#### FIEBRE ASTMH 2021



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## Fighting adult mortality through etiology of fever studies: Description of high mortality in an adult inpatient population in Mozambique





Justina Bramugy<sup>1</sup>, Sham Lal<sup>3</sup>, Marta Valente<sup>1,2</sup>, Sara Ajanovic<sup>1,2</sup>, Oliver Baerenbold<sup>3</sup>, Heidi Hopkins<sup>3</sup>, David Mabey<sup>3</sup>, Quique Bassat<sup>1,2,4,5,6</sup> <sup>1</sup> Centro de Investigação em Saúde de Manhiça (CISM), Maputo, Mozambique. <sup>2</sup> ISGlobal, Hospital Clínic - Universitat de Barcelona, Spain. <sup>3</sup> London School of Hygiene and Tropical Medicine, London, United Kingdom <sup>4</sup> ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Spain; <sup>5</sup> Pediatric Department, Hospital Sant Joan de Déu (Universidade de Barcelona), Barcelona, Spain; <sup>6</sup> CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain.

#### Background

Fever is a common symptom leading to health care seeking and hospital admission in Africa. Mortality rates in febrile adult inpatients in Mozambique are high and are associated with high underlying prevalence of co-morbidities like HIV and cardiovascular diseases, and delays in care-seeking. Better characterization of febrile teenage and adult patients in terms of clinical presentation, diagnostic laboratory findings, and outcomes may be important for a more evidence-based evaluation of current clinical management algorithms, with the aim of decreasing preventable mortality.

#### Methods

The observational study "FIEBRE: Febrile illness evaluation in a broad range of endemicities" recruited febrile patients in Mozambique, Zimbabwe, Malawi and Lao PDR to identify infectious causes of fever and antimicrobial susceptibility of bacterial pathogens. Comprehensive clinical and laboratory testing was conducted, including local and centralised analyses in reference laboratories.

We hereby present mortality data from adult Mozambican outpatients and inpatients (Jan 2019-Feb 2021) at Manhiça District Hospital, Mozambique.

- Patients presenting with fever were enrolled and provided clinical data, pharyngeal swabs and a venous blood sample; selected participants also provided a urine sample (those who had urinary symptoms and all HIV positive).
- Laboratory assessments target infections that are treatable and/or preventable.
- Selected point-of-care tests (POCT) [urine dipstick, malaria and HIV testing, serum cryptococcal antigen (CrAg) and urine lipoarabinomannan (uLAM), as well as blood and urine cultures and antimicrobial susceptibility testing, were performed on site.
- On day 28, patients provided a second venous blood sample for serology and information on clinical outcomes.

Further diagnostic assays were performed at international reference Laboratories including:

 blood parasites; bacterial, mycobacterial and fungal bloodstream infections; typhus group and spotted fever group Rickettsia spp; Orientia tsutsugamushi; Coxiella burnetii; Leptospira spp; Brucella spp; Borrelia spp that cause relapsing fever; Leishmania spp; and arboviruses (1)

(1)- Hopkins H, Bassat Q, Chandler CIR, et al. Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE): protocol for a multisite prospective observational study of the causes of fever in Africa and Asia. BMJ Open 2020;10:e035632. doi:10.1136/bmjopen-2019-035632

#### Results

During the study period, a total of 792 teenage (>15 yo) and adult patients were recruited (445 (56,1%) outpatients, 347 (43,8%) inpatients). 92 died within the first 28 days of recruitment, yielding a case fatality rate of 11.6%.

Table 1: Adult Study Population, by site

Table 2: Demographic and clinical characteristics of patients by day 28 outcome

N= 700

34.0 (25.0,

16.0, 90.0

170 (97%)

162 (86%)

N = 92

41.0 (33.0,

6 (3.4%)

22 (10%)

27 (14%)

Overall

N = 792

35.0 (26.0,

16.0, 90.0

176 (100%)

219 (100%)

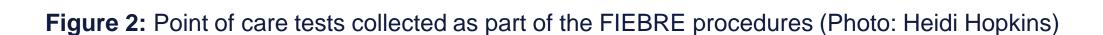
189 (100%)

	lungtions	Outpations	
Variable	Inpatient N = 347	Outpatient N = 445	Varia
Age (years)			Age (ye
Median (IQR)	38.0 (29.0, 52.0)	31.0 (24.0, 41.0)	Median
Range	16.0-90.0	17.0-76.0	
Age group, n (%)			Rar
15 - <25	53 (15%)	123 (28%)	Age group
25 - <35	84 (24%)	135 (30%)	15 -
35 - <40	90 (26%)	99 (22%)	25 - 35 -
45 - <55	45 (13%)	46 (10%)	45 -
55 - <65	47 (14%)	28 (6.3%)	55 -
65+	,	,	65
	28 (8.1%)	14 (3.1%)	Gender,
Gender, n (%)			Fem
Female	192 (55%)	335 (75%)	Ma
Male	155 (45%)	110 (25%)	Patient grou
Temperature (°C)			Inpat
Median (IQR)	38.2 (37.8, 38.9)	38.0 (37.7, 38.4)	Outpa
Range	37.5, 41.0	37.5, 40.5	Temperatu
Day 28 outcome n (%)	, -	,	Median
Alive	262 (76%)	438 (98%)	Rar
Dead	85 (24%)	7 (1.6%)	HIV status
HIV status, n (%)	33 (2170)	1 (11070)	Posi
Positive	187 (54%)	186 (42%)	Nega Unkn
	,	,	Indeter
Negative	153 (44%)	252 (57%)	HIV result PC
Unknown	4 (1.2%)	3 (0.7%)	ind
Indeterminate	3 (0.9%)	4 (0.9%)	ne
			pc
Figure 4 FIFD	DE attacks 2	la la alcalé de e C a la C	/R #'

