The Pharmaceutical Society of Uganda

Implementing the Anti-Microbial Resistance National Action Plan at Fort Portal Regional Referral Hospital, Western Uganda

The Maternal Sepsis Intervention

Summary Report and Policy Recommendations

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EXECUTIVE SUMMARY AND KEY POLICY NOTES & RECOMMENDATIONS

Executive Summary

This report summarises the findings of the Maternal Sepsis Intervention (MSI) at Fort Portal Regional Referral Hospital. The MSI formed part of a larger Antimicrobial Stewardship Project which ran between 2018 and 2020. This project was funded through the Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS[1]) Scheme, which is funded by the UK Department of Health and Social Care (DHSC) through the Fleming Fund, and managed by the Tropical Health Education Trust (THET) and the Commonwealth Pharmacists Association (CPA), for the benefit of the UK and partner country health sectors.

The organisations involved in designing, implementing and evaluating the project included the Uganda Pharmaceutical Society, Fort Portal Regional Referral Hospital, the University of Salford and Knowledge for Change.

The full project report and a paper are available on an Open Access basis:

Ackers, H.L., Ackers-Johnson, G., Welsh, J., Kibombo, D. and Opio, S. (2020) Anti-Microbial Resistance in Global Perspective, Palgrave. (https://link.springer.com/book/10.1007/978-3-030-62662-4)

Ackers, H.L., Ackers-Johnson, G., Seekles, M., Odur, J. and Opio, S. (2020) Opportunities and Challenges for Improving Anti-Microbial Stewardship in Low- and Middle-Income Countries; Lessons learnt from the Maternal Sepsis Intervention in Western Uganda. *Antibiotics* 2020, *9*, 315; doi:10.3390/antibiotics9060315. (https://www.mdpi.com/2079-6382/9/6/315)

The MSI was supported by laboratory research and training in molecular-based identification of antimicrobial resistance in *Staphylococcus aureus*, for which an open access pre-print is available:

Antibiotic resistance profiles and population structure of disease-associated *Staphylococcus aureus* infecting patients in Fort Portal Regional Referral Hospital, Western Uganda doi: https://doi.org/10.1101/2020.11.20.371203

[1] https://www.thet.org/our-work/grants/cwpams/

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Section 1: Introduction

1.1 Project Funding

The project was funded through the Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS[2]) Scheme, which is funded by the UK Department of Health and Social Care (DHSC) through the Fleming Fund, and managed by the Tropical Health Education Trust (THET) and the Commonwealth Pharmacists Association (CPA), for the benefit of the UK and partner country health sectors. The main intervention took place between March 2019 and December 2020.

1.2 The Project Team

The MSI was co-led by Professor Louise Ackers (University of Salford and Chair of Trustees, Knowledge for Change), Samuel Opio (Pharmaceutical Society of Uganda) and Ibrahim Mugerwa (AMR Surveillance Coordinator at the AMR-National Coordination Office - National Health Laboratories and Diagnostic Centre - Ministry of Health). The project leads were gratefully supported by a multi-disciplinary team, as acknowledged below:

- Professor Louise Ackers, Chair in Global Social Justice, University of Salford and Knowledge for Change
- Joe Odur, Pharmacist, Knowledge for Change and Fort Portal Regional Referral Hospital
- Dorothy Gashuga, Midwife, Knowledge for Change
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- Allan Ndawula, Project Manager, Knowledge for Change
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- Ibrahim Mugerwa, AMR National Taskforce (Uganda)
- Alan Muwazae, Senior Pharmacist, Fort Portal Regional Referral Hospital
- Gavin Ackers-Johnson, PhD Researcher, University of Salford and Knowledge for Change
- Miriam Nantamu, PhD Researcher, University of Salford
- Dr Maaike Seekles, Advisor in Statistical Analysis, University of Salford

1.3 Project Objective

"How can we improve antimicrobial stewardship in a Ugandan public referral hospital in a way that improves patient outcomes (in this case associated with maternal sepsis) and demonstrates sustainability through cost effectiveness?"

1.4 Why Maternal Sepsis?

The MSI took a holistic approach to identify and respond to the underlying contexts within with antimicrobial resistance flourishes. Maternal mortality presented as a major priority for FPRRH with many mothers dying as a result of sepsis much of which results from Surgical Site Infection. Table 1 shows the volume of antibiotics prescribed for hospital acquired infection and figure 1 shows the consumption of oral antibiotics in post-natal and gynaecology wards:

[2] https://www.thet.org/our-work/grants/cwpams/

	Gynaecology	Post-natal
Total no. of patients	22	20
Percentage of patients on antibiotics	45%	90%
Of those patients on antibiotics:		
Percentage of antibiotics for Community Acquired Infection	20%	6%
Percentage of Antibiotics for Health Care Acquired Infection	50%	0%
Percentage of antibiotics for medical prophylaxis	0%	0%
Percentage of antibiotics for surgical prophylaxis	10%	94%
Percentage of antibiotics for unknown indication	20%	0%

Table 1: Antibiotic Prescribing on Post-natal and Gynaecology Wards in FPRRH (Source: Results of G-PPS, May 2019 as reported to FPRRH IPC Committee)

