Proceedings of the Kabarak University International Conference on Trends and Opportunities in Addressing Global health Challenges 7th and 8th October 2020 Nakuru, Kenya.

Pattern of Antibiotic Prescription for Upper Respiratory Tract Infections among Under-Fives in Outpatient Clinics in Tharaka-Nithi County

Musa SARUTI[1], B Jason BROTHERTON[2], Kipsaina CHEBIWOT[3]
[1]*Kabarak University, P.O. Box Private Bag, Kabarak, 20157, Kenya*
Tel: +254 795016268, Email: msaruti@kabarak.ac.ke
[2]*Kijabe Hospital, P.O. 20, Kijabe, 00220, Kenya*
Email: jb042107@gmail.com
[3]*Kabarak University, P.O. Box Private Bag, Kabarak, 20157, Kenya,*
Email:ckipsaina@kabarak.ac.ke

Abstract: The World Health Organization (WHO) qualified antimicrobial resistance (AMR) as one of the principal threats to public health globally and inappropriate antibiotic prescription is its modifiable contributor. Therefore assessing antibiotic prescriptions for URTI is an acceptable way to analyze the appropriateness of the prescriptions. However, there is a paucity of data regarding the pattern of antibiotic prescriptions in rural hospitals in Kenya. This study seeks to profile the pattern of antibiotic prescriptions among under-fives with URTI in Tharaka-Nithi County, Kenya.

This was a retrospective charts review of under-fives treated from November 2018 to December 2019 for URTI in outpatient clinics in Chogoria and Chuka hospitals. A systematic sampling of 385 charts was carried out using the table of Robert and Morgan based on the total of 5000 URTI cases recorded. Charts of children with suspected bacterial infections were excluded, and for cases of tonsillitis, only children with a modified Centor score ≤3 were included. The binary logistic regression was used to assess the association between variables with the calculation of Odd ratio with a CI of 95% using SPSS 24.

This study found that 70.4% of under-fives with URTI were prescribed antibiotics. The prescriptions were associated with the diagnosis of tonsillitis as part of the URTI, OR 21(95%CI 4.52-99.3); the level of education of the prescriber with clinical officers prescribing more than medical officers, OR 15.9(95%CI 6.98-36.2) and the patient's proximity to the hospital, OR 1.77(95%CI 1.22-2.77).

Antibiotics were prescribed to 70.4% of URTI cases. This percentage was higher than the 30% expected by WHO and was significantly associated with the diagnosis of tonsillitis, the level of education of the prescriber and hospital accessibility. There is a need to train clinicians about the indications of antibiotic prescriptions and to implement antimicrobial stewardship programs in rural facilities.

Keywords: Upper Respiratory Tract Infection, Under-fives, Antibiotic prescription

1. Introduction

Upper respiratory tract infections (URTI) are acute, self-limiting viral infections of the upper respiratory tract which present with sneezing, nasal congestion or discharge (rhinorrhea), sore throat, cough, low-grade fever, headache, and malaise. More than 100 serotypes of rhinoviruses are responsible for most cases (Heikkinen & Järvinen, 2003). Bacterial complications happen only in 0.5-10%, usually from Group A Streptococci (Rezal et al., 2015). Therefore, there is no reason for routine prescription of antibiotics to treat URTIs because they have no clinical benefit. However, clinicians frequently prescribe antibiotics without indication. (Alves Galvão, Rocha Crispino Santos, & Alves da Cunha, 2016).

When microorganisms are repeatedly exposed to antimicrobials (AM), they change over time and become resistant. Consequently, Antimicrobial Resistance (AMR) leads to high morbidity and mortality in patients with infectious diseases (Bell et al. 2014). Because of this consequence, the Public Health England stated that by 2050, AMR would be responsible for ten million deaths every year, and this will lead to an estimated cost of around 66 trillion pounds (Health Matters, 2014). The magnitude of AMR and its associated morbidity and mortality make it one of the significant threats to global public health (WHO, worldwide country situation analysis, 2015).

We aimed to conduct this study in rural Tharaka-Nithi County. In rural areas, faith-based and public hospital play a role in primary care, yet, there is a paucity of data regarding antibiotic prescriptions. This study seeks to profile the pattern of antibiotic prescriptions among under-fives with URTI in Tharaka-Nithi County, Kenya. The findings will help in the battle against AMR by increasing awareness about appropriateness of antibiotic prescriptions in rural areas.

2. The problem

The inappropriate prescription of antibiotics is a significant contributor to AMR, and this situation is real worldwide (World Health Organization, 2015). Examining prescriptions for childhood URTI is an acceptable strategy to assess the rationality of antibiotic prescription, as most URTIs have a viral aetiology (Alves Galvão et al., 2016). Concerning the inappropriate prescription of antibiotics, according to a systematic review conducted by the World Health Organization (WHO), almost half of patient encounters in primary health care centres in Sub-Saharan Africa received Antibiotics. This prescription rate is significantly higher than the WHO threshold of 30% (Ofori-Asenso, Brhlikova & Pollock, 2016, p. 2) and the European one of 20% (Williams et al. 2018). This WHO review was conducted after a systematic review conducted in 2015 that indicated a high prevalence of AMR in Sub-Saharan Africa (Leopold, van Leth, Tarekegn & Schultz 2014, p. 2340). This evidence suggests a potential association between inappropriate prescription and antibiotic resistance in Africa.