Figure 1: FIEBRE study nurse with adult patient



00 110	102 (0070)	21 (1170)	100 (10070)
45 - <55	81 (89%)	10 (11%)	91 (100%)
55 - <65	58 (77%)	17 (23%)	75 (100%)
65+	32 (76%)	10 (24%)	42 (100%)
Gender, n (%)			
Female	481 (91%)	46 (8.7%)	527 (100%)
Male	219 (83%)	46 (17%)	265 (100%)
Patient group, n (%)			
Inpatient	262 (76%)	85 (24%)	347 (100%)
Outpatient	438 (98%)	7 (1.6%)	445 (100%)
Temperature (°C)			
Median (IQR)	38.0 (37.7, 38.6)	38.2 (37.9, 38.9)	38.0 (37.7, 38.6)
Range	37.5, 40.6	37.5, 41.0	37.5, 41.0
HIV status, n (%)	·	·	
Positive	316 (85%)	57 (15%)	373 (100%)
Negative	373 (92%)	32 (7.9%)	405 (100%)
Unknown	5 (71%)	2 (29%)	7 (100%)
Indeterminate	6 (86%)	1 (14%)	7 (100%)
HIV result POCT, n (%)	( )	, ,	
indet	6 (86%)	1 (14%)	7 (100%)
neg	342 (92%)	28 (7.6%)	370 (100%)
pos	89 (79%)	24 (21%)	113 (100%)
(Missing)	263	39	302
Malaria POCT, n (%)			
indet	2 (40%)	3 (60%)	5 (100%)
neg	637 (88%)	87 (12%)	724 (100%)
pos	61 (97%)	2 (3.2%)	63 (100%)
CrAg POCT, n (%)	3 . (3 . 70)	_ (3.270)	33 (13370)
indet	43 (81%)	10 (19%)	53 (100%)
neg	391 (84%)	75 (16%)	466 (100%)
pos	5 (83%)	1 (17%)	6 (100%)
(Missing)	261	6	267
uLAM POCT, n (%)	201	U	201
indeterminate	2 (100%)	0 (0%)	2 (100%)
negative	222 (89%)	27 (11%)	249 (100%)
positive	20 (87%)	3 (13%)	23 (100%)
(Missing)	456	62	518
Diabetes, n (%)	<del>-100</del>	UZ	010
,	383 (87%)	59 (13%)	442 (100%)
no Unknown	300 (91%)	28 (8.5%)	328 (100%)
		5 (23%)	22 (100%)
yes Sickle cell, n (%)	17 (77%)	J (2J /0)	22 (100%)
· ·	615 (00%)	71 (100/)	686 (1000/)
NO Unknown	615 (90%)	71 (10%)	686 (100%)
Unknown	18 (86%)	3 (14%)	21 (100%)
yes Pland quiture regulte, n	67 (79%)	18 (21%)	85 (100%)
Blood culture results, n (%)			
contaminated	10 (67%)	5 (33%)	15 (100%)
negative	594 (92%)	52 (8.0%)	646 (100%)
positive	43 (83%)	9 (17%)	52 (100%)
(Missing)	53	26	79





#### **Discussion and conclusions**

- The FIEBRE multi-site study will provide an invaluable set of data on febrile illness across Africa and Asia
- Mortality among adult Mozambican inpatients with febrile illness remains unacceptably high
- Malaria plays an important role in febrile illness, but a minor role in terms of teenager and adult mortality
- Tuberculosis remains highly prevalent as a cause of febrile illness in this population, but with low short-term associated mortality
- Cryptococcal invasive diseases affected ~1% of patients in this population with very high prevalence of HIV (47%)
- Invasive bacterial infections were detected in 6.6% of patients, with a high associated mortality. However, the low yield of a single blood culture may have led to an important underestimate of the real burden
- HIV infection significantly increased the risk of dying among our febrile patients (p<0.001)
- Most deaths were related to preventable and treatable opportunistic infections in the context of underlying HIV infection
- Comprehensive strategies to address HIV infection at all stages (prevention, diagnosis and treatment) are needed to decrease mortality.
- While awaiting final centralized diagnostic results from reference laboratories, local laboratory results already reveal a number of causes of preventable deaths
- The detailed analysis of all patient's results will provide a roadmap upon which to base policy change to improve the management of fever in teenagers and adults, and ultimately increase their survival

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## The main pathogens causing febrile illness and implications for fever management in Laos; preliminary results from the FIEBRE study





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#### Introduction

Management of febrile illness in Laos typically relies on clinical assessment and empiric treatment, as laboratory confirmation is often not available, except for malaria and dengue rapid tests. The standard empirical treatment of inpatients with sepsis or febrile illness in Laos is parenteral ceftriaxone. Vientiane Provincial Hospital in northern Laos was one site of the multicentre FIEBRE (Febrile Illness in a Broad Range of Endemicities) study which performed a comprehensive evaluation of the causes of febrile illness in inand outpatients of all ages. We aimed to describe the leading pathogens diagnosed from FIEBRE patients recruited in Laos.

#### Study methods

- Prospective observational study, conducted between October 2018 and 2020, in Vientiane Provincial Hospital, Lao PDR.
- In- and out-patients with fever, aged 2 months and above were recruited. Matched community controls were enrolled to enable calculation of attributable fractions.
- Blood and nasopharyngeal specimens were tested using pathogen-based diagnostics:
  - a) Performed at or near the point of care: blood culture and malaria RDT/blood smear microscopy;
  - b) Performed at reference laboratories: Arboviruses, respiratory pathogens, rickettsial diseases, histoplasma and Leptospira
- Patients' usual care and antibiotic prescriptions from hospital clinicians were documented by the study team.
- Results of point of care tests (POCTs) and blood cultures performed at Mahosot hospital were reported immediately.