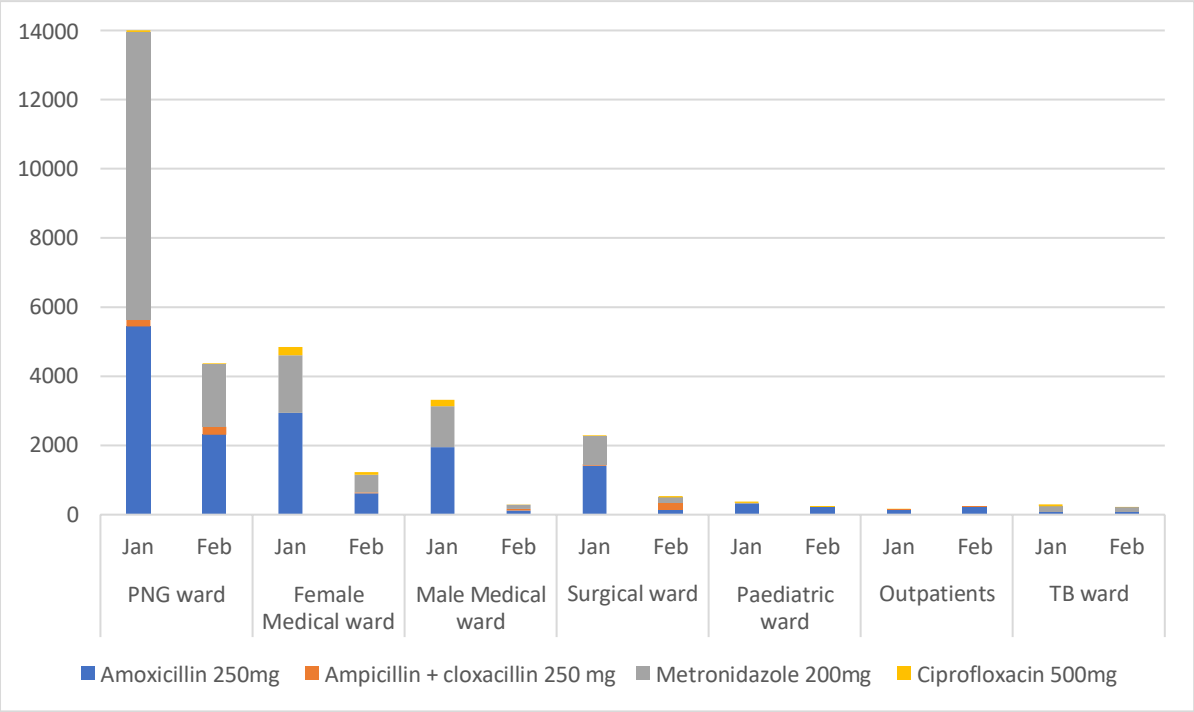


Figure 1: Supply of Oral Antibiotics to All Wards in January and February 2020

1.5 Tackling AMR through Maternal Sepsis

AMR is a pervasive but somewhat intangible and invisible threat to patient care; focusing on an area of immediate clinical and political priority to the hospital facilitated more active engagement. This supported an emphasis on maternal sepsis on the linked post-natal and gynaecology ward. Interventions commenced with attention to Infection-Prevention-Control followed by an emphasis on the diagnosis and treatment of sepsis and wound management.

1.6 Tackling AMR through Improved Knowledge of Circulating Resistance

Specific knowledge of local AMR epidemiology is required to inform evidence-based improvement of antibiotic stewardship measures. A pilot study combining routine antimicrobial susceptibility testing with whole genome sequencing of *Staphylococcus aureus* isolates from wounds highlights the need for early identification of pathogens and their antibiotic susceptibility, to support evidence-based prescribing.

Section 2: Key Impacts

2.1 Maternal Mortality

The combination of more effective multi-disciplinary team-working with on-going mentoring (as the principal training mechanism) has had a major impact on sepsis-related maternal mortality:

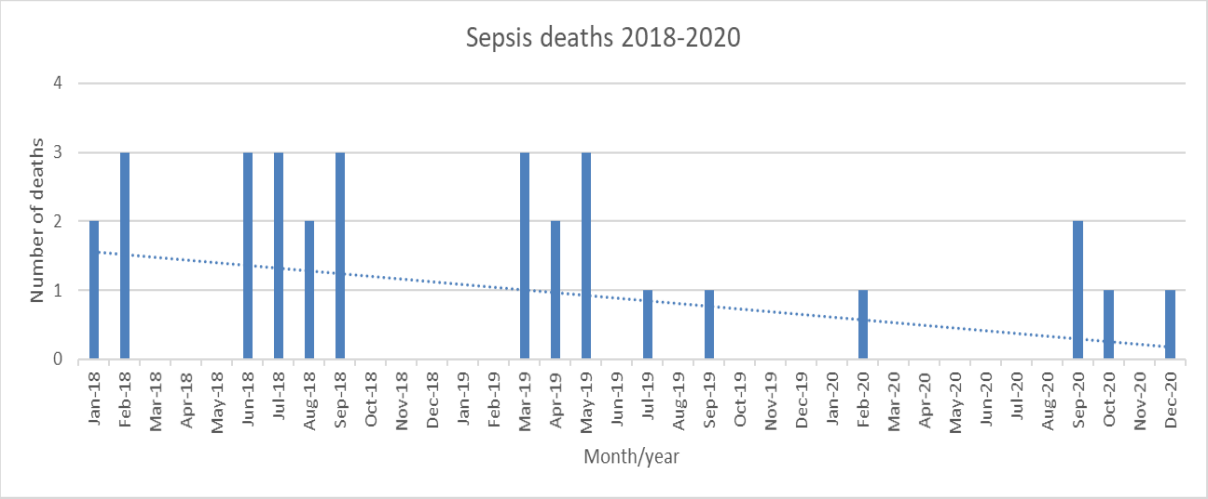


Figure 2: Sepsis as a Cause of Maternal Death in FPRRH

Figure 2 shows the decline in maternal mortality. The 3 cases occurring since project commencement in July involved women referred in from distant health facilities and often facing major delays.

Health workers were keen to cite examples of patients whose lives had been saved because of (their) improved practice. They were not only delighted and highly motivated by their ability to save these women's lives, but the experience also provided direct affirmation of the value of behavioural changes on the wards.

"We have had 4 complicated cases this week. We thought the patients would die and they walked out happy. There was a patient we thought would pass away, but she survived as she got the appropriate antibiotics." **(Midwife)**

2.2 Impacts on Patient Stays and Theatre use

"Patient stays have really reduced on the ward and we produced evidence on this last year. Patients were staying for over 30 days on the ward prior to the project – now in many cases after culture and sensitivity testing[1] and closing the wounds they can then go home after 10 days. We have reduced patient stays on the ward and even in terms of costs, shorter stays and fewer attendants on the wards." **(Laboratory Scientist)**

The MSI has reduced the duration of patient stays on the ward, the use of operating theatres (for secondary wound closure) and the volume of readmissions:

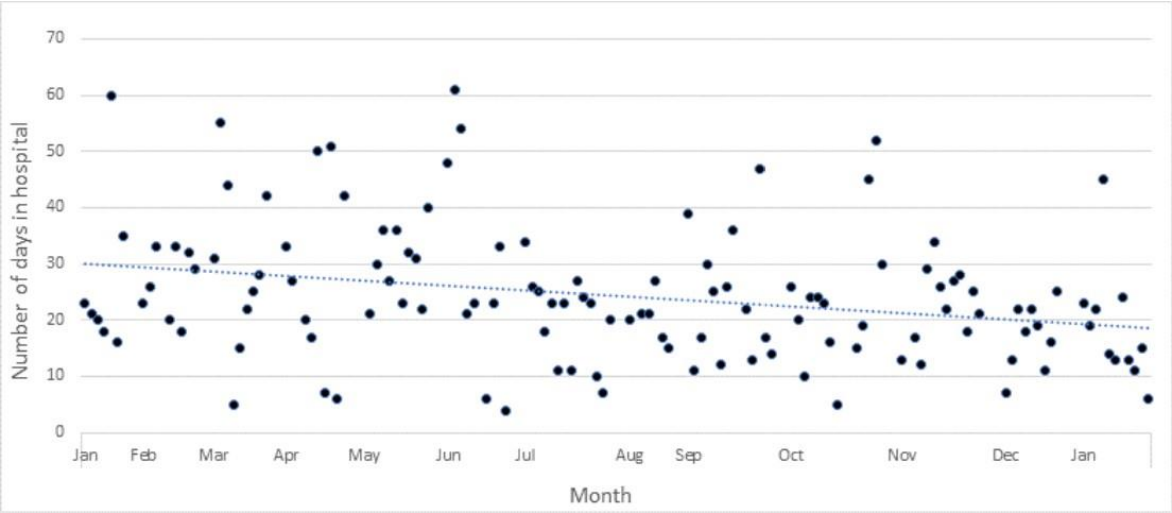


Figure 3: Length of Stay based on Date of Operation

2.3 Impacts on Hospital Budgets

"Hospital-acquired sepsis accounts for a large proportion of additional hospital days, standing out as one of the most expensive and most clinically complex conditions to treat".
(Slawomisrki et al 2017:16).

