Antibiotic use and prescription patterns in a semi-rural first line health centre in Mariakani, Kenya.

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Master of Family Medicine

Masterproef Huisartsgeneeskunde

Academic year/ Academisch jaar: [2019 – 2020]

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Preface

As part of my final assignment, I chose to submit a dissertation in line with my interests in primary care, infectious diseases and global health. During my last year of medical school, I had the opportunity do an internship in Mabati Medical centre, a private primary healthcare centre in Mariakani, Kenya. Learning from, and working closely together with the local staff, encouraged me to subscribe for a postgraduate in Tropical Medicine. The positive experience I had in the centre left me wanting to return a service. I would like to take the opportunity to highlight that the centre and its committed employees are delivering accessible quality healthcare for the entire community at a highly subsidized cost. My intention is to contribute in their continual improvement process towards delivering higher quality care, not to counter or misrepresent the quality care they deliver on a daily basis. Through this research I hope this can be achieved.

Acknowledgements

Foremost, I wish to recognize the invaluable guidance of my promotor, prof dr Erika Vlieghe. She made the research concrete and provided continuous support. I wish to thank her for her insightful comments, encouragement and inspirational enthusiasm.

My completion of this project could not have been accomplished without my local mentor and co-promotor dr Kishor Mandaliya. There are not enough superlatives to describe his inexhaustible energy and commitment. Thank you for guiding me through the tedious administrational processes with admirable patience, for your knowledgeable feedback and for the pleasant conversations during our long car drives.

I would also like to express my gratitude to the whole team of Mabati Medical Centre for their cooperation and warm welcome, to Margaret Muthoni for her help with the presentations and her support, to Christophe Van Dijck for his last minute emendations and special thanks to the administrator of the centre Clara Shuma, for her excellent excel-work and all the tasty snacks. You have deserved your chocolate!

Finally, to my loving parents: my deepest gratitude. For all the opportunities they have provided and for their never-ending support and continuous encouragement in all my endeavours.

Abstract

Background

Widespread use of antibiotics is a major driver of antimicrobial resistance. The majority of AB misuse occurs at community and primary care level, for which available data is particularly scarce. To address this research gap, this single-centred study focused on quantitative and qualitative aspects of antibiotic use in Mabati Medical Centre, a semi-rural private primary healthcare clinic in Mariakani, Kenya.

Method

A mixed methods study used routinely collected data from ambulatory patients to assess the use of antibiotics in Mabati Medical Centre over a 12 month period, from July 1, 2018 to June 30, 2019. For the measurement of antibiotic consumption the Defined Daily Doses (DDD) were calculated from monthly pharmaceutical consumption reports. Quality of antibiotic prescription behaviour was assessed with a point prevalence survey. The survey included all patient visits (receiving an antibiotic) on 52 selected weekdays, i.e. one every week. The quantitative data were processed using Excel 365 and descriptive statistics were applied. The qualitative part comprised three in-depth interviews with healthcare staff. These helped to interpret the quantitative data in its context and to identify improvement opportunities. The transcripts were coded and the most significant findings organised into an organigram.

Results

The 3,667 selected patient visits were prescribed a total number of 9,603 medical prescriptions, implying 2.69 (0-6) prescriptions on average per encounter. Overall, a total of 2,884 antibiotic prescriptions were dispensed over 2,237 (60.62%) patient visits (on average 1.3 antibiotic prescribed per encounter) and only 31 (1.08%) injectable antibiotics were prescribed. The antibiotic indication was in accordance with the guidelines for 655 (22.71%) prescriptions and for 568 (19.69%) more prescriptions the indications would have been in accordance with the guidelines if the clinical presentation was severe. Of these 1,223 (arguably) appropriate antibiotic prescriptions 563 (46.03%) were the first choice antibiotic according to the guidelines. Upper respiratory tract infection was the most common indication for which antibiotics were prescribed with 366 diagnoses. The most consumed antibiotic was amoxicillin-clavulanate with 56.13 DDD/100 patient visits, accounting for 15.76% (482,012 Ksh) of the annual drug expenditure. Both knowledge as ‘know-do’ gaps contributed to inappropriate prescription patterns. In Mabati Medical Centre, habits (‘mazoea’), perceived patient expectations, availability and over-the-counter prescription behaviour emerged as the most relevant determinants influencing antibiotic usage.

Conclusion

The study uncovered antibiotic overuse and inappropriate prescribing. Findings exposed shortcomings and barriers impeding qualitative prescribing behaviour. To effectively tackle these gaps a multiple intervention strategy would be most successful. Ideally, a nationwide whole system approach should be implemented to curb antimicrobial resistance on all levels. From this study several context-adapted recommendations emerged to combat antimicrobial resistance and improve delivered care.

Abstract

Inleiding

Grootschalig gebruik van antibiotica is een belangrijke oorzaak van antimicrobiële resistentie. Hoewel de eerstelijnszorg verantwoordelijk is voor het grootste deel van de antibioticaconsumptie, zijn onderzoeksgegevens er schaars. Dit onderzoek analyseert daarom het antibioticagebruik In Mabati Medical Centre, een semi-ruraal privé eerstelijnsgezondheidscentrum in Mariakani, Kenya.

Methode

In deze *mixed methods* studie werd het antibioticagebruik in het centrum over een periode van 12 maanden, van 1 juli 2018 tot 30 juni 2019, geëvalueerd aan de hand van routinematig verzamelde data van ambulante patiënten. Om de antibioticaconsumptie te meten werd, op basis van de maandelijkse gebruiksregisters van de apotheek, het aantal *Defined Daily Doses* (DDD) van de antibiotica berekend. De kwaliteit van het voorschrijfgedrag werd geëvalueerd aan de hand van een puntprevalentieonderzoek. Alle patiënten die een antibioticavoorschrift kregen op een van de 52 geselecteerde weekdagen (1 dag per week), werden vergeleken met alle patiënten die zich diezelfde dag presenteerden. De kwantitatieve gegevens werden verwerkt met behulp van Microsoft Excel 365 en beschrijvende statistiek. Drie diepte-interviews met medisch personeel dienden om deze data in de lokale context te interpreteren en optimalisatiemogelijkheden te identificeren. De transcripten werden gecodeerd en de belangrijkste bevindingen werden geordend in een organigram.

Resultaten

Bij de 3.667 geselecteerde consulten werden in totaal 9.603 geneesmiddelen voorgeschreven: gemiddeld 2,69 (0-6) voorschriften per consult. Hiervan waren er 2.884 antibioticavoorschriften verstrekt voor 2.237 (60,62%) consulten: gemiddeld 1,3 antibioticum per consult. Er werden slechts 31 (1,08%) parenterale antibiotica voorgeschreven. De antibioticavoorschriften waren geïndiceerd volgens de richtlijnen voor 655 (22,71%) voorschriften en 568 (19,69%) voorschriften hadden potentieel correcte indicaties (indien de klinische presentatie ernstig was). Van deze 1.223 (mogelijk) correct geïndiceerde antibioticavoorschriften waren er 563 (46,03%) de eerste keuze volgens de richtlijnen. De meest voorkomende diagnose was de bovenste luchtweginfectie met 366 (12,69%). Met 56,13 DDD/100 consultaties bleek amoxicilline-clavulaanzuur het meest gebruikte antibioticum, goed voor 15,76% (482,012 Ksh) van de jaarlijkse geneesmiddelenuitgaven. Zowel kennishiaten als *'know-do' gaps* beïnvloedden het voorschrijfgedrag. Concreet werden hierbij beschikbaarheid van medicatie, gewoonte ('mazoea'), (perceptie van) verwachtingen van patiënten en vrij verkrijgbare medicatie in apothekers en drogisten als belangrijke determinanten geïdentificeerd.

Conclusie

Deze studie constateert ongepast voorschrijfgedrag en antibiotica overconsumptie. De bevindingen onthullen diverse algemene en context specifieke drempels die kwalitatief voorschrijfgedrag belemmeren. Deze drempels vereisen een specifieke aanpak die verschillende strategieën combineert om de diverse factoren die van invloed zijn op het ongepast voorschrijfgedrag te viseren. Idealiter gebeurt dit aan de hand van een nationaal multisysteem-actieplan om antimicrobiële resistentie op alle niveaus te bestrijden. Op basis van de bevindingen van dit onderzoek, formuleerden we verschillende contextuele aanbevelingen om antimicrobiële resistentie te bestrijden en de zorg in het centrum te verbeteren.

Abbreviatons and acronyms

AB	Antibiotic
AMR	Antimicrobial resistance
DDD	Defined daily dose
KEML	Kenya Essential Medicine List
LMICs	Low and middle-income countries
MMC	Mabati Medical Centre
OTC	Over-the-counter
PHC	Primary Healthcare Centre
PPS	Point prevalence survey
RTI	Respiratory tract infection
WHO	World Health Organisation

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1. Introduction

Antimicrobial resistance (AMR) is emerging rapidly, threatening healthcare systems worldwide (1–4). Since the discovery of penicillin in 1928 there has not been a single antibiotic (AB) molecule against which micro-organisms have not developed resistance. This resistance is a natural phenomenon following the logic of Darwin's model of natural selection. However, this process is accelerated by AB (mis)use in the human, veterinarian and agricultural field. Antimicrobial resistance is acknowledged as a global public health threat, leading to increased mortality and cost, longer hospitalisations and indirect adverse effects on productivity (1,4,5). Although the rate of AMR is undeniably overtaking pharmaceutical innovation, 50% of AB prescriptions is considered unnecessary (6). Hence, to contain this public health threat, global efforts should prioritize rational use of ABs. The novel coronavirus outbreak, COVID-19, is currently reminding us about the devastating potential of a pandemic. It is clear that the most powerful and cost-effective response is to anticipate potential future threats by investing in global health security. Without pressing global efforts to fight AMR, the risk of a pandemic emerging from multi-drug resistant pathogens is real. In addition, without action, we might be heading to a pre-AB era where otherwise treatable could once again be fatal (2,4,5).