#### Results

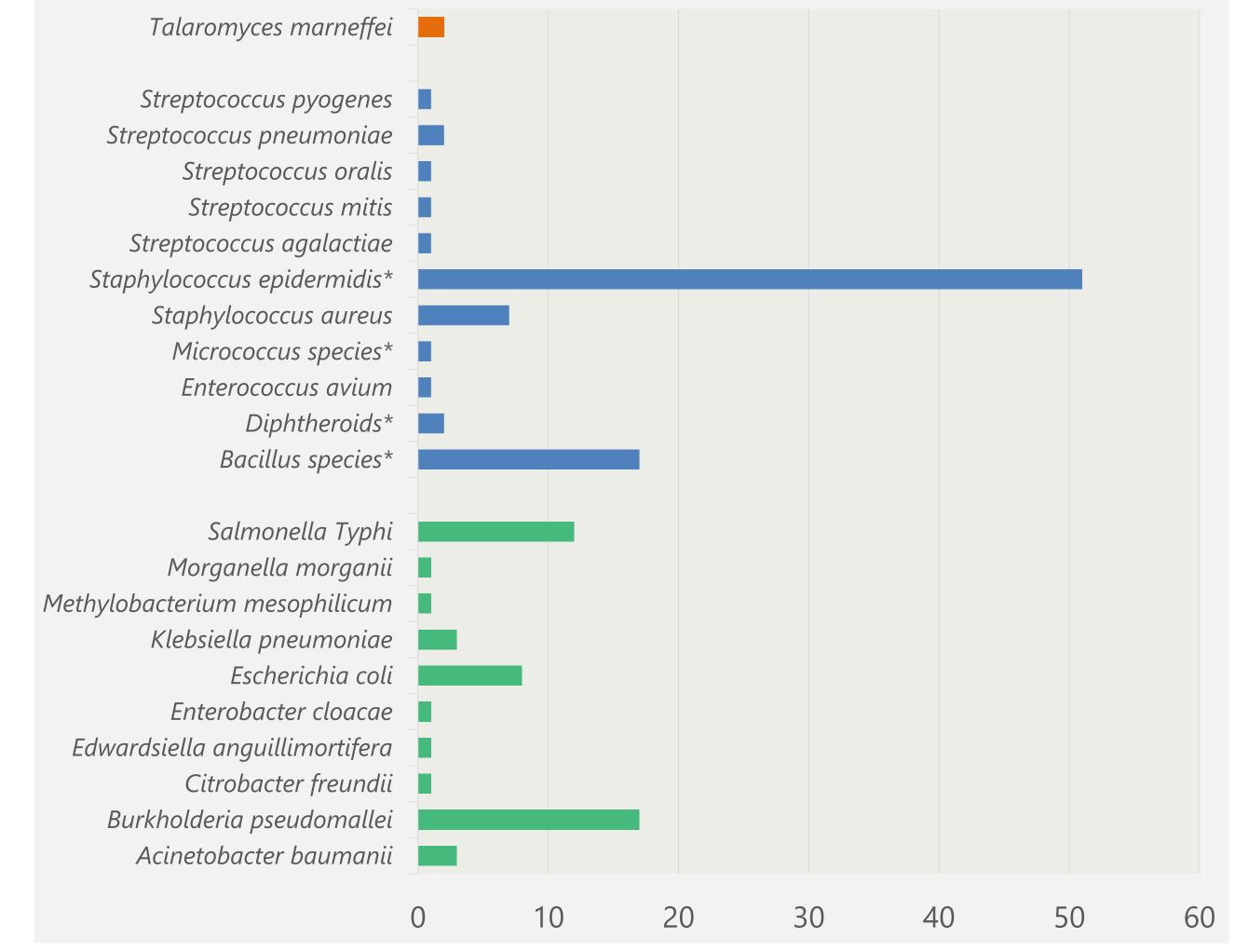
Preliminary results of investigations performed in Laos (blood culture, pending confirmation, malaria rapid test & microscopy) are reported:

• 1,980 blood cultures from 1,972 patients, 135 (6.8%) isolates were identified. Of these, 17 (12.6%) grew Burkholderia pseudomallei, 12 (8.9%) Salmonella Typhi, 8 (5.9%) Escherichia coli (5 were ESBL-producing), 7 (5.2%) Staphylococcus aureus (2 were Methicillin-resistant S. aureus), 3 (2.2%) Klebsiella pneumoniae, 2 (1.5%) Streptococcus pneumoniae, and 2 (1.5%) Talaromyces marneffei [Fig. 1]. No positive test for malaria.

Preliminary results from the international reference laboratories:

- 5/382 (1.3%) blood samples were positive for Histoplasma-Ag. From 1,556 samples, 218 (14%) were PCR-positive for dengue with no patients confirmed PCR-positive for Japanese encephalitis, Zika or chikungunya viruses [Table 1].
- Of 669 nasopharyngeal samples tested so far, 218 (32.6%) tested positive for respiratory viruses. (Results from controls to follow).
- 1,207 (61.4%) patients received antibiotics. Among 1,431 antibiotic prescriptions, 837 (58.5%) were for cephalosporins [Fig. 2].