Critically, from a sustainability perspective, it has reduced the financial costs associated with nosocomial infection. This report identifies Policy Recommendations to support further improvement and the transfer of this to other wards and hospitals. It also identifies Policy Challenges confounding progress on antimicrobial stewardship in Ugandan Regional Referral Hospital Settings.

"When sepsis is managed then the resources used to manage these patients reduce drastically. By reducing long stays, which brings about savings, you have contributed to the hospital budget with real term savings".
(Hospital Manager)

Section 3: Prevention First: Infection Prevention Control and Antimicrobial Stewardship

3.1 IPC as a Priority in AMS

The first and essential step in any AMS intervention MUST always be to ensure that optimal IPC is in place. Prevention is always better and cheaper than cure. The first priority was to make a detailed (and continuing) assessment of IPC including hand hygiene and infrastructure audit.

> *"Antibiotics have become …. a quick fix for hygiene in settings of minimised resources".*
> **(Denyer-Willis and Chandler, 2019:1)**

3.2 Improvements in Hand Hygiene

Adapted WHO Tools demonstrated significant improvements in staff behaviour and infrastructure. This impacted health worker motivation – so critical to behaviour change.

	Hand Washing			**Hand Gel**		
Cadre	Opportunities	Actual	Compliance	Opportunities	Actual	Compliance
Midwives	54	18	33%	54	23	43%
Intern Doctors	36	2	6%	36	8	22%
Senior Doctors	12	2	16%	12	4	33%

Table 2. Hand Hygiene Compliance in October 2019 on PNG ward at FPRRH (Source: Adapted WHO Hand Hygiene Compliance Audit)

	Hand Washing			**Hand Sanitiser**		
Cadre	Opportunities	Actual	Compliance	Opportunities	Actual	Compliance
Midwives	26	20	76%	26	23	**88%**
Intern Doctors	12	7	58%	12	11	**91%**
Nurses	12	8	66%	12	7	**58%**

Table 3: Hand Hygiene Compliance in March 2020 on PNG ward at FPRRH (Source: Adapted WHO Hand Hygiene Compliance Audit)

3.3 Improvements in Basic Infrastructure

On-going attention to basic and essential infrastructure provided the opportunities for improved behavioural change in areas including hand hygiene; wound management; use of sepsis isolation areas; attendant management; the ability to sterilise gauze and instruments on the ward and to undertake minor operations on the wards (rather than waiting for precious and expensive theatre slots):

	Score	Percentage
Audit 1 (October 2019)	37/63	58.7%
Audit 2 (January 2020)	50/63	79.4%
Audit 3 (March 2020)	61/63	**96.8%**

Table 4: Results of IPC Infrastructure Audit (Source: Infrastructure Audit)

Images 1 and 2: Sepsis area before and after decoration, signage and provision of doors.

Images 3, 4 and 5: Replacement of old trolleys and essential equipment

"The new trolleys have really helped. We can now sort our equipment out and this eases our work. The instruments in the evacuation room means we can now do procedures that used to take a long time to do as we had to sterilise equipment between cases. Mothers can be treated much more quickly, get better and leave the next day. This takes pressure off theatre too. We now have enough instruments and receivers (kidney dishes) to use. We had very few so if we used them, we had to wait for another cycle to sterilise them before we used them again". **(Midwife)**

3A. Policy Note/Recommendation: IPC is a Necessary and Foundational Investment

Improving access to opportunities for hand hygiene (access to basic disinfectants Sodium hypochlorite (jiK), water, soap and hand gel) and basic infrastructure (sinks, trolleys, screens, instruments and autoclave facilities) coupled with improved signage and basic refresher training are key to IPC. Where health workers believe that a primary objective is to protect them from nosocomial infection, the uptake is very high and highly cost-effective. Improving the working environment and safety creates an appetite for team working.

"IPC is improving - even when we cannot wash our hands, we all now have our own hand gel so after any procedure or examination we use this alcohol. It has made life safer for us". **(Midwife)**

health worker

safety creates an appetite for team working.

3.4 Stock-Outs of IPC Consumables

Regular and predictable stock-outs of all basic consumables (including soap, hand gel, jiK and iodine, gauze and cotton wool) undermine IPC. Training and disciplining people for not adhering to IPC guidelines, when they do not have access to the materials that are required compounds health worker demotivation and cannot build a positive IPC culture. Identifying ways of managing stock-outs would be far more efficient (cheaper) than dealing with the consequences of nosocomial infection.

Image 6 (left): Empty Hand Gel Dispenser under Ugandan MOH Guidelines on Hand Washing

3B. Policy Note/Recommendation: Improve procurement systems for basic IPC equipment and consumables to avoid the regular and predictable stock-outs which undermine IPC

3.5 Attendant Management

One of the key concerns raised in relation to Infection Prevention and Control on the wards is the constant influx of large numbers of attendants. Managing attendants and other visitors, such as pastors for example, is a challenge for most Ugandan public facilities. Although they play an essential role in caring for their relatives and friends, the sheer numbers in already congested wards; the fact that many eat on the floors and sleep in the ward at night and sit on patient beds makes it very hard to reduce sources of infection. It also makes it much harder for health workers to work efficiently and effectively moving around the ward. The project has introduced a range of measures to try to manage this traffic more effectively including locks on doors; advertising and trying to police visiting hours.