The phenomenon of AMR is widespread. Nonetheless, the major differences in grade of resistance and speed of distribution are striking. In low and middle-income countries (LMICs) such as Kenya, the situation is alarming. Poor infection prevention and control, difficult access to clean water and migration all contribute to this emerging threat (3,7). Conversely, the training of health care providers, the availability of diagnostic means and access to high-quality medication play a vital role in maintaining our antimicrobial agents (1,3,8). Throughout the years, several stewardship strategies and interventions have been demonstrated to be successful (4). Multi-strategy programs have proven to be most effective and since interventions are context dependent, an analysis should be made to determine the situation and characteristics of an institution prior to implementing a program. In addition, antimicrobial stewardship interventions ideally target both the knowledge gap and the 'know-do' gap. The knowledge gap refers to essential expertise, including clinical knowhow, lab interpretation and keeping up with clinical guidelines, while the 'know-do' gap refers to several context specific factors (i.e. habits, patient expectations, profit incentives, etc.) that impede clinicians to deliver the care they know is appropriate (4,9). Since the design of antimicrobial stewardship should be chosen to fit within its context, it is crucial to distinguish these gaps and understand the causes. Although the majority of AB use occurs at community and primary care level, the data for these levels is particularly scarce (1,10–13). In this single centre study, we analysed annual pharmaceutical consumption reports and drug availability to measure overall consumption, we used routinely collected electronic data to assess the quality of prescription behaviour and we conducted in-depth interviews to better understand the context and identify improvement opportunities.

2. Methodology

2.1 Setting

The study was conducted in Mabati Medical Centre (MMC), a first-line health centre in Mariakani, located along the major highway between Mombasa and Nairobi on the border of the provinces of Kilifi and Kwale (Figure 1). This private Medical Centre was established by the Safal Mabati Rolling Mills company fund in the year 2000. They provide consultations including treatment at a fixed fee for service rate of 350 KSh (approximately three euros). Originally only providing care to employees and their families, they now serve the entire community. On average the centre registers 20,000 patient visits per year.

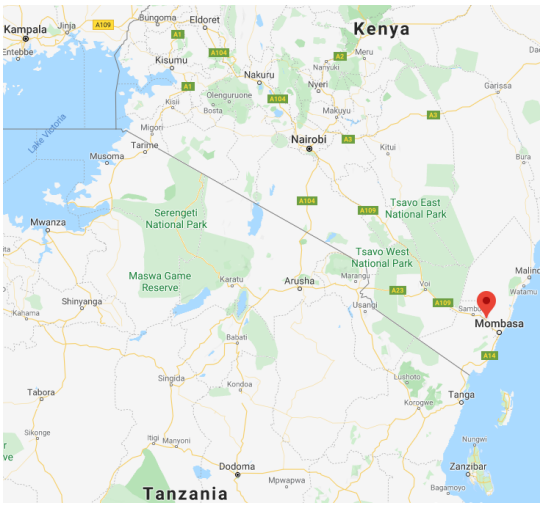


Figure 1 Location of the medical centre in Mariakani, Kenya (14). (Google Maps™)

2.2 Study Objectives

The primary objective of this study was to determine the patterns of prescribing practices in MMC. This was subdivided into the following specific objectives:

1. Asses availability of medicines. Measure AB consumption and expenditure.
2. Assess AB prescription quality.
3. Assess healthcare workers' ideas on current practice and AMR. Identify improvement opportunities.
4. Issue recommendations to combat AMR and improve quality use of antibiotics.

2.3 Study design

This was an observational, single-centred study. Routinely collected data from ambulatory patients over a 12-month period, from July 1, 2018 to June 30, 2019 were analysed. It is a mixed methods study comprising two quantitative parts, i.e. the measurement of AB consumption and an analysis of the quality of prescription behaviour, and a qualitative part in which in-depth interviews were used to explore the context and its improvement opportunities.

2.3.1 Measurement of AB consumption and assessment of AB availability

First, the theoretical and real availability of medication in MMC's pharmacy was assessed by comparing the inventory with the pharmaceutical stock; medicine storage was evaluated (see Appendix 1). Next, the Kenya Essential Medicine List (KEML), was remodelled into a checklist, i.e. the appropriate levels of care, corresponding with the delivered care of MMC, were selected and copied into a form (see Appendix 2) (15). Third, based on monthly drug expenditure reports, the annual expenditure on AB was calculated and compared to the total annual drug expenditure. Finally, based on monthly pharmaceutical consumption reports, the defined daily dose (DDD) per 100 patient visits was calculated from all antimicrobial molecules. The DDDs were calculated according to the official World Health Organisation (WHO) guidelines (16).

2.3.2 Analysis of the quality of the prescription behaviour

To characterize the use of ABs, a point prevalence survey (PPS) design was employed for the retrospective audit of AB prescriptions. The protocol and data collection tools for these were based on both The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance and the WHO methodology (see Appendix 3) (17,18). The source for the PPS were electronic medical records, drug dispense records and patient visiting records, routinely collected on Microsoft Excel sheets by local staff. These were de-identified, coded, cleaned and merged into one "mother database" to gather the following information:

- Molecule and dosage.
- Branded drugs vs generics
- Patient profile (age, sex)
- Administration (IV, IM, po)
- Indication

The indication was assessed by the principal investigator and the diagnosis was correlated with the national guidelines. Depending on the diagnosis, each prescription was divided into one of the following categories: indication in accordance with the guidelines; indication not in accordance with the guidelines; indication is unknown, indication in accordance with the guidelines if severe clinical presentation (e.g. tonsillitis, diarrheal disease, etc.). Subsequently, for all 'indication in accordance with guidelines' and 'indication in accordance with guidelines if severe clinical presentation', the AB of choice was compared with the guidelines (19).

The target population included all ages, both male as female sexes. To cover patient visits over a whole year, 52 subsequent weekdays (one day per week, Mon. - Fri.) were cross-sectionally selected for analysis, i.e. Monday 2nd July, 2018; Tuesday 10th July, 2018; Wednesday 18th July, 2018; etc. In case the selected weekday was a holiday, exceptionally, the next day was selected, after which the regular algorithm continued, e.g. Wednesday 2nd January, 2019 instead of Monday 1st January, 2019; Wednesday 9th January, 2019, etc. Figure 2 displays a flowchart of the selected patient visits. For each selected day the following was calculated: the denominator 'b' includes all patients who presented themselves on the selected day, the numerator 'a' includes all patients who presented themselves on the same day and were prescribed ABs (see Eq. 1). The group 'ABs' covers all systemic antimicrobials with activity against bacteria, fungi, protozoa (including malaria) and viruses (see Appendix 4 for a complete list).

$$\text{PPS} = \frac{\text{All patients receiving an antimicrobial prescription}}{\text{All patients presenting on the day of the survey}} = \frac{'a'}{'b'}$$

Equation 1 Calculation of AB administered patient visits in relation to total patient visits with a PPS

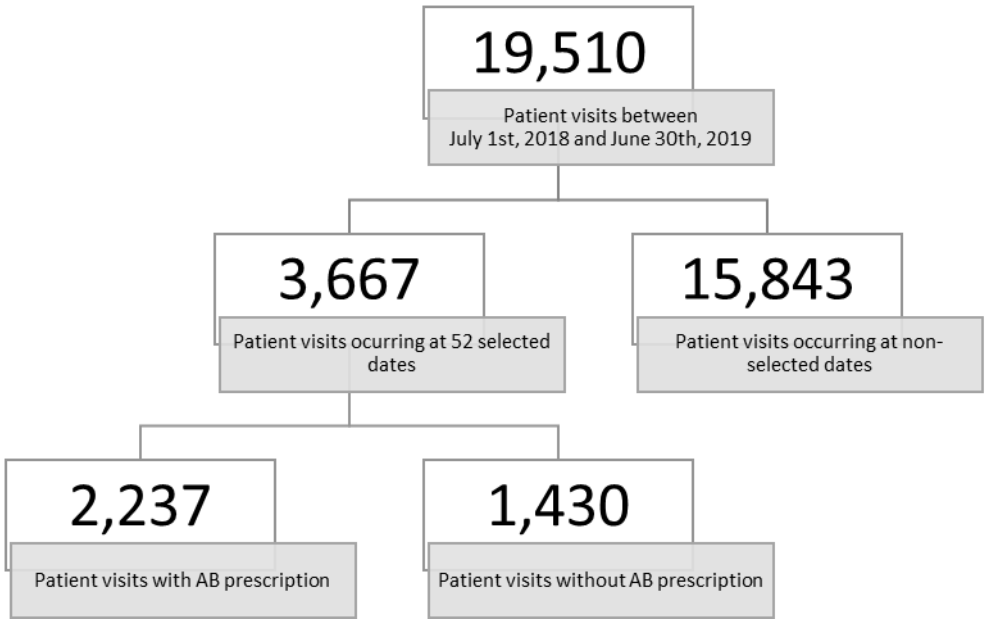


Figure 2 Flowchart of the selected patients visits for the PPS.

2.3.3 Qualitative analysis

Three explorative semi-structured key informant interviews were conducted to analyse the current function of the centre, explore determinants influencing antimicrobial use and identify improvement opportunities. In a discovery-oriented matter, open ended questions served to explore the ideas and perspectives of the respondents on specific topics. The six common challenges (structural, political, cultural, educational, emotional and physical) of quality healthcare formed an integral part of the topic lists, each drafted and customized to the interviewee (20). A pharmacist, a clinical officer and a lab technician were invited to participate based on their expertise and experience. Individual face to face interviews were preferred over focus groups to reduce bias of social pressure between informants' positions and specialities.

2.4 Data analysis

The quantitative data were analysed using Microsoft Excel 365. Descriptive statistics were applied, and data were presented using counts and percentages. The semi-structured interviews were transcribed using standard verbatim transcription. The transcripts were analysed using thematic/inductive analysis by the principal investigator. The used coding criteria were repetitions; remarkable information; known theories; relevant information and particular information considered important by the interviewee. Once coded, the data were categorised and the categories were labelled. These labels were different for each interview. The most significant findings from the labels were subtracted and organised into an organigram.

2.5 Ethical considerations

Approval for this study was obtained from the Ethics Committee of the Antwerp University Hospital on February 18, 2019 (reference letter n°18/47/534), Coast Provincial General Hospital on June 22, 2019 (Ref. ERC-CGH/MSc/VOL.I/57), the Kilifi County Department of Health Services on August 7, 2019 (Ref. HP/KCHS/VOL.XL/157) and was officially authorized by the administrator of MMC, Ms Clara Shuma, on July 22, 2019.

3 Results

3.1 Measurement of AB consumption and assessment of AB availability

3.1.1 Survey of formulary and pharmacy stock

All activities in the pharmacy (consumption reports, stock and purchases) were electronically recorded. In the pharmacy the medication was stored in a systematic manner, ABs were stored in locked cupboards and air conditioning kept the rooms at a constant temperature (see Appendix 1 for pictures of the pharmacy). Upon formulary review, inconsistency was noted between the theoretical and real availability of the medication. Out of the 237 pharmaceutical products mentioned in the formulary, 157 were actually present, 25 were out of stock and 55 were permanently unavailable. Moreover, 16 of the 23 essential ABs listed in KEML were present (see Appendix 2 for checklist). Two antibacterials, i.e. benzathine benzylpenicillin and cefixime, one antiprotozoal, i.e. diloxanide and four antimalarials, i.e. quinine; dihydroartemesinine + piperaquine; sulfadoxine pyrimethamine and artesunate for injection were not available. Artemether was in use as a parenteral antimalarial instead of artesunate. All ABs present were generic drugs.