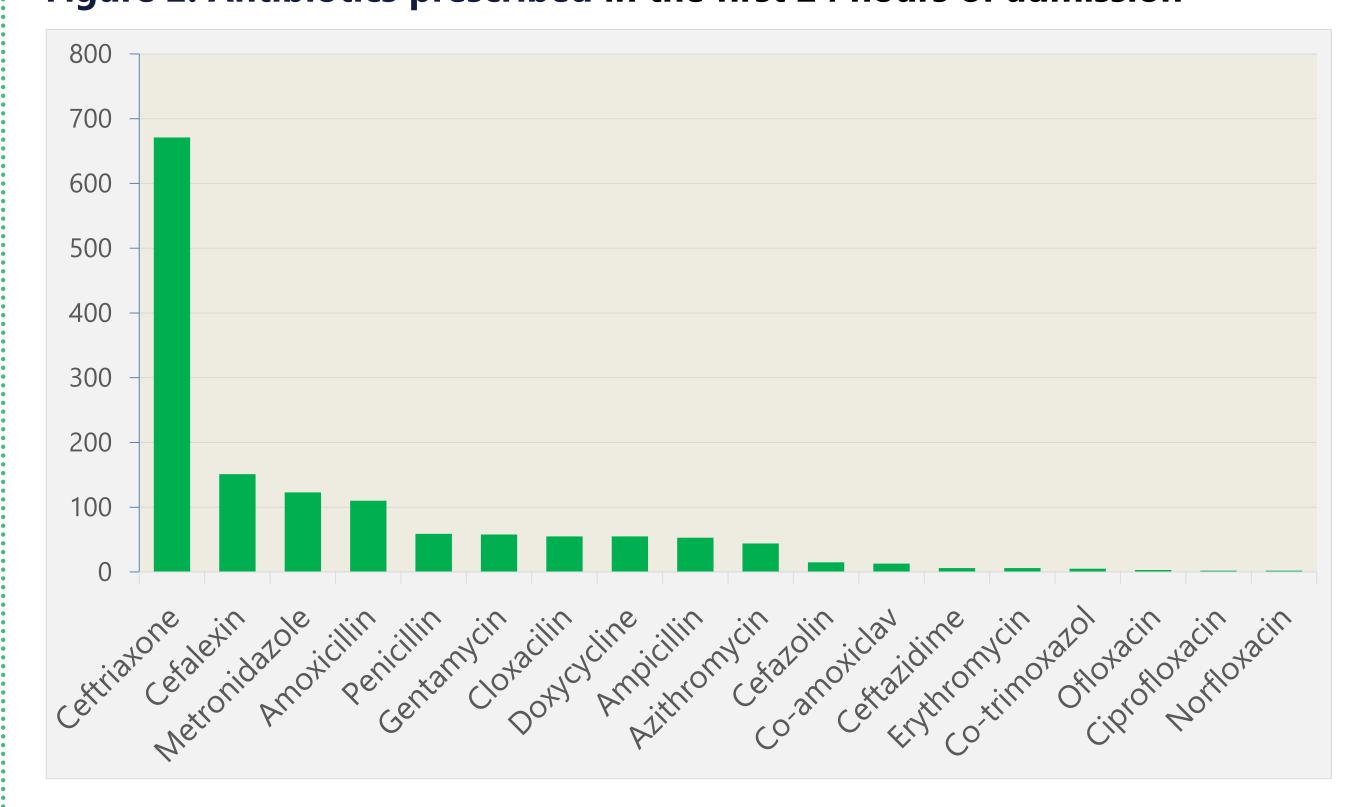
\*considered as contaminant organisms

**Table 1: Preliminary results of Arbovirus testing** 

	Patient	Patients, N=1556	
	Confirmed	Presumptive	
Results for each virus analysed separately			
Dengue virus	218 (14%)	147 (9.4%)	
Japanese encephalitis virus	0	125 (8%)	
Zika virus	0	9 (0.6%)	
Chikungunya virus	0	101 (6.5%)	
Overall results (PCR is confirmatory over Ab)			
Dengue virus	218 (14%)	92 (5.9%)	
Japanese encephalitis virus	0	37 (2.4%)	
Zika virus	0	1 (0.1%)	
Chikungunya virus	0	43 (2.8%)	
Multi (POS for >1 V)	0	76 (4.9%)	
Overall positive	218 (14%)	249 (16%)	

Viral RNA detection using real-time RT-PCR; specific ELISAs to look for serological evidence of Infection, with confirmation by microneutralization (pending). Confirmed = PCR positive, Presumptive = ELISA IgM positive.

#### Figure 2: Antibiotics prescribed in the first 24 hours of admission



#### Conclusion

- From these preliminary results, we confirm that malaria is no longer a leading cause of fever in northern Laos.
- Dengue was a common reason for presentation to the hospital with fever, reflecting the fact that there was an epidemic in the country while the study was recruiting.
- We demonstrated melioidosis, enteric fever and ESBL-producing Enterobacterales bacteraemia as causes of bloodstream infection in this part of Laos, with important implications for empiric prescribing in severely ill patients with sepsis.



FIEBRE-Laos team recruiting control participants at home,

#### **References:**

• Hopkins H, Bassat Q, Chandler CI, et al.; FIEBRE Consortium. Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE): protocol for a multisite prospective observational study of the causes of fever in Africa and Asia. BMJ Open. 2020 Jul 21;10(7):e035632. doi: 10.1136/bmjopen-2019-035632. Erratum in: BMJ Open. 2020 Aug 31;10(8):e035632corr1. PMID: 32699131; PMCID: PMC7375419.

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FIEBRE is funded by UK aid from the UK government; the views expressed however, do not necessarily reflect the UK government's official policies.





















# Understanding antimicrobial resistance through the lens of antibiotic vulnerabilities in primary health care in rural Malawi





## Eleanor E MacPherson,<sup>1,2</sup> Joanna Reynolds,<sup>3</sup> Chimwemwe Phiri,<sup>1</sup> John Mankhomwa,<sup>1</sup> Justin Dixon,<sup>4</sup> Clare I.R. Chandler <sup>4</sup>

1. Malawi-Liverpool-Wellcome Trust, 2. Liverpool School of Tropical Medicine, 3. Sheffield Hallam University and Capacity Q 4. London School of Hygiene and Tropical Medicine

#### Background

- Diminishing effectiveness of antimicrobials raises serious concerns for human health
- Policy makers grapple to reduce the overuse of antimicrobial medicines
- Yet antibiotic access is patchy in low resource contexts
- Understanding how care is constituted is critical for optimising antibiotic use

#### Methodology

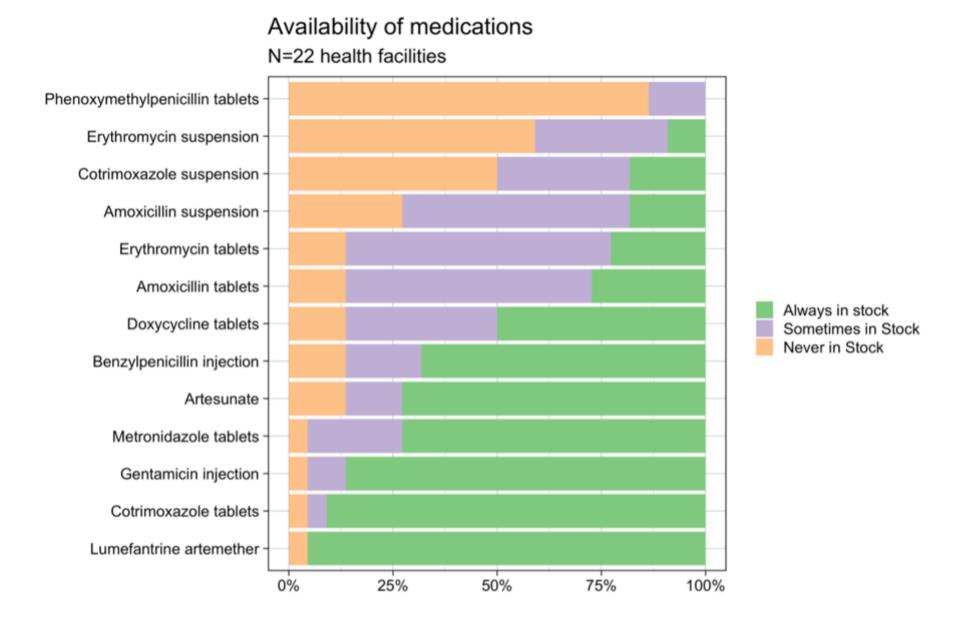
- This study aimed to understand the context of antimicrobial prescribing in primary health care clinics in rural Chikwawa District, Malawi
- Fieldwork took place over 18 months (2018-2020)
  - 22 health facilities surveyed
  - 1348 health worker-patient consultations observed
  - 45 staff and patients interviewed in-depth

### Results

- Care was centred around provision of an antimicrobial
- Chronic lack of essential medicines and other resources
- Donor funded antibiotics such as cotrimoxazole were one of the only constants
- Clinic interactions were tightly scripted, no time for discussions or questions with patients
- We develop the lens of antibiotic vulnerabilities: multiple ways in which the vulnerabilities of medicines, people and systems intersected in extreme scarcity

"We struggle to secure so many drugs. We only have cotrimoxazole, that's all we have to give. We give it out all day because that is all we have to give." Health care worker in rural Chikwawa





#### Discussion

- Antibiotics are central and essential to primary care
- Case management must be expanded to a wider definition of care
- As targets to reduce antibiotic prescribing take a more prominent role in global policy we must track the ramifications of this for the delivery of care to ensure that efforts to stem resistance do not undermine the goal of improved health for all.