> *"We are focusing on health workers, but the big issues are attendants and patients. We need to comprehensively look at sources of infection".*
> **(IPC Committee Chair)**

3C. Policy Note/Recommendation: Attendants as Vectors of Infection

Hospitals should work with local communities and the IPC Committees to develop systems to improve the management of attendants and educate visitors and attendants so that they understand the risks associated with their behaviour. This is urgently needed during COVID-19. Knowledge for Change has recently made a film which is being used in FPRRH to try to encourage attendants to modify their visiting behaviour during COVID-19: https://youtu.be/fqo3L8aleZ0

Image 7: Attendants waiting outside the ward on shared benches
Image 8: Attendants waiting inside the ward on very soiled mattresses
Image 9: New signage to restrict attendants' entry to wards

Section 4: Wound Management and Culture and Sensitivity Testing

4.1 Motivating Health Workers to Manage Infected Wounds

"The saddling of responsibility for hygiene with individuals who have limited ability to change the environment in which 'good hygiene behaviour' is expected to operate leaves these individuals to find solutions that are more feasible and within their control, such as the use of antibiotics"
(Denyer Willis and Chandler, 2019:3)

Health workers' concerns about the risks they put themselves under when dealing with infected wounds coupled with a lack of knowledge about wound management and the role that culture and sensitivity testing plays in timely healing discouraged attention to wound care. Prior to the project, women were left with gaping septic wounds and spent weeks on the ward often enduring extensive waits for theatre slots for secondary closure. The response to poor healing was often to continue courses of (ineffective) empirical prescribing; no swabbing of wounds was taking place despite the encouragement of the laboratory staff.

Improved IPC coupled with mentoring encouraged midwives and nurses to engage actively in wound management. Swabbing rates improved significantly and as wounds began to heal much more quickly and lose the foul odour, staff were motivated to improve their practice.

Wound closures began to take place on the ward reducing the need to use theatres and increasing the satisfaction of the junior doctors involved.

4.2 Timely and Comprehensive Laboratory Testing

A well-supported laboratory system allows for the comprehensive testing of samples, and confidence in the results. Timely turnaround of laboratory results supported by the presence of pharmacists on the ward working in multi-disciplinary teams with nurses, midwives and doctors created a very positive working environment. Being part of a team that is improving patient outcomes is a critical driver of behaviour change. It also created the basis for rational (evidence-based) prescribing and the opportunity for more targeted and less wasteful use of antibiotics.

Time frame	Suspected Sepsis Cases	Culture and Sensitivity Tests Performed	% Tested
January 1st, 2019 - July 8th 2019	50	0	0%
July 9th, 2019 – July 21st 2019	16	3	19%
July 22nd 2019 – January 31st 2020	76	74 (2 had missing data)	95%

Table 5. Volume and Proportion of Suspected Sepsis Cases Sent for Laboratory Testing (Source: FPRRH Laboratory)

"I have seen a very great improvement. Yes, there are bottlenecks, but we have really achieved a lot. Restricting our discussion to post-natal; the utilisation of diagnostics in regard to microbiology previously was very low. The staff didn't appreciate the value of prescribing on the basis of a laboratory report. Prescribing practices were poor; how often did the doctors come to check patients? They were wasting time. People believed we can use antibiotics the way the Ministry has put them into the clinical guidelines but some of these are not working so they really need to be guided by the bacterial reports. The uptake is really good" **(Laboratory Scientist)**

4.3 The Importance of Wound Care to AMS

Providing access to inoffensive wounds and mentoring on wound management (including observing and dressing wounds) creates the environment for wound monitoring and swabbing.

"Before [the project] staff did not have the idea about wound swabbing; they didn't understand culture and sensitivity testing. That's where a lot of improvement has come. They now understand the science and take an interest and ask, 'why is this mother not getting better?'. They have learnt about resistance. Midwives are now taking the lead in managing patients; they used to wait for doctors to make decisions, but the doctors only appear once in a while, so they waited for them instead of acting – now they act". **(Pharmacist)**

4A. Policy Note/Recommendation: Wound Care, Nursing and Evidence-based Prescribing

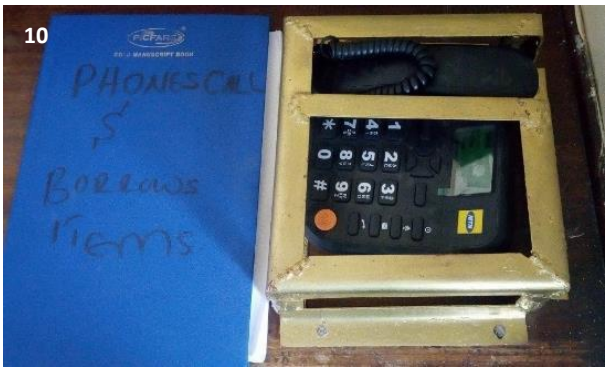
Midwives and nurses play an important role in antimicrobial stewardship, especially in ensuring that samples for culture and sensitivity are collected and sent to the laboratory for analysis. Efforts should be made to improve their capacity in wound management, particularly surgical site infections.

4.4 Timely Communication

Even where laboratory tests had taken place, serious communication problems prevented rational prescribing. A key problem was the fact that doctors put their personal mobile numbers on laboratory forms and were often not available when results came in to make timely changes to prescriptions. Relying on staff to use their own mobile phones creates serious communication deficits.

4B. Policy Note/Recommendation: Communication is Essential to Timely, Evidence-Based Prescribing

A clear communication pathway and SOP detailing the movement of laboratory results from the laboratory to the ward and into the patient's file is necessary. The provision of fixed telephones is essential for communication in hospitals. Making communication the role of the in-charge nurse and providing a fixed telephone (attached to the desk) with clearly enforced rules on use creates the opportunity to improve the reporting of laboratory test results direct to the ward.



"Now we use the phone that was bought for us to call the laboratory and also to receive results – it is TOO GOOD! Before we had the phone, we had to move from our ward to the laboratory - if we wanted to speak to the laboratory or take a sample we had to walk up there". **(Midwife)**

Image 10: Fixed landline provided to enable effective communication between ward and laboratory staff

4.5 Team-Working and Wound Management

"Pharmacy will tell you there is no point in them coming unless there are cultures". **(Midwife)**

Laboratory results provide a critical focal point for what pharmacy teams in the UK refer to as 'huddling.'[3] Gardner et al (2018) characterise huddling as a mechanism to 'support inter-professional communication and collaborative practice' (2018;16). Effective wound management and communication of laboratory results to the ward creates the opportunity for pharmacy engagement in antibiotic prescribing.

4.6 The (Neglected) Role of Pharmacy in Ugandan Public Hospitals

4C. Policy Note/Recommendation: Culture and Sensitivity Results are the key to Clinical Pharmacy Engagement

The data collated from patient notes showed that, once the intervention was in place, pharmacists reviewed the pharmacotherapy in 91.8% of cases where test results were taken and showed a bacterial growth.[4]

4D. Policy Note/Recommendation: Pharmacists play an essential role in guiding prescribing

Include pharmacists in clinical decision - making and integrate pharmacists into the core patient care team. Pharmacists should be present on the wards and attend ward rounds as part of the bigger patient care team.