3.1.2 Expenditure to ABs

The total cost of the annual AB consumption, i.e. from July 1, 2018 to June 30, 2019, was 1,150,450 Ksh, accounting for 37.62% of the total annual pharmaceutical budget. Among the ABs used, amoxicillin/clavulanate use comprised the largest cost with 482,012 Ksh, accounting for 15.76% of the total expenditure (see Table 1 and Figure 3).

Table 1 Annual AB expenditure at MMC between July 1, 2018 and June 30, 2019

AB molecule	Annual expenditure in Ksh	Annual expenditure in percentage of total MMC pharmacy expenditure
Amoxicillin-clavulanate	482,012	15.76
Flucloxacillin	99,175	3.24
Amoxicillin	108,570	3.55
Ampicloxacillin	119,906	3.92
Ceftriaxone	39,631	1.3
Other ABs	301,156	9.85
Total	1,150,450	37.62

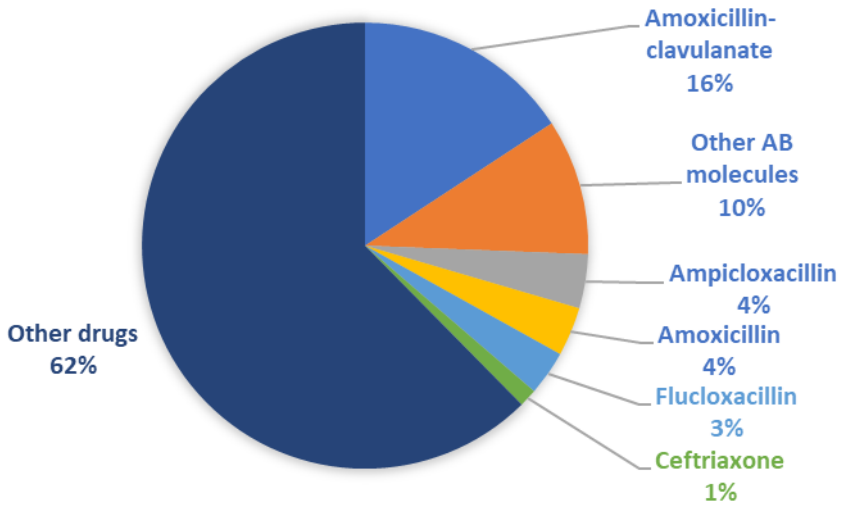


Figure 3 Relative share of AB consumption in relation to annual pharmaceutical expenditure at MMC between July 1, 2018 and June 30, 2019.

3.1.3 Defined Daily Doses

Annual AB consumption, expressed as DDD/100 patient visits and calculated from monthly pharmacy consumption reports are presented in Table 2. In Appendix 5, the definition of DDD is clarified and the annual DDD/100 patient visits from July 1, 2018 to June 30, 2019 of all ABs are illustrated. Amoxicillin-clavulanate consumption was the largest with 56.13 DDD/100 patient visits and the overall use of ceftriaxone was lower with 3.53 DDD/100 patient visits. Figures 4 and 5 show the monthly trend in AB consumption throughout the year. Although these findings were in line with the overall consumption, there was an apparent month-to-month variability. In August the overall consumption was much lower.

Artemether-lumefantrin consumption was high in December (200 DDD/100 patient visits) in contrast with January, May, June and August, when consumption dropped to zero DDD/100 patient visits. Artemether injection knew a peak in consumption in the month of May, to remain at zero for the rest of the year. Moreover, the high usage of amoxicillin-clavulanate in October, November, December and June, and the single rise of mebendazole use in September, were noteworthy. Overall, the usage of parenteral ABs (ceftriaxone, benzyl penicillin, artemether) was low.

Table 2 Defined daily dose and DDD/100 patient visits of the most consumed AB from July 1, 2018 to June 30, 2019 in MMC

AB Molecule	DDD	DDD/100 patient visits
Amoxicillin-clavulanate	10,950.66	56.13
Amoxicillin	8,895	45.59
Artemether-Lumefantrin	7,061	36.19
Ampicloxacillin	6,632.19	34
Co-trimoxazole	5,899.25	30.24
Ciprofloxacin	4,717	24.18
Artemether	2,042.29	10.47
Metronidazole	1,995.33	10.23
Mebendazole	1,783.5	9.14
Erythromycin	1,451	7.44
Albendazole	990	5.07
Ceftriaxone	688.5	3.53
Cefuroxime	440	2.26

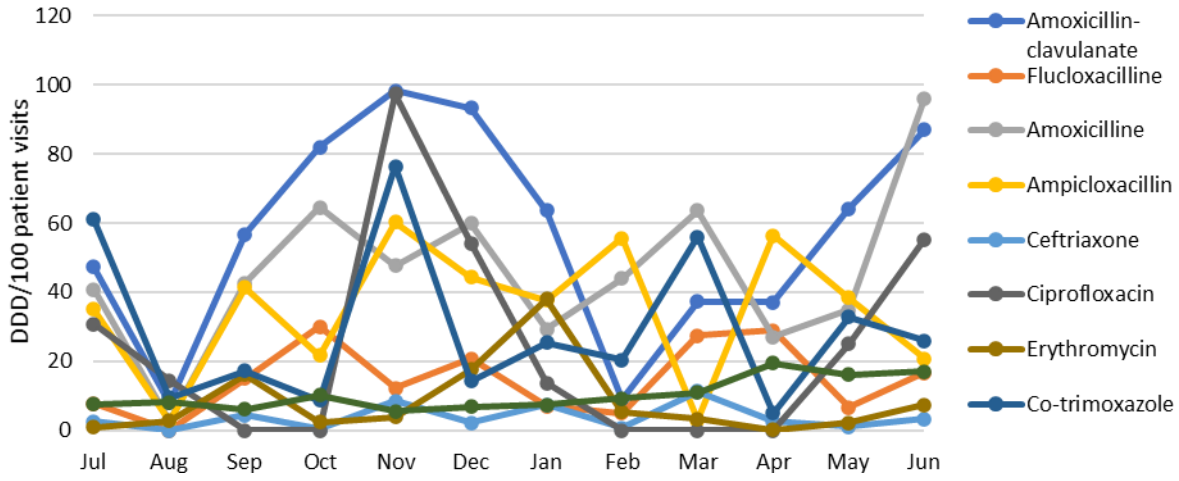


Figure 4 Monthly trend of DDD/100 patient visits for the most commonly consumed antibacterials from July, 2018 to June, 2019

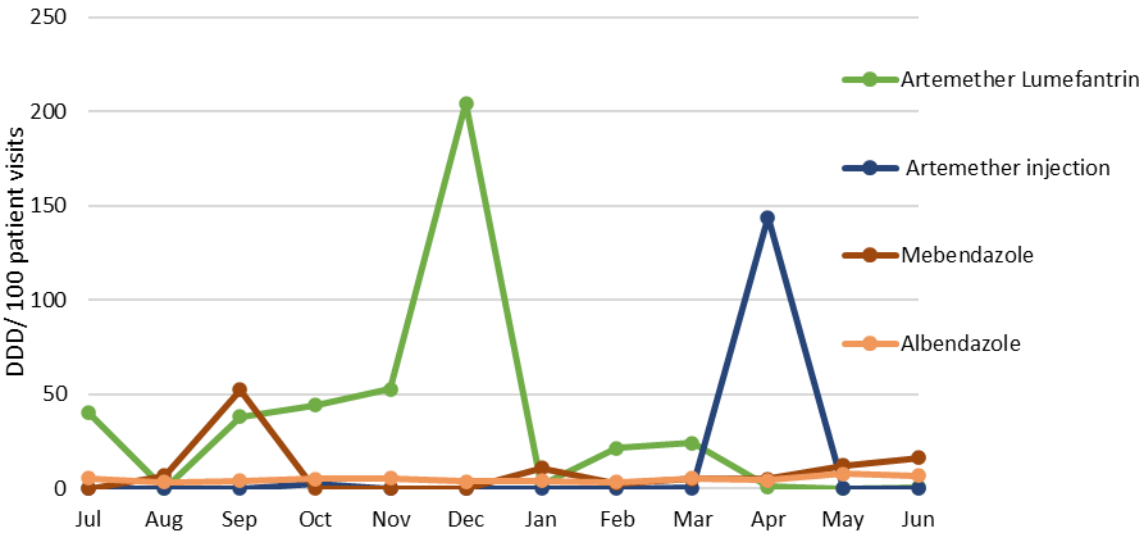


Figure 5 Monthly trend of DDD/100 patient visits for the antimalarials and antihelminthics from July, 2018 to June, 2019

3.2 Analysis of the quality of the prescription behaviour

3.2.1 Point prevalence survey

Figure 2 displays the process of patient visit selection. The characteristics of all patient visits, the selected patient visits and their analysed prescriptions are presented in Table 3. A total of 9,603 medical prescriptions (including ABs) were prescribed over the 3,667 selected patient visits (i.e. a mean of 2.69 (0-6) prescriptions per patient visit). On 2,235 of the 3,667 selected visits (60.6%) a total of 2,884 ABs were prescribed (i.e. on average 1.3 AB per patient visit). As shown in Figure 6 there was considerable month-to-month variability of the proportion of visits with AB prescription, with 47% being the lowest and 75% being the highest proportion. Males dominated with a total of 2,039 patient visits (55.60%). However, females received 1,537 (53.29%) of the 2,884 ABs prescribed.

$$\mathrm{PPS} = \frac{\text{All patients receiving an antimicrobial prescription}}{\text{All patients presenting on the day of the survey}} = \frac{2237}{3667} = 0.6062$$

Equation 2 Result of all antibiotic administered patient visits in relation to total patient visits over the 52 selected weekdays

Table 3 Characteristics of patient visits and AB prescriptions, selected for quality assessment.