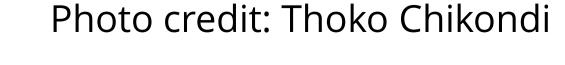








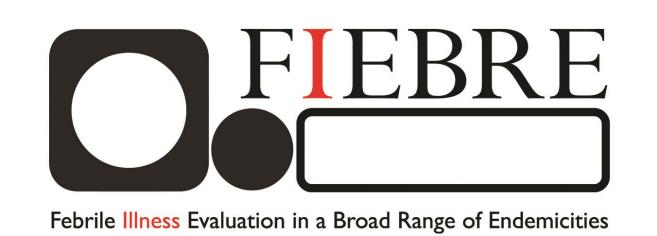








# Sex Work, Antibiotic Use & the Management of Sexually Transmitted Infections in Harare, Zimbabwe: An Ethnographic Study





Salome Manyau\*<sup>1, 2</sup>, Justin Dixon<sup>1</sup>, Norest Mutukwa<sup>2</sup>, Faith Kandiye<sup>2</sup>, Paula Palanco Lopez<sup>1</sup>, Eleanor E MacPherson<sup>3</sup>, and Clare I R Chandler<sup>1</sup>

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#### Background

- The dramatic increase in antibiotic resistant infections is a key challenge of our time
- This is a pressing issue for sexually transmitted infections (STIs) such as gonorrhoea and syphilis
- Sex workers face a heightened STI transmission risk, but often have poor access to healthcare and have been shown in previous studies to use antibiotics regularly.
- Historically sex workers have been negatively framed as a deviant population.
- Understanding the lived realities of sex workers in low resource settings and the ways in which they access and use antibiotics in the era of increasing drug resistant infections is critical for effective and equitable action.



Illegal shacks used for sex work n Harare

#### Aim

 We aimed to understand the context of antibiotic use by sex workers within an informal setting in Harare.

#### **Research Questions**

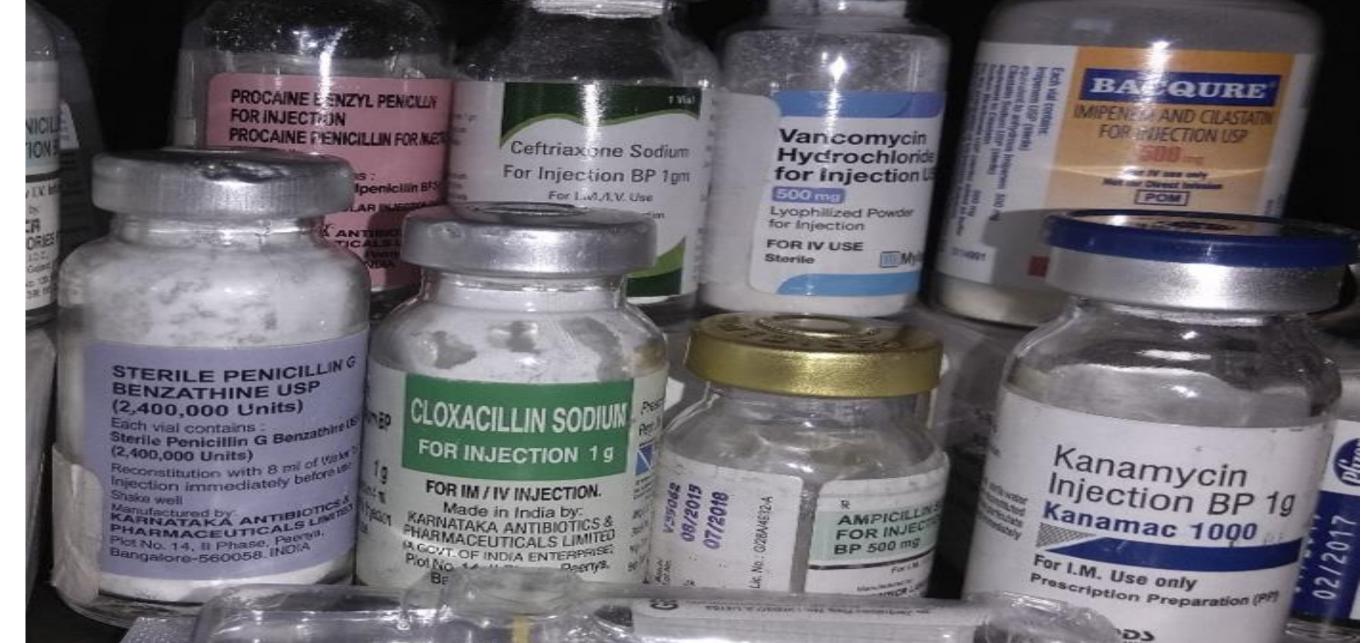
- What are the roles of antibiotics in sex work?
- What is the history and the local context that explains the patterns of antibiotic use?

#### Methodology

- Ethnographic fieldwork was carried out from June-November 2019 in Harare's oldest township, Mbare, including:
- Immersive observation of the lives of sex workers and residents living within the sex workers' zone.
- o In-depth interviews (IDIs) with 25 female sex workers
- In-depth interviews with 5 residents
- Archival research of the history of public health in the management of STIs and sex workers in Zimbabwe.
- Thematic analysis involved coding and theoretical abstraction
- Ethical approval was obtained from the Medical Research Council of Zimbabwe and LSHTM

#### **Findings**

- Regular access to free antibiotics provided a 'quick fix' for care and productivity, enabling them to continue working despite regular occupational exposure to STIs
- Many women who were not sex workers and thus not eligible to attend the NGO were unable to access antibiotics for STIs (often contracted via partners paying for sex) because of prohibitive costs and stigmatizing treatment.
- Our historical analysis revealed continuity between the current reliance on antibiotics to 'fix' gaps in care and productivity and older colonial public health strategies for managing sex work and the spread of STIs.



#### Findings

- Sex workers were familiar with and regularly used antibiotics like ciprofloxacin, metronidazole, doxycycline, and ceftriaxone for STIs
- These antibiotics were largely prescribed by a northern-funded NGO clinic devoted to sex workers, towards which they felt considerable belonging in contrast to stigmatizing experiences at public clinics.