4.7 Pharmacy Staffing in Ugandan Public Hospitals

At the time of the project, only 2 pharmacists were employed at FPRRH. This number ofpharmacists employed in Regional Referral Hospitals is insufficient to support the extension of clinical pharmacy services to the wards. Pharmacists in public hospitals have to spend most of their time on stock management (some of which could be undertaken by task-shifted cadres under supervision). This undermines motivation and under-utilises expertise.

Employing more pharmacists is essential to ensure evidence-based prescribing and reduce AMR. This would prove cost-effective/saving. The employment of an inventory manager in pharmacy stores has helped to release the senior pharmacists to engage in clinical pharmacy on the wards andtis an example of good practice in task-shifting.

4E. Policy Note/Recommendation: Pharmacy Staffing and Clinical Pharmacy Roles

The PSU urges the Ministry of Health to consider increasing the number of pharmacy staff at RRHs. Employing more pharmacists is essential to ensure evidence-based prescribing and reduce AMR. It could be cost-effective/saving.

4.8 The (Neglected) Role of Laboratories in Ugandan Public Hospitals

Laboratory Capacity: FPRRH has an exemplary laboratory supported by the Infectious Diseases Institute (IDI). It did not suffer from lack of consumables, equipment or staff. However, hospital reliance upon IDI was very high raising questions about sustainability.

4F. Policy Note/Recommendation: Laboratory Effectiveness and AMR

Hospital management should consider attaching hospital laboratory technicians, for agreed and extended periods of time, to the IDI laboratory to support capacity-building through mentoring and co-working. In other RRHs laboratory capacity is a key weakness in the chain limiting potential for culture and sensitivity testing and rational prescribing.

[3] http://www.pulsetoday.co.uk/pulse-intelligence-your-practice/regulation/how-our-morning-huddles-improved-practice-teamworking/20037047.article

[4] Patient Records (January 2019-January 2020).

"We did culture and sensitivity testing (in Mbale) but we had to use a private laboratory that charged 30,000 shillings per case. About 50% of people were able and willing to pay for this service. The hospital microbiology laboratory did not function; they lacked consumables, culture medium …."
(Laboratory Scientist)

4.9 The Value of Antibiograms

At the start of the MSI all prescribing in FPRRH was done on an empirical basis, grounded in prior learning and circumscribed by awareness of antibiotic availability. In practice, this meant very heavy reliance on two antibiotics that were routinely prescribed for all women.

Culture and sensitivity testing alerts doctors to the limitations of these antibiotics and, with the advice of pharmacists, the wider suite of (potential) options. Sensitivity testing, complemented by new molecular research[4], showed that appropriate and sufficient laboratory consumables are essential to inform the hospital antibiogram, and to keep it updated. This research found evidence of likely development of resistance should bacteria be exposed to certain antibiotics, indicating the need for close control of antibiotic prescription of "at-risk" antibiotics and an improved and regularly updated antibiogram.

This supported rational prescribing for individual patients. In suspected sepsis cases an initial empirical prescription is still indicated prior to receiving lab results.

"On the basis of the increased swabbing we are now in a position to have an antibiogram. This will be very informative. The sample size is now very adequate. The antibiogram will be good for the clinicians to guide prescribing and it will be good for the patients". **(Pharmacist)**

4G. Policy Note/Recommendation: The Introduction of a Hospital Antibiogram to guide Empirical Prescribing

The MSI supported the collection of sufficient samples to generate, for the first time, a hospital antibiogram that can play a key role in guiding empirical prescribing in future. This is playing a critical role in limiting unnecessary and empirical prescribing and targeting antibiotics more effectively.

4H. Policy Note/Recommendation: Bi-annual Updating and Communicating Antibiogram Data

Whilst the generation of the first antibiogram marks a huge success; antibiograms require continual up-dating and an active communication mechanism to guide prescribers, the majority of whom are intern doctors on short rotations. This emphasises that the antibiogram needs to be supported with sufficient and appropriate laboratory testing materials to remain updated and complemented with molecular methods of detection where possible and appropriate. We propose that all hospitals with culture and sensitivity testing capacity should update their antibiograms every two years. In addition, all hospitals with testing capacity (General Hospitals – Referral Hospitals) should endeavour to create an antibiogram. This will inform antimicrobial resistance trends within the country.

This also points to the need for more active supervision and mentoring of intern doctors by senior medical staff in the use of the antibiogram; this is seriously lacking at present in Uganda. Engaging pharmacists and midwives/nurses in this process on a multi-disciplinary team (MDT) basis will improve communication and practice.

Section 5: Access to Antibiotics and Supply Chain Management

5.1 Inadequate supplies of antibiotics are a major cause of AMR

There is no escaping the reality (that is such common knowledge it is often not even mentioned): supplies received from National Medical Stores (NMS) are often less than what is ordered and wholly inadequate.

> *"Antibiotic stock-outs remain a serious constraint; in many cases patients can only be given the right antibiotics if they pay and many of them can't pay.* ***We have to be very clear, antibioticstock-outs are a key factor fueling AMR****. If we look at the scenario where we have investigations done and antibiotics are available, and the outcomes are good, but if we have done the investigations and the antibiotics are out of stock we won't have a good outcome"* **(Laboratory Scientist)**

5.2 Discrepancies between Order and Supply (Order Fill Rates)

In practice, not all that is ordered by the hospital from NMS is supplied. The 'Order Fill Rate' gauges the delivery performance of total number of items ordered against the total number of items delivered. As clearly seen in Table 6, NMS supplies about 75% of orders:

Financial Year Cycle	Total Items Ordered	Total Items Delivered	Fill rate
CYCLE 1 (July - August 2019	307	236	77%
CYCLE 2 (September – October 2019)	306	232	76%
CYCLE 3 (November – December 2019)	309	226	73%

Table 6: The Order Fill Rate at FPRRH in 2019 (Source: Rx on-line medicines management system (NMS do not provide data for specific medications)

This leads to entirely predictable and almost total 'stock-outs' for up to 3 weeks in every 8-week supply cycle. Mortalities and morbidities - and associated significant costs to the hospital - can be directly attributed to these stock-outs. Additionally, the development of team working cannot happen in a vacuum and if the outcomes of that team-working, in terms of wound care or prescribing decisions cannot be operationalised due to lack of supplies then team-working will become frustrating, demotivating and collapse.