Characteristics of all patient visits from July 2018 to June 2019			Characteristics of the study population (52 survey days)		Characteristics of AB prescriptions (52 survey days)	
Total	19,510		3,667		2,884	
Age						
0-5 y	3,730	19.12%	807	22.01%	757	26.25%
5-10 y	3,025	15.50%	669	18.24%	586	20.32%
18-60 y	10,272	52.65%	1,878	51.21%	1,371	47.54%
60+	1,633	8%	312	8.51%	169	5.86%
Age unknown	848	4.35%	1	0.03%	2	0.07%
Sex						
Male	11,120	57.00%	2,039	55.60%	1,347	46.71%
Female	8,389	43.00%	1,628	44.40%	1,537	53.29%

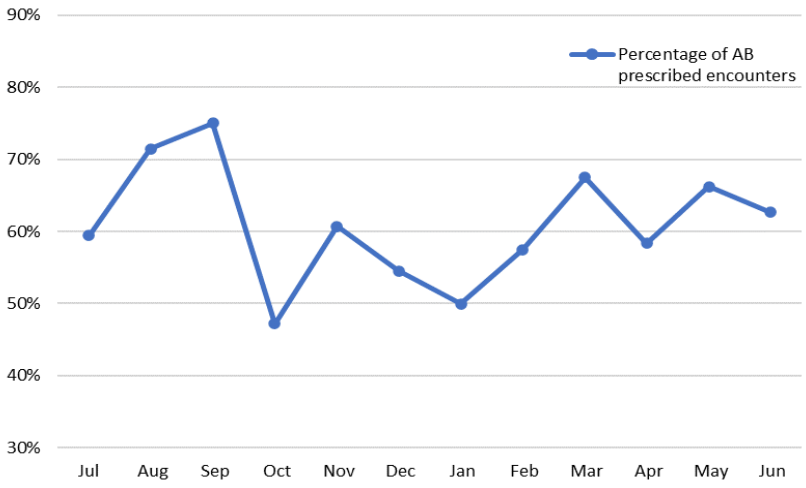


Figure 6 Evolution of monthly proportion of visits at MMC in which an AB was prescribed from July, 2018 to June, 2019.

The results of the analysis of the AB prescriptions are displayed in Table 4. For only 655 (22.7%) of the prescriptions the indication was in accordance with the guidelines. Another 568 (19.7%) prescriptions were justifiable if the clinical presentation was severe and for 1,176 (40.8%) prescriptions the indication was not in accordance with the guidelines while 485 (16.8%) prescriptions were not assessable. For the 1,225 indicated, some questionable, prescriptions only 563 (46.0%) were in accordance with the suggested choice of the guidelines, as illustrated in Figure 7. Assessment of posology proved to be very difficult due to lack of accurate guidelines and incomplete data, i.e. unknown patient's weight and uncertain indications. Therefore, the usual posology of the most commonly prescribed AB was summarised in Appendix 6.

Table 4 Main results of the point prevalence survey, prescription quality analysis of the 2,884 selected AB prescriptions

Total number of AB prescriptions analysed	**2,884**	
Antibiotic indication in accordance with the guidelines	655	22.71%
Antibiotic indication in accordance with the guidelines in case of severe clinical presentation	568	19.69%
Antibiotic indication not in accordance with the guidelines	1,176	40.78%
Antibiotic indication unknown	485	16.82%
Route of administration		
Oral ABs	2,853	98.9%
Parenteral ABs	31	1.08%
Total number of AB prescriptions with arguably correct indications	**1,223**	
Choice of AB in accordance with the guidelines (first choice)	563	46.03%
Choice of AB molecule not in accordance with the guidelines	660	53.97%
Total number of selected patient visits	**3,667**	
Antibiotic injections prescribed	31	0.85%

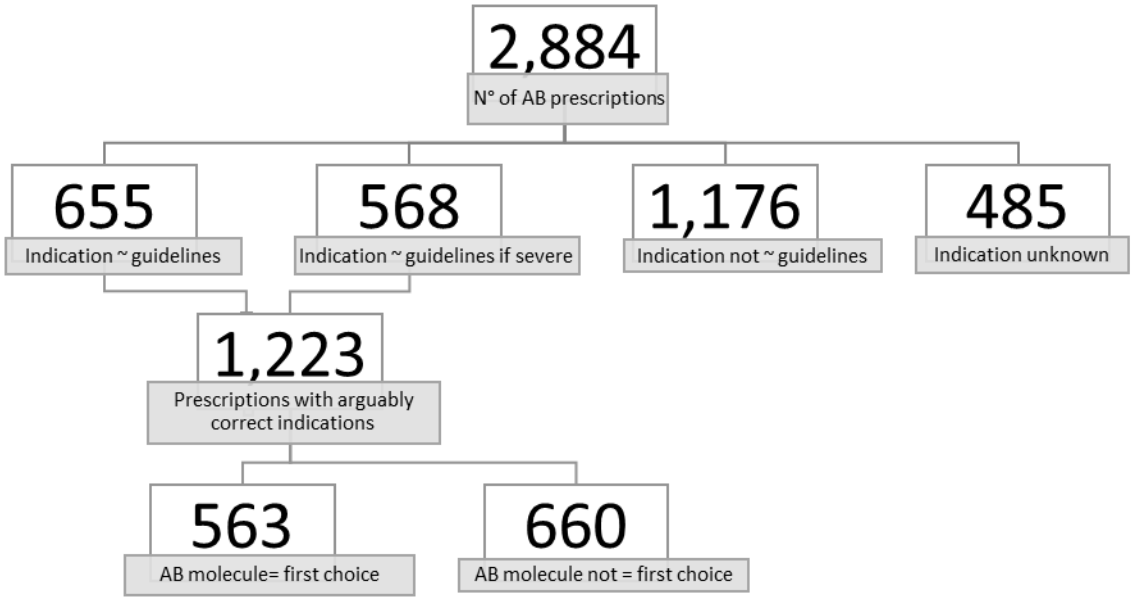


Figure 7 Graphical overview of the quality analysis of the 2,884 selected AB prescriptions.

3.2.2 Most common diagnoses for which ABs were prescribed

Figure 8 illustrates the main diagnoses for which AB were prescribed. Patients on ABs were mainly diagnosed with respiratory tract infections (RTI), representing 653 (22,64%) diagnoses among which 366 (12,69%) upper RTI, 144 (4,99%) pneumonias and 143 (4,96%) undefined RTIs. Urinary tract infections accounted for 168 (5,83%) diagnoses, malaria 155 (5,37%) and gastro-intestinal infections 253 (8,77%) among which 114 (3,95%) gastritis. The ten most common diagnoses, presented in Table 5, accounted for 1,418 (49,2%) of the 2,884 diagnoses. The other 50% was a heterogenous group of primary care pathologies ranging from specific diagnoses (i.e. ear infection, diabetes mellitus, etc.) to vague descriptive complaints (i.e. febrile illness, open wound, hormonal imbalance, etc.).

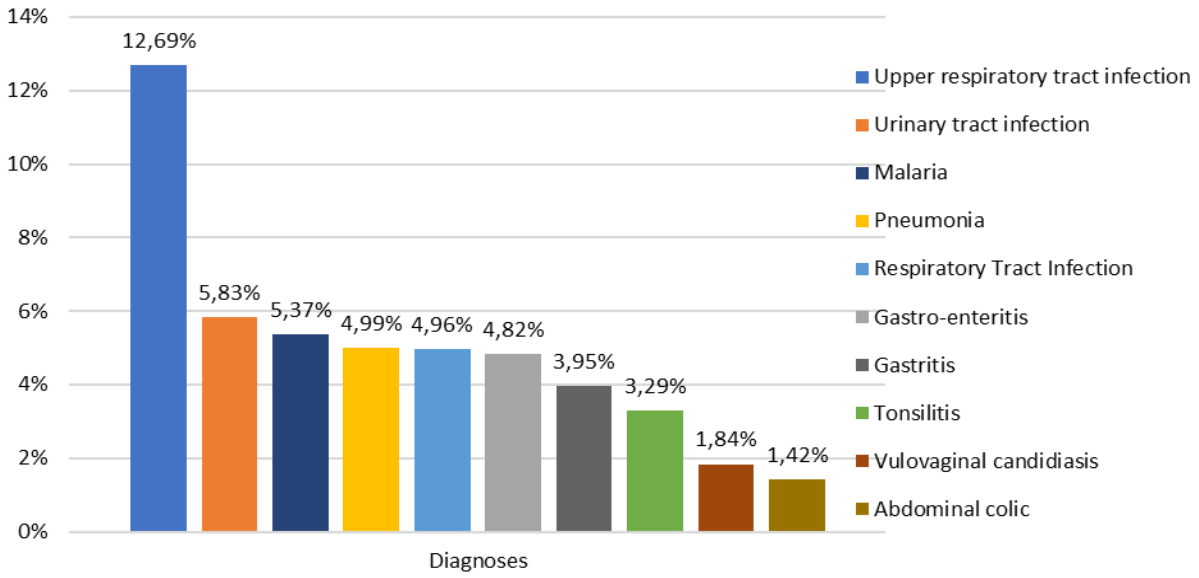


Figure 8 Top ten most common indications for the 2884 analysed AB prescriptions

Table 5 Ten most common diagnoses for which ABs were prescribed

Diagnosis	**Number of diagnoses**	**In relation to the total number of 2,884 AB prescriptions**
Upper respiratory tract infection	366	12.69 %
Urinary tract infection	168	5.83 %
Gastro-enteritis	139	4.82 %
Pneumonia	144	4.99 %
Respiratory tract infection	143	4.96 %
Tonsillitis	95	3.29 %
Malaria	155	5.37 %
Vulvovaginal candidiasis	53	1.84 %

Diagnosis	Number of diagnoses	In relation to the total number of 2,884 AB prescriptions
Gastritis	114	3.95 %
Abdominal colic	41	1.42 %
Other	1,466	50.83 %

3.3 Qualitative analysis

Three in-depth interviews provided interesting views concerning drug storage, consumption and prescription behaviour in the centre. The duration of the interviews ranged between 33 and 45 minutes. The questions and content differed for each candidate due to the different professional background of the interviewees. In Appendix 7 the main findings were summarised into an organigram per interview. Table 6 provides an overview of characteristic quotes that support the respective statements.

3.3.1 Prescribing habits

All interviewees agreed too many ABs were prescribed. However, regarding reasons for AB overuse and determinants influencing prescribing behaviour, opinions differed. The prescribing patterns were prescriber dependent and were affected by drug availability (see Table 6, Quote1, Interview1). Patient demand may impact AB prescription, especially when accustomed to a particular drug. Explanations for the high consumption of amoxicillin-clavulanate were perceived risk of failure of smaller-spectrum ABs due to AMR, patient satisfaction, convenience (one tablet BID versus two tablets TID for amoxicillin, see Appendix 6) and habit (‘mazoea’ in Swahili). For RTIs the main argument to prescribe an AB was the productiveness and colour of the sputum (Q2I2). Patient history and clinical examination were found to be the principle determinants influencing prescribing behaviour although medical imaging results; microbiological data; patient characteristics i.e. age; and patient satisfaction were also mentioned. This was in contrast with another testimony, questioning evidence based judgment of the prescribers and suggesting mass prescription emerged from poor interpretation of microbiological data and non-adherence to the guidelines (Q3I3).