Sex workers clinic was made for us, they saw that in our job, sex workers were suffering, we had no money for medicine, and the nurses at the public clinics were treating us like we were not human, so our clinic provides us with medicine and care for free." (Fadzi, Sex Worker 32 years)



#### **Discussion and Conclusion**

- Programs for sex workers, while valued by these women, were narrow, exclusionary and enacted a pharmaceuticalised form of governance that hangs on the efficacy of antibiotics.
- Sex workers navigated fragmented landscapes of NGO and state healthcare in the face of regular occupational exposure to STIs.
- Attention to individual behaviour risks overlooking the limitations of the ways in which STIs have been managed through vertical programmes.
- Programs need to move away from a narrow focus on sex workers – whether empowering, admonishing or abolishing – as this obscures the social, economic and epidemiological connections between sex workers, wives, husbands, health systems and society at large.
- Further effort is needed to reconsider integrated services, recognising the legacies that shape the challenges of integration.





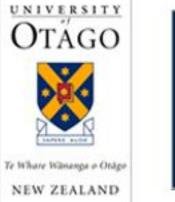
















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## High mortality in adult patients with HIV admitted with fever to hospitals in Malawi, Mozambique and Zimbabwe – results from the FIEBRE study





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1 London School of Hygiene and Tropical Medicine, United Kingdom, 2 Biomedical Research and Training Institute, Zimbabwe; 3 ISGlobal, Hospital Clínic - Universitatde Barcelona, Spain; 4 Centro de Investigação em Saúde de Manhiça (CISM), Mozambique, 5 Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Malawi, 6 Liverpool Schoolof Tropical Medicine, United Kingdom

#### **BACKGROUND**

Despite important advances in HIV diagnosis and roll-out of antiretroviral therapy (ART) in sub-Saharan Africa, HIVassociated conditions continue to be a major cause of hospitalisation and death. The aim of this study was to compare mortality and causes of death among HIVinfected and uninfected adults hospitalised with febrile illnesses in Malawi, Mozambique and Zimbabwe.

#### **METHODS**

This is a preliminary analysis including patients aged ≥15 years who were admitted to seven hospitals in Malawi, Mozambique and Zimbabwe and enrolled into the FIEBRE (Febrile Illness Evaluation in Broad Range of Endemicities) study evaluating infectious causes of fever. Participants provided detailed clinical information and samples were collected for laboratory diagnosis of infections. A follow-up visit was conducted at 28 days to assess patient outcome. Causes of death were assessed by combining information from hospital records, family reports, and the FIEBRE study data. Autopsy reports were not available and among patients who died after hospital discharge, the information was provided by the family.

#### **RESULTS**

Among 940 adult patients admitted to hospital, the median age was 35 years (IQR 26-49) and 498 (53.0%) were female. HIV status was determined in 926 (98.5%); 383 (41.4%) were HIV-infected Outcome information was available for 889 patients and of those 122 (13.7%) died. Mortality at 28 days was 22.4% and 7.1% (p<0.001) in patients with and without HIV, with 69.8% of the deaths occurring among patients with HIV.

#### **RESULTS**

The most common causes of death among HIV-infected individuals in whom a cause of death was available (n=73) were tuberculosis in 29 (39.7%) and other conditions associated with advanced HIV infection in 37 (50.7%). Conditions associated with advanced HIV were central nervous system disease where the cause was not identified (n=10), cryptococcal meningitis (n=8), Pneumocystis jirovecii pneumonia (n=3), Kaposi sarcoma (n=3). In 13 patients death was attributed to advanced HIV however, a specific cause was not reported. Figure 1 shows the causes of death among patients with HIV.

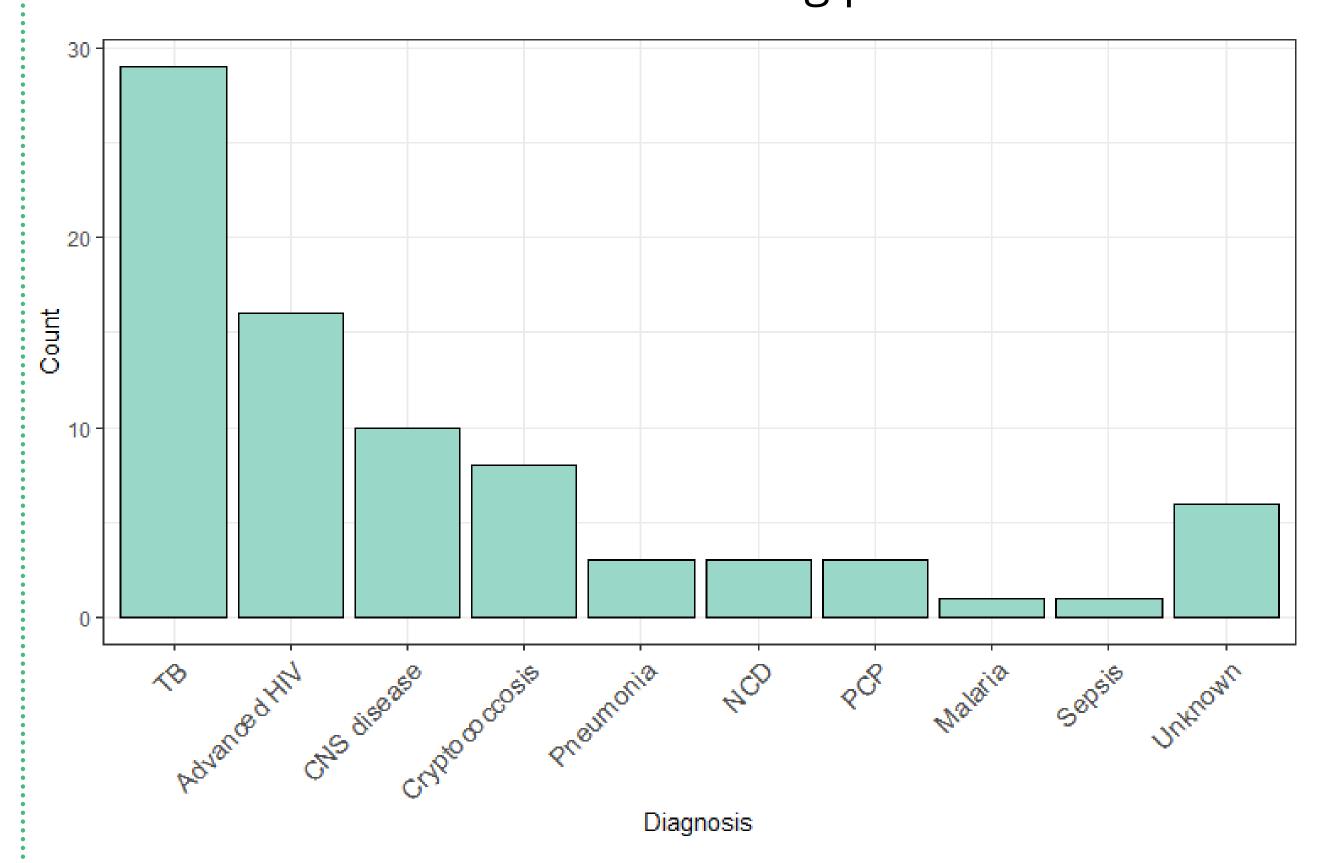


Figure 1 Causes of death among participants with HIV NCD: non-communicable diseases; PCP: Pneumocystis jirovecii pneumonia; TB: tuberculosis.