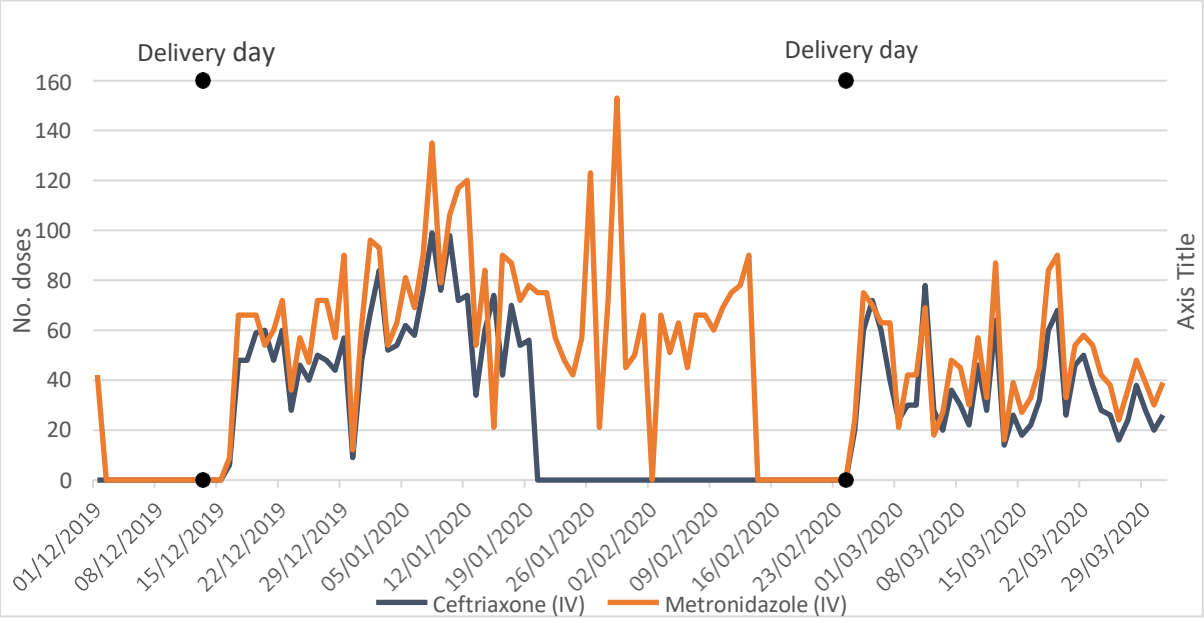


Figure 4: Supplies and Stock-outs: Dispensing of IV Ceftriaxone and Metronidazole from In-Patient Pharmacy to PNG Wards at FPRRH (01/12/2019 - 29/03/2020)

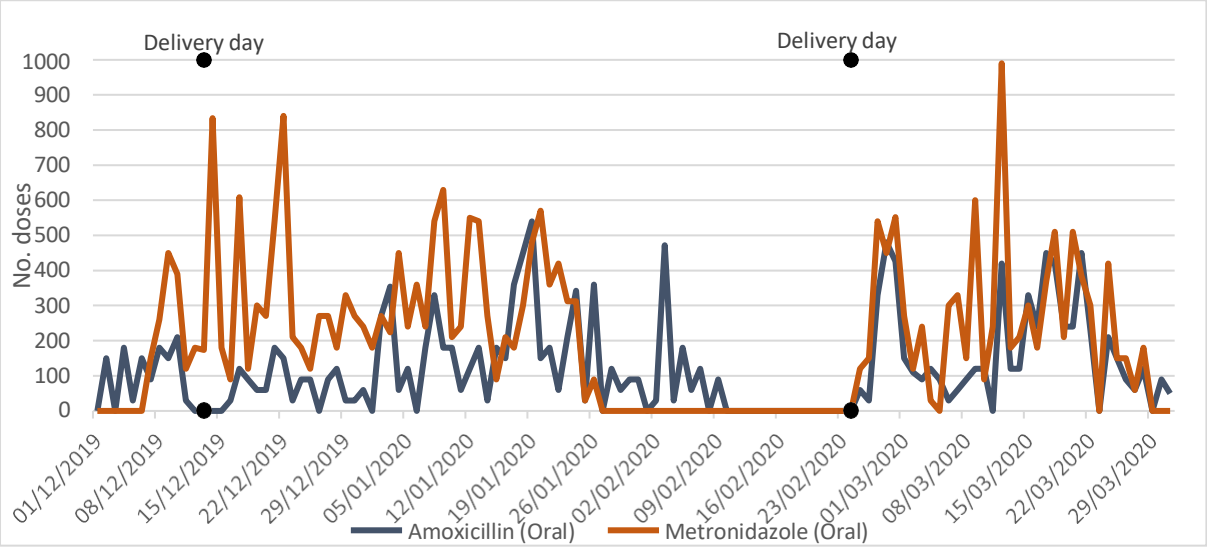


Figure 5: Supplies and Stock-outs: Dispensing of Oral Amoxicillin and Metronidazole from In-Patient Pharmacy to PNG Wards at FPRRH (01/12/2019 - 29/03/2020)

5.3 Monitoring Antibiotic resistance requires appropriate supply of laboratory consumables

Improved IPC practices, including increased testing of swabs for appropriate treatment, requires increased supply of appropriate testing materials, such as antibiotic disks for sensitivity testing. Microbiology needs to be part of the ordering process to ensure that there is timely and sufficient procurement of lab-related supplies.

5A. Policy Note/Recommendation: Overwhelming and Costly Stock-Outs

The Pharmaceutical Society of Uganda and the Hospital Management Team should lobby National Medical Stores and the Ministry of Health to improve the system of supplies to Ugandan Regional Referral hospitals. Table 7 shows the results of a GPPS survey prior to project commencement indicating how many patients did not receive prescribed antibiotics due to stock-outs:

	Gynaecology Patients (n=22)	Post-natal Patients (n=20)
No. of patients on antibiotics	10	18
No. of patients documented to have received all prescribed doses in last 24 hours	4	0

Table 7: Patients Receiving the Prescribed Antibiotic Dose (Source: Results of G-PPS, May 2019 as reported to FPRRH IPC Committee)

When items are 'out-of-stock' patients are advised to source essential items of equipment (catheters, spinal needles, gauze, jic, and drugs and scans) privately. Often operations are conditional on them complying and will be delayed if they are unable to do so even if this poses a risk to life. This situation makes it impossible to gauge real antibiotic consumption in the hospital; it also increases patient stays and complications incurring major costs to the hospital, way beyond the actual costs of the items. Fundamentally it undermines the Ministry of Health's commitment to universal health care and erodes health workers' morale.

The highly centralised and rigid NMS system (with NMS even holding hospital budgets) is a major contributory factor removing any autonomy from the hospital management to attempt to solve this

bi-monthly challenge.

5B. Policy Note/Recommendation: Pharmacy Engagement and Access to Antibiotics

Notwithstanding major structural problems in the supply of anti-microbials, pro-active pharmacy engagement in the MSI, supported by Laboratory Testing, facilitated greater agility and 'lateral thinking' to improve access to optimal antibiotics. This was achieved through the greater efficiencies brought about by utilisation of the RX stores management system and augmented through exploitation of pharmacist knowledge of alternative antibiotic 'silos' linked to specific donor programs (in TB, for example). In practice many areas of antibiotic supply currently sit out of the main stores system. Whilst this may meet the needs of donors this is not in line with effective and holistic management of resources in a public hospital. It also leads to misuse of supplies which often go beyond their expiry date.