3.3.2 Availability

Drug stock-outs occurred frequently and had a direct impact on the prescribing behaviour. Clinical officers either adapted their primary choice according to the availability or referred patients to an external pharmacy. A tedious ordering process, prescribing habits, patient visit fluctuations, disease outbreaks and insufficient buffer-stock all affected AB availability (Q4I1).

3.3.3 Antimicrobial resistance

Interviewees reported that AMR was becoming progressively eminent. One interviewee described AMR as a lack of clinical response after AB treatment, while another observed various resistant antibiograms in stool and urine cultures (Q5I3). All agreed that over-the-counter (OTC) prescribing behaviour was an important driver of AMR. Patients often consulted chemists first and only presented themselves at the centre when symptoms persisted, usually after an initial treatment with AB: always empirical and often inappropriate, i.e. poor drug choice, dosage and quality control. One interviewee referred to poverty as the most important fuelling factor (OTC drugs are cheaper)

whereas the others blamed corruption. Someone claimed the Pharmacy and Poisons Board was allowing uneducated pharmacists to practice and was tolerating prescription drugs being sold OTC in return for bribes (Q6I3).

3.3.4 Future perspectives

The interdisciplinary communication in the centre seemed to be going well. Nevertheless, interviewees had various suggestions to tackle some of the identified pitfalls. First, improve availability by simplifying the complex process of ordering medication and respecting a sufficient buffer stock (Q2I1). Next, address prescribing habits by retraining staff on the current guidelines and interpretation of lab results, perform clinical audits to monitor (Q7I3). Third, it was pointed out that, if available, clear guidelines would be respected and implemented in practice (Q8I2). On a national level there was consensus that OTC prescription behaviour was compromising good clinical practice. The Pharmacy and Poison's board should ensure that all pharmacies are run by professionals, conduct thorough inspections and close down clandestine chemists (Q6I3). In addition, AMR sensitization campaigns should be implemented to inform patients and motivate them to seek professional healthcare.

Table 6 Interview quotes per label.

Quote	Label
Q1 "Yes, the prescribing behaviour is a fact. We keep a variety of drugs. But then a particular clinical officer prefers a particular drug. So, when it's there, they prescribe just that. If we run out, that is when they switch." I1	Prescribing habits
Q2 "If it is a productive cough, we ask: "Which colour has the sputum?". If it is creamy and yellowish we start the treatment for a bacterial infection because we think of a pneumonia. If the patient comes with a cough for a few days and it is productive but colourless, watery, then we scope this as either viral or allergic" I2	
Q3 "So I feel like: yes, the results come out. But my major concern is the interpretation of these results, interpretation is a key thing. " "We draft very nice policies etc but implementing them, that is where the challenge is." I3	
Q4 "Now first of all, I would say we need a shorter lead from the time we made the order to the time we receive the order. This is causing most of the stock-outs, because it's a tedious process" I1	Availability
Q5 "There are some particular drugs that are totally resistant. And this is replicating itself, I see it in urine cultures from different people. So, for me that is an indicator that it could be that most of these patients, especially those with chronic urinary tract infections, tend to have used a lot of antibiotics" I3	AMR
Q6 "They should make sure to close down, clamp and maybe arrest and prosecute some of these who are selling this. But the problem is they end up getting bribed when they show up to these small chemists and shops. Therefore, they're not doing what they're mandated to do. From my own of point of view, that is one of the factors that has actually largely contributed to AB resistance. I think for me it is the main factor because you can easily access drugs anywhere at any point. "I3	

Quote	Label
Q7 "Generally I feel like, to counter this type of antibiotic misuse, retraining and this kind of clinical audit could be useful" I3	Future perspectives
Q8 "I think a guideline has passed through great brains in the medical field before it was passed to us. I believe in them, I believe in the protocols that are there from the medical field by different medics. So, if at all those guidelines come, 100%. I would trust them." I2	

4 Discussion

This single centre study analysed AB consumption and prescribing behaviour in an exhaustive manner. The most important results regarding AB overuse, inappropriate practice patterns, identified pitfalls and improvement opportunities will be discussed in this section. The main recommendations that emerged from this study are summarised in Table 7.

4.1 Measurement of AB consumption and assessment of AB availability

Overall the availability of drugs was acceptable and the pharmacy stock well organised. The formulary was comprehensive but should be updated, given that some medication was removed from the list. Most of the essential ABs, as recommended by KEML, were present. Nevertheless, the absence of benzathine benzylpenicillin and artesunate injection were remarkable. Benzathine benzylpenicillin is suggested as first choice treatment for several infections in the national guidelines and, according to WHO's AWARE classification, is part of the 'Access' group and should thus be widely available (21). Artesunate IV/IM is the primary choice for all adults and children presenting with severe malaria according to the most recent WHO guidelines (2015) for the treatment of malaria; "If artesunate is not available, use artemether in preference to quinine for treating children and adults with severe malaria" (22). National guidelines recommend parenteral quinine rather than artesunate/artemether for the treatment of severe malaria, which is outdated because parenteral artesunate has shown a substantial reduction in mortality compared to parenteral quinine and is simpler and safer to use (22,23). It is therefore recommended to include benzathine benzylpenicillin and artesunate in the formulary.

On the one hand, the DDD/100 patient visits is a useful measure to follow up AB consumption within a centre over the years, as well as it is a useful universal tool to compare drug consumption with other facilities, regions and countries. On the other hand, reliable data to benchmark the results with are often lacking, as is the case for MMC (to our knowledge no previous research has measured DDDs in a primary healthcare centre (PHC) or outpatient clinic in Kenya). Nevertheless, it proves useful to compare the different ABs among each other. In Kenya, as in most LMICs, broad-spectrum ABs (e.g. amoxicillin-clavulanate) are frequently being overprescribed (9,24). Amoxicillin-clavulanate was most commonly prescribed at MMC, consuming 16% of the total annual drug expenditure with 56.13 DDD/100 patients. This is particularly remarkable since the drug is rarely a first-choice molecule according to the guidelines (19). In addition, it is inconsistent with results of a similar studies in Mbagathi district Hospital (Kenya) and PHCs in Ghana. These studies reported amoxicillin and metronidazole, amoxicillin, cotrimoxazole and flucloxacillin being more frequently prescribed than amoxicillin clavulanate (25,26). In the outpatient department of Makueni county referral hospital (Kenya), amoxicillin clavulanate did not occur in the top five most commonly used AB (27).

The high usage of amoxicillin clavulanate in MMC could be attributed to the perceived risk of AMR or the differences in mortality and morbidity characteristics of the population. Nevertheless, it also indicates that prescribers did not strictly comply with the current guidelines. As indicated above (see 3.3.1), (perceived) AMR; (perceived) patient demand; convenience and habit ('mazoea') were given as the main explanations. Regardless, de-escalation from oral broad-spectrum ABs (amoxicillin-clavulanate) to more narrow-spectrum ABs (amoxicillin, nitrofurantoin) is desirable.

The strong month-to-month variability observed in consumption could mainly be explained by seasonal diseases; patient fluctuations and stock-outs, though this does not explain all observed variation. To illustrate, the peak in consumption of mebendazole was attributed to an outreach project, targeting lymphatic filariasis in Mombasa and Kwale counties. The remarkable low consumption of parenteral ABs (e.g. 3.5 DDD/100 patient visits for ceftriaxone) is discussed underneath.

4.2 Analysis of the quality of the prescription behaviour

This study showed that 2,237 out of 3,667 (60.62%) encounters led to at least one AB prescription. This corresponds to the nationwide trend of AB (mis)use in Kenya, reporting percentages from 68.4% to 76.7% (27,28). Other studies analysing outpatient prescribing practices published 72.9% in Makueni County Referral Hospital (MCRH) and 68.1% in Mbagathi District Hospital (25,27). A WHO analysis of medicine use in LMICs showed that the percentage of encounters in which AB were prescribed is lower in other countries, e.g. for Colombia, Tanzania, India and Mali they estimated 30%, 46.43%, 50.77% and 58.6%, respectively (28). This is still significantly higher than the admissible range of 20.0-26.8% as suggested by the WHO (29). A situational analysis on the AB use in Kenya reported the following provider related factors for AB misuse: lack of diagnostic means; improper training; fear of bad treatment outcome and profit incentives (30). However, several additional determinants have been described, i.e. a high patient-doctor ratio; outdated guidelines; medicine availability; difficulty in observing patient progress; (perceived) patient demand; habit; sociocultural factors and organizational policies (4,10,31,32). Diagnostic means are appropriate in MMC and since they charge an all-in-one fee for service, profit incentives are less likely to contribute significantly. Interpretation of lab results, non-adherence to guidelines, habits ('mazoea'), patient expectations and convenience emerged as important influencing factors in MMC in particular (as stated in section 3.3).

Out of the 2,884 AB prescriptions analysed, the PPS reported 655 appropriate AB prescriptions and 568 potentially appropriate AB prescriptions (see Figure 7). Overall for 46.03% of all AB prescriptions with arguably correct indications, the first choice AB molecule was prescribed. These results indicate substandard quality of AB prescribing. Which is also evident from the most common diagnoses for which ABs were prescribed. Out of the top ten diagnoses only pneumonia, malaria and urinary tract infections are absolute indications for ABs. Respiratory tract infections accounted for 22.64% of all diagnoses, half of these were upper RTIs. Since most uncomplicated RTIs are caused by viruses, ABs are not recommended (24). Nevertheless it is the primary reason for AB prescription worldwide. A recent study concerning AB usage in private PHCs in Kenya reported that commonly encountered infectious conditions, i.e. RTI, urinary tract infections and diarrheal disease, result in an AB prescription in over 90% of patient encounters (4,9).

