0.353	48/425 (11%)
Unprotected well/spring	5/225 (2%)	6/100 (6%)	2/100 (2%)	0.181	13/425 (3%)
Surface water (including rainwater collection)	4/225 (2%)	2/100 (2%)	0/100 (0%)	0.556	6/425 (1%)
Tube well with powered pump	2/225 (1%)	1/100 (1%)	1/100 (1%)	1.000	4/425 (1%)
Treat water with chlorine	**19/225 (8%)**	**5/100 (5%)**	**0/100 (0%)**	**0.004**	**24/425 (6%)**
No. household members					
Children	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.395	2.0 (1.0-3.0)
Adults	2.0 (2.0-3.0)	3.0 (2.0-4.0)	2.0 (2.0-4.0)	0.907	3.0 (2.0-4.0)
Electricty					
Electricity available in house	119/225 (53%)	41/100 (41%)	58/100 (58%)	0.357	218/425 (51%)
Main cooking fuel					
Charcoal	161/225 (72%)	63/100 (63%)	88/100 (88%)	0.291	312/425 (73%)
Wood	**61/225 (27%)**	**35/100 (35%)**	**11/100 (11%)**	**0.004**	**107/425 (25%)**
Electricity	3/225 (1%)	2/100 (2%)	1/100 (1%)	0.869	6/425 (1%)
Animals at home?					
Any animal	**71/225 (32%)**	**43/100 (43%)**	**15/100 (15%)**	**0.004**	**129/425 (30%)**
Poultry	46/71 (65%)	34/43 (79%)	10/15 (67%)	0.800	90/129 (70%)
Dogs	18/71 (25%)	11/43 (26%)	9/15 (60%)	0.201	38/129 (29%)
Other	11/71 (15%)	9/43 (21%)	5/15 (33%)	0.413	25/129 (19%)
Goats	12/71 (17%)	7/43 (16%)	1/15 (7%)	0.830	20/129 (16%)
Cattle	2/71 (3%)	3/43 (7%)	0/15 (0%)	0.406	5/129 (4%)

Note:

ART = Antiretroviral therapy, CPT = Co-trimoxazole preventative therapy, EFV: Efavirenz, 3TC: Lamivudine, TDF: Tenofovir. Numeric values are median (IQR)) unless otherwise stated. P-values are to assess for differened across the three groups: Fisher's exact test across the groups for categorical variable, and Kruskal-Wallace test for continuous variables.

[*] ART status includes HIV reactive only as denominator

[†] Missing CPT data for two participants.

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Chapter 6

Whole genome sequencing of ESBL *E. coli* carriage isolates

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Chapter 7

Gut mucosal carriage of ESBL-E in Blantyre, Malawi

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