5C. Policy Note/Recommendation: Expansion of RX System to Internal Pharmacy Stores

At the present time, the RX system only covers the supply chain between National Medical Stores (NMS) and the main pharmacy stores. In practice, a somewhat haphazard system operates to distribute medicines and supplies throughout the hospital. In-patient pharmacy is involved in the distribution of most supplies to wards. Although the supplies from main stores to in-patient pharmacy are captured on the RX system; the distribution from in-patient pharmacy to patients and wards continue to use handwritten files.

Specific 'systems' are also in place for wards such as the neo-natal unit and for those wards supported by foreign donors. This is a very cumbersome and opaque system and steps should be taken to bring the whole supply system into the RX frame to support effective AMR surveillance and optimal efficacy.

5D. Policy Note/Recommendation: Improving Agility and Holistic planning through Public-Private-Partnership

Knowledge for Change, a key NGO partner in the MSI linked to FPRRH through a Memorandum of Understanding (MOU) has proposed a PPP system to enable FPRRH to access supplies in emergency situations from other suppliers (including Joint Medical Stores). In this case, K4C has loaned FPRRH funds to support the provision of hand gel to key wards during the MSI and also the COVID-19 pandemic. The loan will be recovered through social enterprise mechanisms linked to K4C's undergraduate placement scheme. We would encourage other foreign partners to consider developing similar PPP mechanisms as an alternative to unconditional 'donations' that are then effectively siloed.

5E. Policy Note/Recommendation: Access to Medicines at Night and On-Site Accommodation for Pharmacy Interns

On-going problems were experienced due to the lack of available pharmacy at night times restricting timely access to drugs (and antibiotics in particular). The pharmacy team proposed the opening of a night pharmacy, but pharmacy interns were reluctant to accept night working given the risks associated with this and the fact that pharmacy interns are not allocated accommodation at the hospital . Hospital management should consider reviewing its policy of not allocating accommodation on site to pharmacy interns in order to support access to night pharmacy.

Section 6: Behaviour Change and Knowledge Translation Mechanisms

"Sincerely the trend has changed. Maternity was the ward we laughed at and now it is the ward we all envy" **(Nurse)**

6.1 The full report discusses the mechanism of Health Partnership engagement in detail. In particular, it notes K4C's commitment to **co-present mentoring** as the optimal mechanism for knowledge mobilisation. It also critiques the use of one-off formalised training interventions, often taking place out of the hospital or off the ward and the allowances associated with these. Research indicates these approaches to partnership working are rarely if ever successful.

6A(i). Policy Note/Recommendation: Supporting Behaviour Change requires more than Training

In many areas where real change has been seen in the MSI this was not a result of a prior knowledge deficit (or lack of skill). This is particularly true in discussion of hand hygiene. The early emphasis on infrastructure audit to ensure health workers have the essential materials and equipment to support positive behaviours was instrumental in bringing about change. This then drove the thirst for more knowledge, often beyond their traditional roles bridging the specialist skills of individual disciplines to support effective multidisciplinary teamworking. **Knowledge does not drive change; change drives knowledge.**

6A(ii). Policy Note/Recommendation: Supporting Behaviour Change and Knowledge Transfer through Mentoring

"Sometimes there can be ego – that the doctor or pharmacist thinks, 'I am the overall boss so I can't be directed on what to do' but with the data that goes down" **(Pharmacist)**

Building resilience to AMR (in common with other complex health interventions) demands holistic, multi-professional, team working. We encourage organisations funding interventions and hospitals engaging in partnerships to consider the balance of knowledge mobilisation methods (combining informal mentoring and co-working approaches and formal training) appropriate to their goals. Continuous presence of co-working project staff and professional volunteers enhances team-working

6A(iii). Policy Note/Recommendation: Supporting Behaviour Change through Respectful Team-working

"We are working hand-in-hand together as a team. Before the doctor was not there but nowadays doctors are responding. [The change] is because of the teamwork those people introduced. They showed us good leadership. They would follow-up and afterwards they call the doctor and he comes even if they first deny we call again even the senior doctors. They come – it is a big change" **Midwife**

Effective team working challenges professional hierarchies and empowers lower cadres of staff. When team working is based on collegiality, recognition of respective skills and the role they can play in helping (especially doctors) to achieve their goals efficiently can drive change.

6A(iv). Policy Note/Recommendation: Removing Per Diems to support sustained Behaviour Change

The use of per diems has distorted incentives for training. It often results in the wrong staff (often only senior) staff being trained and pollutes team relationships. We urge all foreign organisations and the Ugandan Ministry of Health to stop making payments for training (and use those funds to augment health worker pay and conditions).

6.2 Staff Rotations, Intern/Student Mobilities and Clinical Supervision

We have emphasised the importance of seeking changes in *organisational (ward) culture* and not individual capability as such. Without such changes to the underlying culture even the most motivated and capable individuals will become frustrated. Building effective Infection Prevention Control and Anti-Microbial Stewardship cultures is complex enough in itself. Maintaining such a culture requires critical mass and strong inter-personal relationships and trust.

The fluidity caused by regular staff rotations; influxes of short-term interns and students (typically with no accompanying supervision from senior doctors or partner education institutions) has the potential to undermine that culture. This is a serious risk to sustainability. Intern doctors play a critical role in RRH settings in the delivery of patient care. The MSI suggests that interns commonly receive no induction and very little supervision from senior doctors and are left to manage on their own.

Orientation of interns is important both for their learning but also to maintain the IPS and AMS culture. At present the responsibility for all orientation rests with the in-charge nurse. This places undue pressure on the in-charge.

6A(v). Policy Note/Recommendation: Improving Management of Doctors

Hospital managers (supported by the Ministry of Health) need to identify a way of managing doctors to ensure that they are routinely present on the wards for their shifts and play an active role in supervising the intern doctors and actively engage with multi-disciplinary teams.

6B. Policy Note/Recommendation: Effective Supervision of Students

Universities and training establishments placing large numbers of students in FPRRH should ensure that they are provided with effective supervision. Effectively oriented and supervised these students provide valuable staff for the ward. In the absence of such supervision, they put a burden on hard-pressed local staff and constitute weak links in the AMS/IPC chain.

Section 7: Integrating and Sustaining the MSI Model

7.1 Hospital management and the Central role of Medicines and Therapeutic Committee in AMS

The Ugandan National Action Plan on AMR places a key emphasis on the role of Hospital Medicines and Therapeutic Committees (MTCs). At the start of the MSI FPRRH did not have a functioning MTC. There was a strong feeling amongst the team that in the absence of MTC validation any policy measures (beyond IPC which are referred to the existing IPC Committee) including any protocols developed (such as the requirement not to release frontline antibiotics in the absence of a lab. test) would not be adhered to.