As introduced before, both knowledge and 'know-do' gaps contribute to indiscriminate prescription behaviour. In spite of the available evidence, showing that sputum colour does not imply therapeutic consequences such as the prescription of AB, the colour of sputa had a decisive influence on prescribing behaviour in MMC (see table 6, Q2I2) (33). Consequently, staff training and issuing up-to-date clinical guidelines are essential in tackling knowledge gaps. However, merely improving knowledge about evidence-based recommendations is not sufficient for adherence. Antibiotics are also being prescribed in spite of better knowledge, driven by behavioural factors i.e. patient expectations; habit or inertia of previous practice; lack of self-efficacy; limited outcome expectancy and an irrational feeling of greater patient safety, or by external factors i.e. medicine availability; financial incentives; and lack of resources or facilities (9,30,34–36). Therefore, efforts must also be made to tackle this 'know-do' gap and allow clinicians to deliver the care they know is appropriate. The identified context-specific barriers (applicable in MMC) are summarised in Table 7.

One frequently recurring determinant was patient expectation. However, prescribers should realise that patients, e.g. with a RTI, expect a proper diagnosis, prognosis and guidance on symptom management, rather than an AB prescription. Healthcare workers often seem to overestimate patient expectations on AB prescriptions and they might prescribe ABs to avoid conflict, paradoxically stimulating the patients idea that ABs are necessary for their illness and nourishing a vicious circle of medicalization of a self-limiting illness (4). Additionally, efforts should be made to provide proper patient information and to raise awareness on AB misuse and its consequences. Patient information must also address the importance of correct usage. Using partial doses, sharing AB with others or hoarding them for future use, will only increase the problem (30).

The PPS showed an average number of medicines prescribed per encounter of 2.69 (0-6) and the percentage of encounters with an AB injection prescribed was 0.85%. These results compare to 2.48 and 1,5%, respectively, in the outpatient clinic of Makueni, but they differ from the recommended 1.6-1.9 and 13.4-24.1% range as recommended by the WHO (27,29). The study in Mbagathi reported 3.85 average prescriptions and 9.5% of their prescriptions were injectables. Injectables come with a higher cost and additional potential complications such as infection at the injection site. They should therefore be reserved for the severely ill patients or when oral therapy is not an option. Together with the low DDD/100 patient visits for parenteral ABs, this percentage further supports the finding that parenteral AB usage is appropriate in MMC. By contrast, with a mean of 2.69 (0-6) prescriptions per patient visit, polypharmacy was obvious. This may result in drug interactions, reduced compliance, unnecessary expenses and there is a positive association with AB prescriptions (4,27,37). Consequently, mitigating medicine overuse benefits the patient on an individual and on a public health level, as it decreases unnecessary healthcare expenses, suffering from iatrogenic complications and the risk of AMR.

4.3 Qualitative analysis

When exploring contributing factors to the documented inappropriate AB prescription behaviour in the centre, a dissatisfaction on national policy and OTC prescription emerged. Corruption and poverty were identified as the main drive of OTC prescription, thus fuelling AMR. Antibiotic misuse as a result of OTC prescription is a documented driver of AMR worldwide, though the frequency of non-prescription use of antimicrobials in the general population is highest in Africa (11). In Kenya more than 70% of pharmacies dispense ABs without a prescription (11,30). Tackling this problem would mitigate indiscriminate use of ABs in general and allow healthcare providers in MMC to deliver more

appropriate care. However, research has shown that restricting OTC sales with fines and closing down businesses, as suggested by interviewees, can have a disappointing impact (10). In neighbouring country Tanzania, the government introduced the accredited drug dispensing outlet program in 2003 to improve access to quality medicines and pharmaceutical services. Again, despite improved standards of practice and knowledge on treatment guidelines, overuse of ABs for common conditions remained problematic (32). Most countries that have effectively decreased non-prescription antimicrobial use combined regulation with expanded access to healthcare (11). Kenya's national action, with a main focus on measures to raise awareness and promote behaviour change, should take this into account (7).

This study confirmed inappropriate prescribing behaviour and identified shortcomings in availability, knowledge and know-do gaps in MMC. Consequently, the interviewees advocated for a less complex supply chain, provide straightforward up-to-date guidelines, retrain prescribers, perform clinical audits and sensitize patients. Although most AB use occurs in the community, there is few evidence available on the effectiveness of AB stewardship interventions at primary care level (10,34). Most experts agree that a combination of different strategies proved most successful, i.e. combining teaching techniques with monitoring. In addition, individual behaviour and decision making is determined by numerous contextual factors across different scales. Ideally a decentred whole system approach, such as Kenya's national action plan, should be implemented in order to maximise gains (10). For instance, education on AB use should not be limited to postgraduate courses for prescribers, it should even more so focus on shaping adequate behaviour of junior doctors, which in turn demands strong political support for a curriculum program to be implemented (38). Nevertheless, small scale stewardship studies can provide valuable data in the combat against AMR and can improve local daily practice. Previous research endorses most of the suggested interventions to tackle the identified shortcomings, ideally by combining several strategies and monitor progress yearly.

4.4 Strengths and limitations

This mixed methods study comes with some limitations. The AB usage assessment was based on MMC pharmacy consumption reports when, on rare occasions e.g. in case of stock-out, prescribers referred to extramural pharmacies. For the PPS, routinely collected data were used, yet incomplete patient records and nonspecific symptomatic descriptions formed a challenge. Even so, it is exceptional for PHCs in Kenya to collect electronic health records so diligently. These efforts allowed for a retrospective assessment of the data, thus mitigating the Hawthorne effect (i.e. when participants of a study modify their behaviour due to their awareness of being observed). Lastly, due to circumstances only three in-depth interviews, including one interview with a clinical officer, were conducted. A larger sample size, including the manager; nurse; etc. would have increased the reliability of this study. However, since all interviewees were highly skilled and experienced employees it was easy to rapidly deduct valuable insights from the interviews. Despite these limitations this study provides valuable insights into the AB usage and prescribing behaviour of MMC, a private semi-rural PHC. To our knowledge this is the first study to report prescribing behaviour in such an exhaustive manner in a semi-rural PHC setting. From this comprehensive analysis several evidence based suggested interventions emerged to improve the quality of care in MMC. In addition, this study addresses a research gap by providing useful data on AB usage, contributing to a better understanding in a setting where data are scarce.

Table 7 Summary of recommendations based on identified barriers.

Identified barriers impeding qualitative prescribing behaviour	Recommendation	Level (local vs national)
Knowledge gap		
• Antibiotic indication not in accordance with guidelines • Flaws in clinical reasoning e.g. colour of sputum as indicator. • Misinterpretation of lab results e.g. malaria treatment despite negative result • Inappropriate choice of AB molecule e.g. overconsumption of amoxicillin-clavulanate	• Retrain clinical officers on AMR and appropriate prescribing behaviour e.g. with online courses. • Monitor progress i.e. perform clinical audits; address guideline-discordant prescribing behaviour; follow-up DDDs • National/government efforts should develop and implement an adapted AMR curriculum to educate on AB (mis)use in both schools and universities • Update and improve access to national guidelines, e.g. user-friendly smartphone application.	L + N
'Know-do' gap		
• (Perceived) patient expectation • Irrational feeling of patient safety • Inertia of previous practice or habit ('mazoea') • Financial incentives? • Medicine availability	• Raise awareness in the community on AMR and the dangers of AB misuse • Raise awareness among prescribers on perceived patient expectations • For both patients and health care workers raising awareness and educating on prudent antibiotic use should start early Shape behaviour > change behaviour	L + N
Availability		
• Stock- outs • Absence of benzathine benzylpenicillin • Absence of artesunate injection • Outdated formulary	• Simplify tedious process of ordering medication. • Increase buffer stock. • Add benzathine benzylpenicillin and artesunate injection to the formulary. • Update formulary to current situation	L
Non-prescribed antimicrobial use		
• Over-the-counter prescribing	• Raise awareness on AMR and the dangers of AB misuse. • Review and enforce regulations. • Expand access to health-care. • Fight poverty and corruption.	N

5 Conclusion

Antibiotic overuse at primary care and population level in LMICs directly contributes to AMR, a global health emergency. This study demonstrated inappropriate AB prescribing behaviour in semi-rural PHC in an exhaustive manner. There was an overconsumption of ABs, the proportion of patient visits in which ABs were prescribed was 68% and the quality of prescription behaviour proved substandard. Although the amount of AB injectables prescribed was appropriate, polypharmacy and AB combination therapy were common. Furthermore, findings emphasized shortcomings and barriers impeding qualitative prescribing behaviour. Not only did this research expose deficiencies of national policy, directly affecting local practice, it also identified possible interventions to mitigate AB misuse and enhance the quality of care in the centre. In Table 7 the recommendations that emerged from this analysis are summarised, many of which are well-founded evidence-based strategies in antimicrobial stewardship. They address both local and national policy, since pressing efforts are vital on every level to curb AMR, ideally through a whole-system integrative approach.

Conflicts of interest

We wish to confirm that there are no known conflicts of interest associated with this study and there has been no financial support for this work that could have influenced its outcome.

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Appendices

Appendix 1: Pharmacy stock of MMC



Picture 1 Pharmacy stock of MMC



Picture 2 Pharmacy stock of MMC



Picture 3 Pharmacy stock of MMC

Appendix 2: Kenya's Essential Medicine List

Meaning of the levels: "The lowest level of the healthcare delivery system at which each particular medicine may reasonably be expected to be appropriately used (ie. after correct diagnosis and a correct decision on management of the condition according to current best therapeutic practice). It is thus the lowest level at which the medicine is expected to be available for use (ie. distributed, stored, prescribed and dispensed)."(15).