In patients without HIV infection, 16 (51.6%) and 15 (48.4%) of deaths were attributed to infectious and noninfectious causes, respectively (Figure 2. Among the most common causes of death from non-communicable diseases were stroke (n=6) and heart failure (n=5).

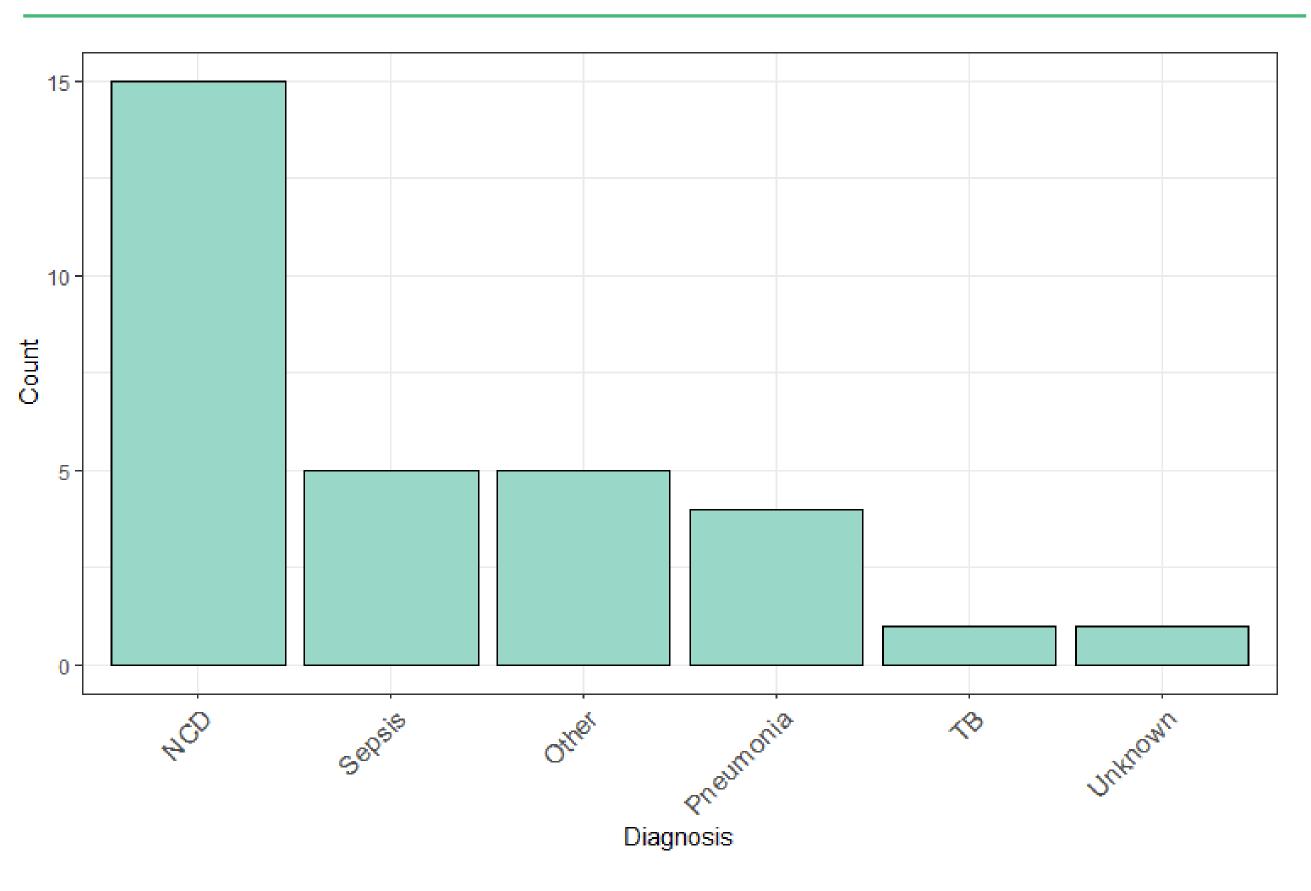


Figure 2 Causes of death among participants without HIV NCD: non-communicable diseases; TB: tuberculosis.

In 11 participants the HIV status was unknwon. In most of these patients (8/11), the cause of death was not recorded with the remainder deaths being due to tuberculosis (n=2) and malaria (n=1).

Overall, 15 participants had an unknown cause of death.

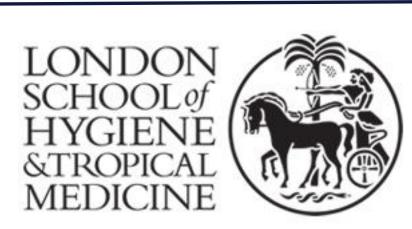
#### CONCLUSIONS

Mortality among adult patients with HIV was three times higher than in HIV uninfected patients. Tuberculosis and other preventable and treatable conditions associated with advanced HIV represented major causes of death in our population. This highlights the need for improved HIV diagnosis, monitoring, therapy and retention in care to decrease HIV-associated mortality.

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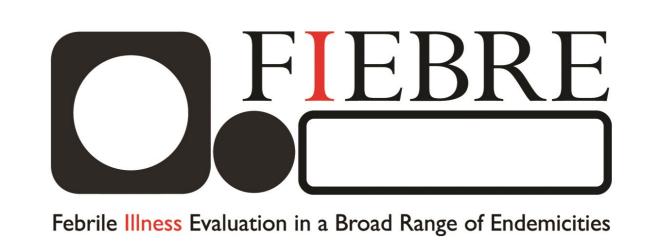




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# Negotiating Myanmar's Law and (Dis)Order amidst Antimicrobial Resistance Policy Implementation – an ethnographic study in Yangon, Myanmar



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#### Background

Date	Event
2015	World Health Organization Global Action Plan on AMR (WHO GAP) published
2017	National Action Plan on Antimicrobial Resistance Myanmar (NAP AMR) drafted
2018	First National Multisectoral Steering Committee Meeting on Combating Antimicrobial Resistance Myanmar
2020	Antimicrobial Resistance as a panel discussion at the Myanmar Health Congress

Table 1. Timeline of Global and Myanmar-focused Antibiotic Regulation

- The WHO's model for governance operates through state surveillance, regulation, and stewardship programmes.
- The WHO GAP expects nation-states to have the capacity and authority for implementation.
- The presumed 'irrational' use of antibiotics is argued by social scientists to be better understood by attending to context.