7A. Policy Note/Recommendation: Mobilising a Hospital Medicines and Therapeutic Committee

The MTC at FPRRH is now in place and creates important opportunities to progress and scale-up the work to other wards and to hospital-wide AMR policy.

7B. Policy Note/Recommendation: Sub-Committees be created under MTC

AMS/AMR teams should be constituted as sub-committees of either the MTC or IPC. These teams/sub-committees will oversee the creation and implementation of Hospital wide antibiotic use policies.

7.2 Sustainability and Cost-Benefit Analysis

In projects such as the MSI where the intervention has been proven to reduce pressure on hospital budgets the intervention is inherently sustainable and the responsibility to ensure continued progress rests with the Hospital and not external partners.

> *"When sepsis is managed then the resources used to manage these patients reduce drastically. By reducing long stays which brings about savings you have contributed to the hospital budget with real term savings. That's an area for me now to look into. We should be able to see in real terms how much savings we have been able to make"* **(Hospital Manager)**

7B. Policy Note/Recommendation: Sustainability and Cost-Benefit Analysis

The Hospital Management team, whilst acknowledging the impact of the MSI in reducing hospital budgets, proposed more thorough attention to ensure accurate cost-benefit analysis of the MSI model.

7.3 Sustainability and Staff Rotations

> *"Our ward is very small, and the volume of patients is overwhelming because the nearby hospitals are not doing c-sections. We have patients now coming from Kyenjojo hospital where they are not doing sections; they just put on the form that they have no anaesthetists".* **Midwife**

The report has emphasised the need for multi-disciplinary teamwork and the role that MDT has played in achieving such positive outcomes. In August 2020 all of the midwives involved in the MSI were routinely rotated to other wards. We accept that this is the cultural norm in Ugandan public facilities. However, these rotations destabilise teams and undermine the positive occupational culture that lies behind behavioural changes. Partial rotations support knowledge exchange and transmission of new learning to other wards whilst retaining sufficient presence on the wards to induct new staff into the ward culture.

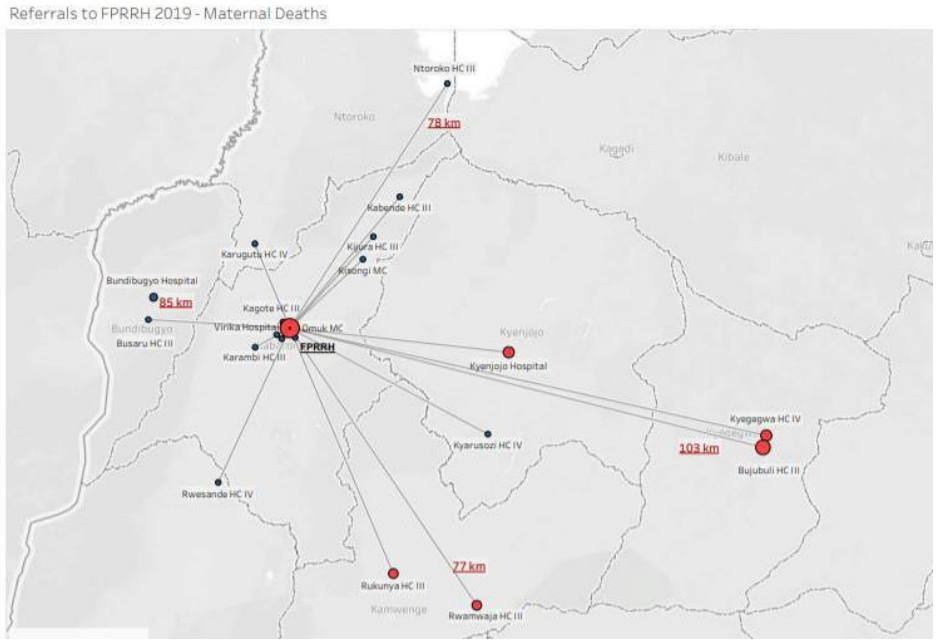
7C. Policy Note/Recommendation: Sustainability and Staff Rotations

The policy of wholesale and frequent rotations should be reconsidered and form the basis of wider multi-disciplinary discussion.

Section 8: Future Work?

8.1 Dysfunctional Referral Systems

The MSI has shown marked success in reducing the deaths of women admitted to labour ward and subsequently operated on in FPRRH. Deaths – and many 'near misses' continue to occur amongst women passing through or by-passing Health Centre IV and hospitals on their journey to FPRRH. Analysis of 1000 admissions identified key areas of concern in Kyenjojo, for example, and in refugee camps. Further work needs to address the causes of referrals and associated delays to prevent the unanticipated arrival of very critical cases, often at night.



District name	Frequency
Bundibugyo	3
Bunyamurwa	1
Bunyangabu	3
Kabarole	15
Kamwenge	6
Kyegegwa	11
Kyenjojo	8
Ntoroko	2

Figure 6: Distances Travelled to FPRRH (Maternal Mortality Cases)

"They are bumping the cases down here simply because their anaesthetists are not there. In the referring centres you will find zero deaths – they will keep a mother there until she is now risky and between leaving there and arriving here… most women die within 1 hour of arriving". **(Stakeholder)**

Section 9: Concluding Comments

Antimicrobial resistance has been described as a 'Terrible Scenario' posing one of the biggest threats to global health, food security and development in the World today. In comparison to other pandemics it is largely invisible and, as such, is rarely seen as a priority. Tagging AMR to one of the major causes of maternal deaths in Uganda has evidenced the potential for major and cost-effective, improvements in anti-microbial stewardship in the Ugandan health system.

We hope that this work and the Recommendations made in this Report will encourage other hospitals and stakeholders in Uganda to identify opportunities to integrate stewardship within current clinical priorities.

References

- Ackers, H.L., Ackers-Johnson, G., Welsh, J., Kibombo, D. and Opio, S. (2020) Anti-Microbial Resistance inGlobal Perspective, Palgrave. (https://link.springer.com/book/10.1007/978-3-030-62662-4)

- Ackers, H.L., Ackers-Johnson, G., Seekles, M., Odur, J. and Opio, S. (2020) Opportunities and Challenges for Improving Anti-Microbial Stewardship in Low- and Middle-Income Countries; Lessons learnt from the Maternal Sepsis Intervention in Western Uganda. *Antibiotics* 2020, *9*, 315; doi:10.3390/antibiotics9060315.(https://www.mdpi.com/2079-6382/9/6/315)

- Antibiotic resistance profiles and population structure of disease-associated *Staphylococcus aureus* infecting patients in Fort Portal Regional Referral Hospital, Western Uganda doi: https://doi.org/10.1101/2020.11.20.371203