The levels in the forms are as follows:
1 = Community Health Services
2 = Dispensary/Clinic
3 = Health Centre

Table 8 Kenya's Essential Medicine List, checklist

Drug	***Dose-form***	***Size***	***Level***	***Availability at MMC pharmacy (Real, Theoretical or None)***
Antihelmintics				
Albendazole	Tablet	400mg	1	R
Praziquantel	Tablet	600mg	2	R
Antibacterials				
Amoxicillin	Disperse Tablet (DT)	250 mg	2	R
	Capsule	500 mg	2	N
Amoxicillin-clavulanate	Disperse Tablet	200mg + 28,5mg	3	R
	Capsule	875mg + 125mg	3	T, Out Of Stock[1]
Benzathine benzylpenicillin	Powder For Injection (PFI)	900mg (1.2M) vial	2	N
Benzylpenicillin	PFI	600mg (1MU) vial	2	R
Cefixime	Tablet	400mg	2	N
Ceftriaxone	Injection	250mg /1g	2	R
Azithromycine	Tablet	250 mg	2	R[2]
	Powder For Oral Liquid (PFOL)	200 mg/5ml	2	N
Ciprofloxacine	Oral liquid	250mg/5ml	3	N
	Tablet	250 mg	3	R
Cotrimoxazole (sulfamethoxazole +	Injection	96mg/ml (10ml am)	3	N

[1] Survey was done 1 day before arrival of new stock, syrup: 156/25mg 5ml and 228/5mg 5ml, tablets: 375 and 625 (OOS)
[2] Split tablets of 500mg

Drug	*Dose-form*	*Size*	*Level*	*Availability at MMC pharmacy (Real, Theoretical or None)*
trimethoprim)				
	Oral liquid	240mg 5/ml		R
	Tablet	240mg 5/ml		R
Doxycycline	Tablet	100mg	2	R
Gentamicin	Injection	10mg/ml 2mg vial	2	N
		40mg/ ml 2mg vial	2	R
Metronidazole	Injection	5mg/ml 100ml vial	3	R
	Oral Liquid	200mg/5ml	2	R
	Tablet	200mg	2	R
Tinidazole	Tablet	500mg	2	R
Anti-TB → Referral				
Anti-Viral				
Aciclovir	Tablet	200mg	2	R
ART → Referral				
Antihelmintics				
Diloxanide	Tablet	500mg	2	N
Tinidazole	Tablet	500mg	2	R
Antiprotozoal				
Artemether + Lumefantrine (AL)	Tablet	20mg + 120mg 80+480mg	1	R
Artesunate (always follow with AL)	Injection	30mg vial/ 60mg vial	2	N[3]
	Rectal capsule	100mg	2	N
Dihydroartemesinine + piperaquine (DHA+PPQ) (2nd line use)	Tablet	40mg + 320	Tablet	N
Quinine	Injection	300mg/ml	2	N[4]
	Tablet	300mg	2	N
Intermittent presumptive treatment in pregnancy (IPTp) Sulfadoxine + pyrimethamine	Tablet	500mg + 25mg	2	N
Anti-microbial molecules present but not on the list				
Ampicilline + Cloxacilline	Tablet	500 mg		

[3] Artemether 80mg injections
[4] Stopped storing it

Drug	*Dose-form*	*Size*	*Level*	*Availability at MMC pharmacy (Real, Theoretical or None)*
Cefadroxil	Tablet	500 mg		
Clarithromycine 50ml	Bottle	50ml		
Erythromycine 250mg	Tablet	250mg		
	Syrup			
Flucloxacilline	Capsules	250 mg		
	Tablet	150 mg		
Mebendazole	Tablet	100 mg		
Nitrofurantoine	Tablet	100 mg		
Norfloxacine	Tablet	400 mg		
Ofloxacine	Tablet	200 mg		
Praziquentel	Tablet	600 mg		

Appendix 3: Data collection tool

Table 9 Point Prevalence Survey (PPS) - Data Collection Tool

Patient ID		
Age (years)		
Sex	M F	
Antimicrobial molecule	1.	2.
Drugs	Branded	
	Generics	
Route of administration	Parenteral (IV, IM)	
	Oral	
	Other	
Dosing, posology and duration of therapy compliant with guidelines (KEML)?	Yes/ No	
Duration of therapy (in days)		
Indication	Unclear	
	Prophylactic	
	Empirical	
	Targeted	
Diagnosis		
Complies with guidelines *	Yes	
	Yes, if severe	
	Unclear	
	No	

Appendix 4: Antimicrobial formulary of MMC

Table 10 Antimicrobial formulary of MMC

Acyclovir 200mg tablets

Albendazole 400mg tablets (8)

Amoxicillin 250mg capsules (1)

Amoxicillin susp 100ml

Ampiclox 500mg capsules (3)

Ampiclox suspension 250mg/5ml syrup

Artemether lumefantrin 24s 20/120mg tablets

Augmentin 156mg.25/5ml syrup

Augmentin 228.5mg/5ml syrup (7)

Augmentin 375mg 375mg tablets

Augmentin 625mg tablets (2)

Azithromycin 500mg tabs

Benzyl penicillin im.u vial

Cefadroxil 500mg tablets

Ceftriaxone 1gm vial

Cefuroxime 500mg tabs

Ciprofloxacin 500mg tablets

Clarithromycin 500mg

Co-trimoxazole 240mg/5ml(bottled) syrup (5)

Co-trimoxazole 480mg tablets (4)

Doxycycline 100mg capsules

Erythromycin 250mg tablets

Erythromycin syrup 100/5mls syrup

Flucloxacillin 250mg capsules (10)

Fluconazole 150mg tablets

Mebendazole 100mg tablets

Metronidazole 200mg tablets (6)

Metronidazole 200mg/5ml syrup (9)

Neonatl ampiclox 90mg/0.6ml suspension

Nitrofurantoin 100mg tablets

Norfloxacin 400mg tablets (10)

Praziquantel 600mg tablets

Tinidazole 500mg tablets

Appendix 5 Annual DDD/100 patient visits

The defined daily dose (DDD) is a statistical measure of drug consumption, defined by the World Health Organization. It is used to standardize the comparison of drug usage between different drugs or between different health care environments. We use it to measure AB consumption and identify the most common used ABs. It can signal irrational drug use early.

$$\text{DDD /100 patient visits} = \frac{\text{DDDs} \times 100}{\text{pt visits}}$$

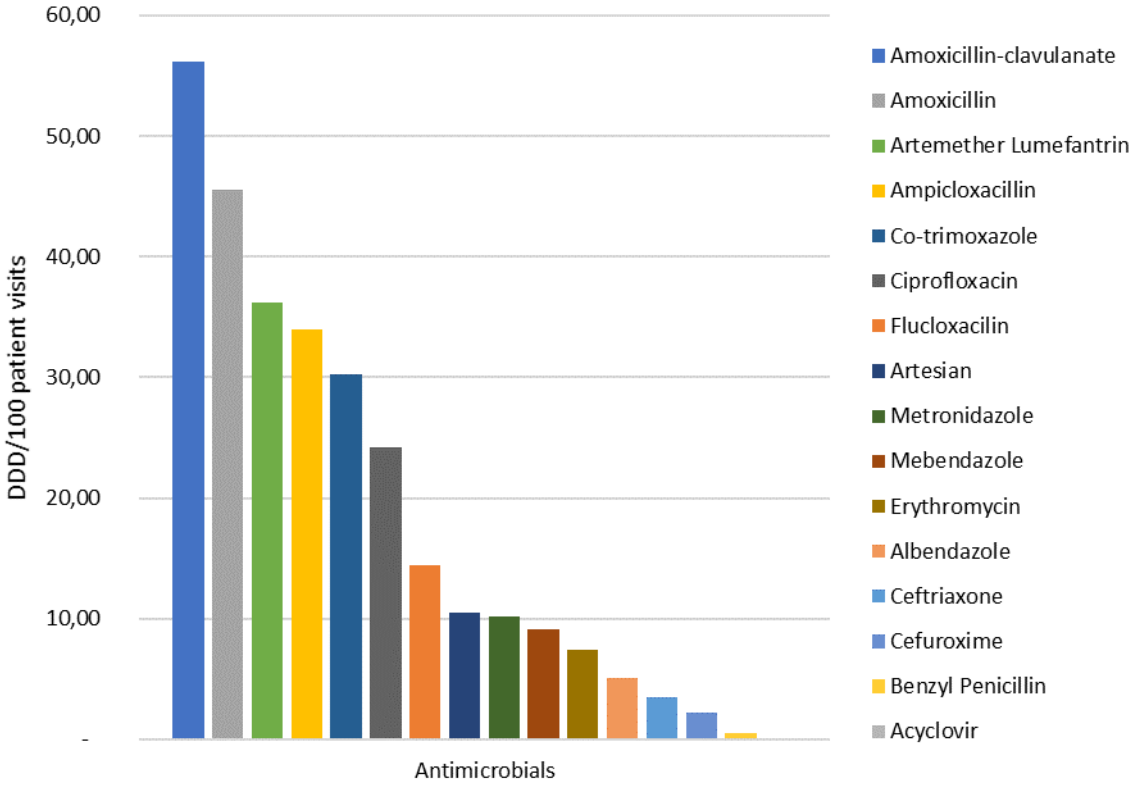


Figure 9 DDD/100 patient visits at MMC of all antimicrobials over 12 month period (July, 2018 to June, 2019)

Appendix 6 Dosing scheme of the most common used ABs in MMC

Dosing scheme most common used AB	**Age 0-5**	**Age 5-18**	**Age 18+**
1. Augmentin (amoxicillin-clavulanate)	Augmentin 228,5 /ml syrup 5ml BID during 5 days OR Augmentin 156,25 mg/ml 5ml BID during 5 days	Augmentin 375mg BID during 5 days	Augmentin tablet 625mg BID during 5 days
2.Amoxicillin	Amoxicillin susp 100ml 2,5 to 7,5 ml TID during 5 days	Depending on weight: as 0-5 or 18+	Amoxicillin tablet 250 mg 2 items TID during 5 days
3. Ampiclox	Ampiclox suspension 250mg/5ml syrup 2,5-5ml QID during 5 days	Depending on weight: as 0-5 or 18+	Ampiclox tablet 500 mg QID during 5 days
4.Co-Trimoxazole	Co-Trimoxazole 240mg/ 5Ml (bottled) syrup 1,5-7,5 ml BID during 5 days	Depending on weight: as 0-5 or 18+ (1 unit BID)	Co-Trimoxazole tablet 480mg 2 units BID during 5 days
5. Artemether Lumefantrin	Artemether Lumefantrin 24s 20/120mg tablets 1-4 units BID during 3 days	Artemether Lumefantrin 24s 20/120mg tablets 1-4 units BID during 3 days	Artemether Lumefantrin 24s 20/120mg tablets 4 units BID during 3 days
6. Metronidazole	Metronidazole 200mg/5ml syrup 2,5-5ml TID during 5 days	Depending on weight: as 0-5 or 18+	Metronidazole 200mg tablets TID during 5 days