#### **Research Aim**

What is the context of antibiotic use in Myanmar? A preliminary explorative ethnographic study

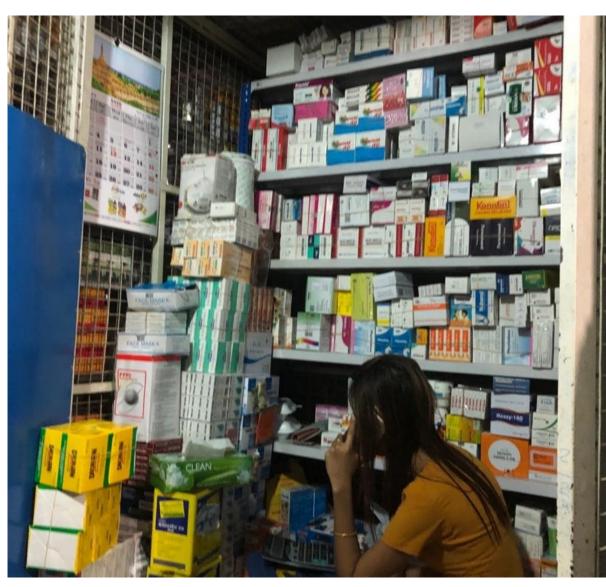


Figure 1. Wholesaler/ drug shop at a market

Burmese socialist era. Journal of Southeast Asian Studies, 44(2), 292-314.

problem of antibiotic overuse. *BMJ global health*, *4*(4), e001590.

References

## **Research Objectives**

- antibiotic policy in practice in Yangon, Myanmar
- 2. To trace and understand the trajectory of medicines within the pharmaceutical industry in Yangon,
- 3. To understand the social role of medicines in the context of labour

- . To explore the implications of
- Myanmar

# antibiotic regulation practice in Yangon (Objective 1)

Disconnect between global AMR discourse and

Global Discourses on AMR	Regulation in Practice in Yangon, Myanmar
'Rational' drug use defined as a biomedically inappropriate use of medicines	'Rational' drug use in practice is shaped by pragmatic social and economic concerns (e.g. taking a cheaper course of medicines regardless of their quality or a biomedical correctness).
Nation-states implied as the most appropriate bodies to promote antibiotic policy	Fragmented sovereignty and on-going civil wars between the state and the citizens mean that the state may not be the most appropriate body for regulation
The assumption that the state will promote health and well-being of its citizens through values of equity and justice	The state is in conflict with it's citizen and has deliberately underfunded healthcare in some regions as a militarisation tactic (Oehlers 2005).
Lack of knowledge of formal guidelines on antibiotic use is a key contributor to antibiotic 'misuse'.	Structural determinants (e.g. pharmaceutical industry, poverty, state regulation) determine which antibiotics are available and where and why people use them more so than knowledge.
Awareness raising as a solution to change 'misuse' behaviours	When factors beyond awareness are determining antibiotic use patterns, targeting awareness raising may be a

Table 2. The Disconnect between global discourses on AMR and Regulation in Practice in Myanmar

• AMR can be understood as a reaction to a 'presumed problem' (Bacchi 2016); the disconnect reflects a Global North / South epistemology

misdirected effort

## Myanmar's Pharmaceutical industry (Objective 2)



Figure 2. Antibiotics collected to saturation in Yangon

- Networks of 'legal' (registered with the state) and 'illegal' medicines market) circulating in Myanmar
- Public (state) discourses on AMR accentuates 'illegal' medicines as the cause of drug resistance.
- 'Illegal' medicines are cheaper and are used in lower-income settings.
- Although public discourses condemn and penalise the 'illegal', in practice the 'illegal' supports the 'legal' where agents of the state themselves are part of the 'illegal' (Chang 2013).
- Corruption and negotiations with the state determine which medicines are available and where as opposed to individual awareness or knowledge.

### A pharmaceutical model of care (Objective 3)

Medicines as Coping Mechanisms for State dysfunction

"But you know [pharmaceutical taxation rates] ... cannot fix it forever because government, our Myanmar's policies, they are changing every time. They are fixing every time. So, sometimes... I said 5%. Sometime 10%. (laughs)" - Manager at a pharmaceutical company

- 'A pharmaceutical centred model of care' (Biehl 2007) as a coping mechanism
- Taking drug cocktails and intravenous/ intramuscular injections of vitamin cocktails because they are cheaper and/or faster then having to access formal healthcare.

Figure 3. Sample of a cocktail of injections or a kyaw se (translation: intravenous)

#### Medicines as 'quick fixes'

- Deliberate underfunding and militarisation of healthcare -- 'Public health in Burma: Anatomy of a crisis' (Oehlers 2005).
- Patients are rendered responsible for their own health.
- Medicines as a 'quick fix for care, productivity and inequality' to substitute for lacking social and healthcare infrastructures (Denyer Willis & Chandler 2019).

#### Conclusion

- Although there have been economic and health improvements during the quasidemocratic period (2011–2021), these developments were not always distributed equitably and were insufficient to reverse decades of neglect. The 2021 military coup, which has created even more dysfunction and decline in the context of the healthcare sector, makes addressing health through other means even more pressing.
- The consequences are that individuals resort to coping mechanisms; one being a pharmaceutical model of care with medicines as 'quick fixes'.
- A lack of attention to these coping mechanisms and a blanketed, disconnected approach to addressing AMR may risk intensifying pressures on Myanmar people (particularly the informal sector but also extends to the entire economy as the formal relies on the informal).



*Open, 6*(2), 2158244016653986.



Bacchi, C. (2016). Problematizations in health policy: Questioning how "problems" are constituted in policies. Sage

Biehl, J. (2007). Pharmaceuticalization: AIDS treatment and global health politics. Anthropological Quarterly, 1083-1126

Chang, W. C. (2013). The everyday politics of the underground trade in Burma by the Yunnanese Chinese since the

Willis, L. D., & Chandler, C. (2019). Quick fix for care, productivity, hygiene and inequality: reframing the entrenched

Oehlers, A. (2005). Public health in Burma: Anatomy of a crisis. *Journal of Contemporary Asia*, 35(2), 195-206.

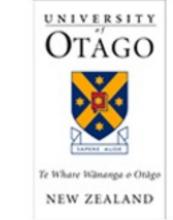
















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