Appendix 7 Main findings per in-depth interview presented in organigrams

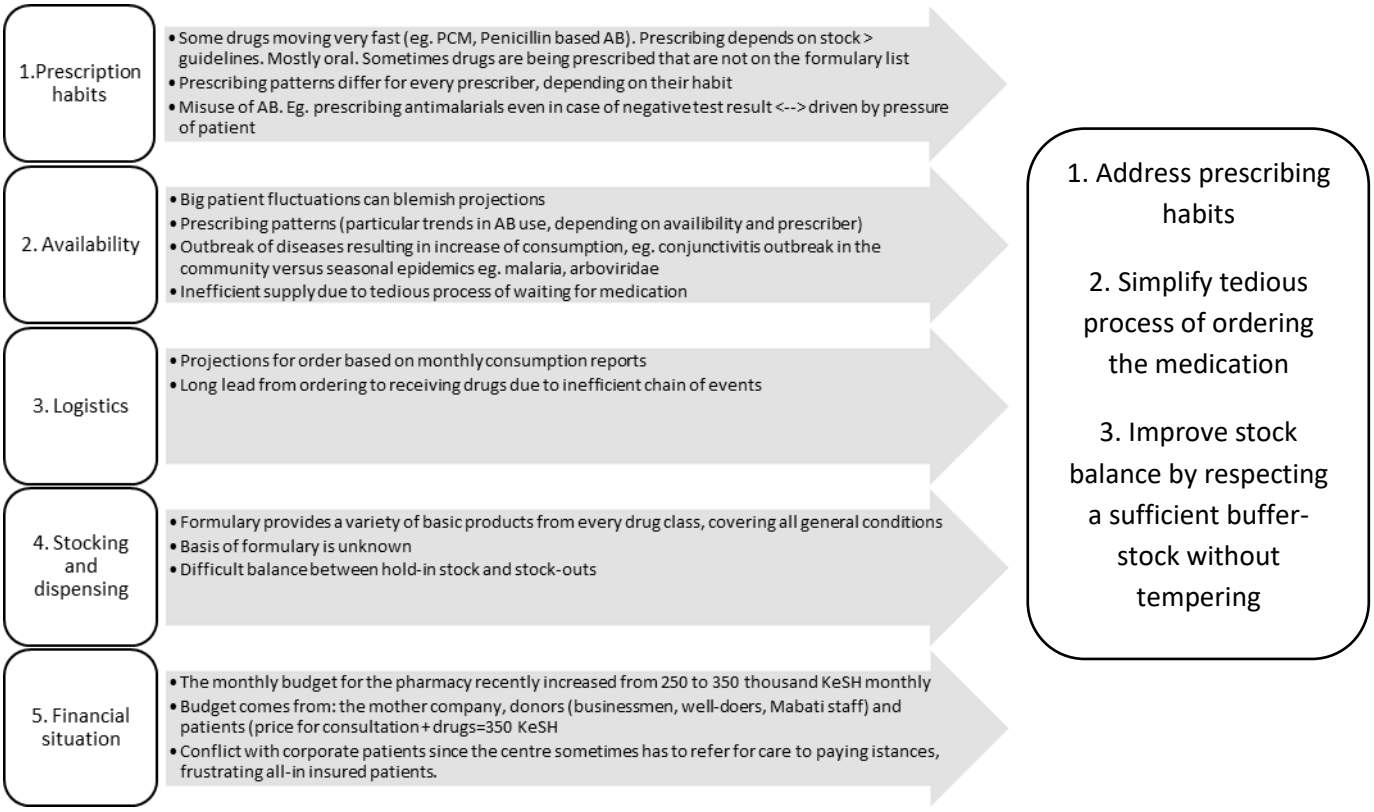


Figure 10 Organigram interview 1

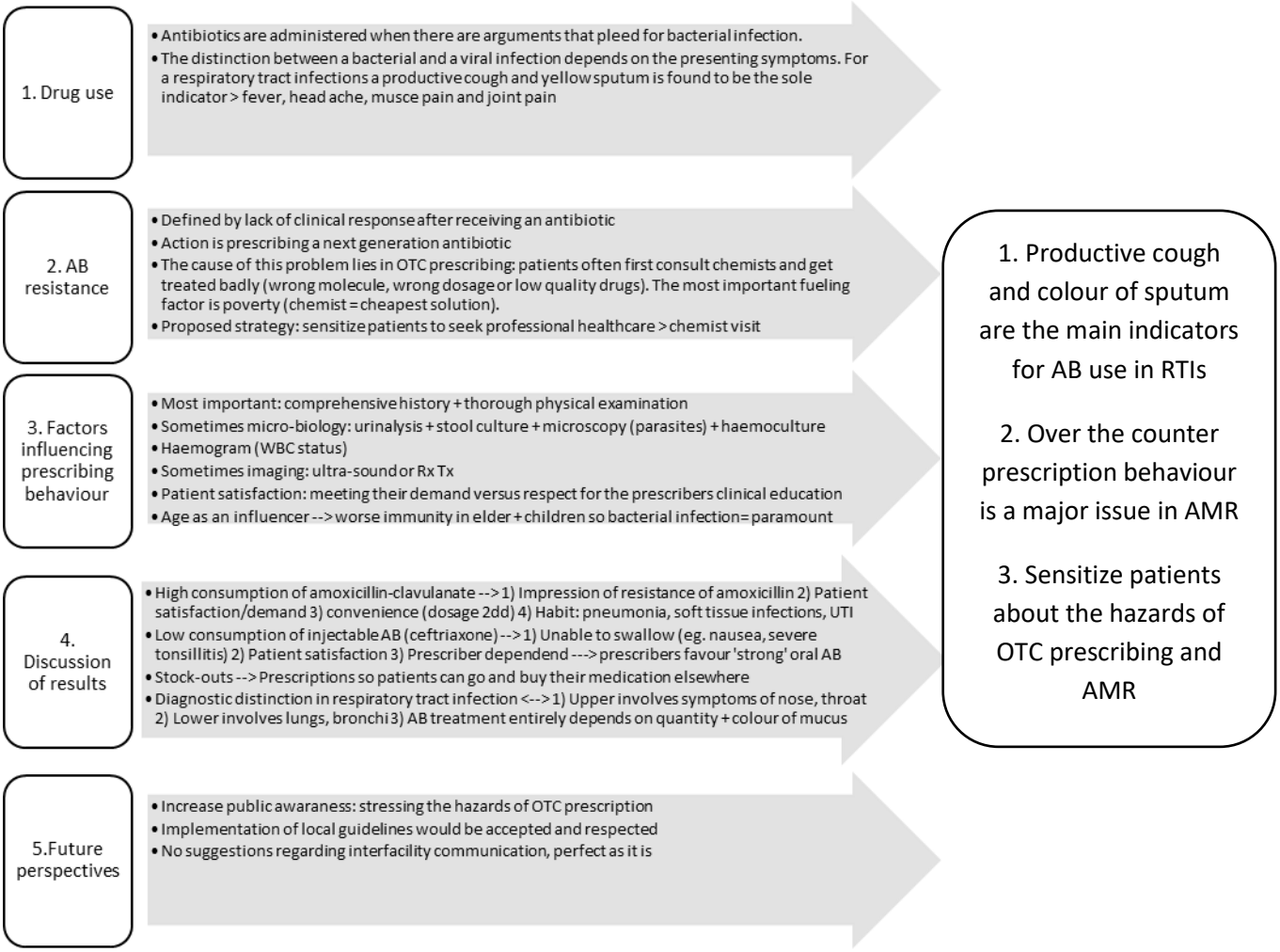


Figure 11 Organigram interview 2

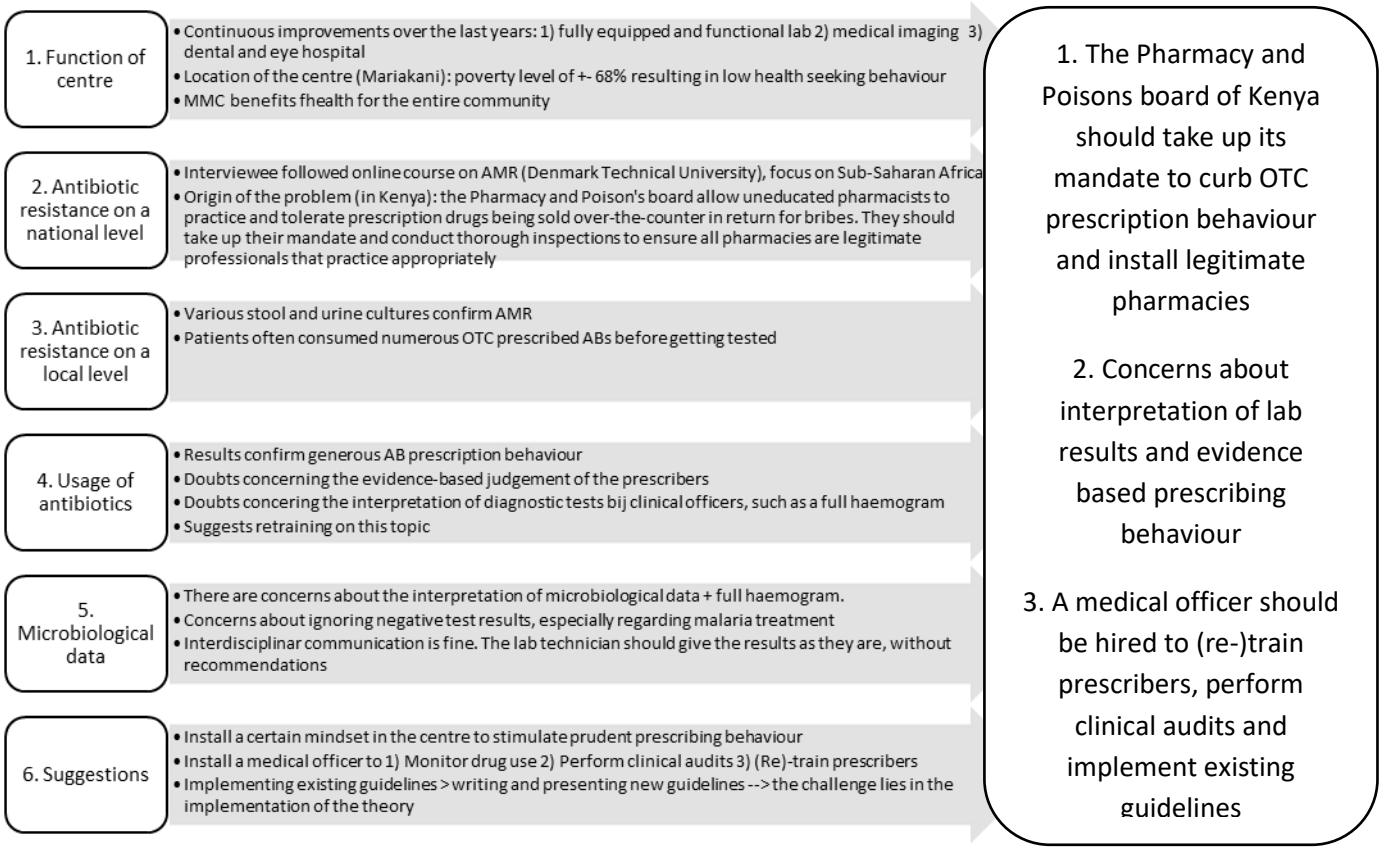


Figure 12 Organigram interview 3