The Global Antibiotic Resistance Partnership (GARP) in Kenya reported a paucity of data about AMR and its contributing factors in Kenya. Therefore, GARP expressed the need for more studies in this area (Kariuki, 2017). An extensive search of the literature published online and in the local universities repository revealed no data on antibiotic prescriptions for Tharaka-Nithi County. However, a chart review of 80 cases of under-fives with URTI treated in one of the largest facilities in Tharaka-Nithi County, found that half of those patients were prescribed antibiotics in the outpatient clinic. This practice is ongoing while literature has confirmed that

viruses are responsible for most cases of URTI and routine antibiotic prescriptions is unnecessary and dangerous for the community (WHO, 2017).

Profiling the pattern of antibiotic prescriptions for URTI in under-fives in outpatient clinics will help to have an evidence based idea about antibiotic prescription and it will inform possible interventions to reduce inappropriate antibiotic prescriptions.

3. Objective

The objective of this study is to profile the pattern of antibiotic prescriptions among under-fives treated for URTI in Tharaka-Nithi County, Kenya.

4. Literature review

The top two diagnoses for which clinicians overprescribe antibiotics are URTI and bronchitis (McAvoy, 1994; Lee et al., 2014). In one study conducted in Greece, Vietnam, Uganda, and Kyrgyzstan, 50 % of children were prescribed antibiotics for URTI (Kjærgaard et al. 2019). Seventy-eight per cent of patients, in another study, received antibiotics for URTI. About thirty per cent of those antibiotics were broad-spectrum antibiotics like amoxicillin/clavulanate and cefuroxime (Ochoa, Eiros, Inglada, & Vallano, 2000; Gonzales et al., 2001). However, virological studies have shown that viruses are the commonest cause of URTI worldwide, including Kenya. The superimposed bacteria were found in around 24% of all URTI in a study performed in Nakuru, Kenya (Matu, 2014). Moreover, a recent systematic review confirmed that antibiotics do not treat viral URTI nor prevent complications such as pneumonia (Kenealy T, 2013). Despite all this evidence, literature shows that 50 to 70% of patients receive antibiotics for URTI (Gonzales et al., 2001; Larrabee, 2002). More so for childhood URTI, 20–90 % are treated with antibiotics, with the large percentage being reported in LMICs. (*ICD-10*, 2011).

In Africa, respiratory symptoms are still the leading reason for antibiotic prescription like elsewhere in the world. In one study conducted in Namibia, 78% of patients treated for URTI were prescribed antibiotics. The high prescription rate was associated with age under-five and the differential diagnosis of pharyngitis, unspecified URTI, and tonsillitis (Kunda and Haoses-Gorases 2015). In Kenya, one study done in private healthcare clinics in slums in Nairobi found that 94 % of all patients were prescribed antibiotics and specifically for URTI it was 97.3% (Kleczka et al. 2019).

The reasons behind these inappropriate prescriptions are complex and with multiple facets (McKay et al. 2016a). Most studies on inappropriate antibiotic prescriptions have been done in western countries and Asia. The target for those studies was mainly general practitioners since they are actively involved in the outpatient management of children with URTI (Rezal et al., 2015). In Kenya, it is mostly COs and MOs who work in outpatient clinics, and there is a paucity of data about inappropriate antibiotic prescriptions in the outpatient clinic of public and faith-based facilities. The two recent studies conducted in Nairobi were conducted in private facilities located in slum areas and did not have actual patients' chart review. Instead, the researchers used online tools with limited information to validate the diagnosis of URTI (Kleczka et al. 2019; Mekuria et al. 2019).

5. Methods

A quantitative, retrospective chart review was undertaken to determine the prevalence of antibiotic prescription for URTIs in Chuka and Chogoria hospitals from November 2018 to

December 2019. The chart review included the demographic characteristics of the patients, their body temperature, the duration of the symptoms, the treatment that was prescribed, and the level of education of the prescriber.

A systematic sampling method was used to select patients' files that fulfilled the inclusion criteria. Since both hospitals were using an electronic medical record in the outpatient clinics, the researcher filtered all patients under five years of age who were treated for URTI from November 2018 to December 2019. A systematic sampling of 385 charts was carried out using the table of Robert and Morgan based on the total of 5000 URTI cases recorded. Charts of children with suspected bacterial infections were excluded, and for cases of tonsillitis, only children with a modified Centor score ≤3 were included. The binary logistic regression was used to assess the association between variables with the calculation of Odd ratio with a CI of 95% using SPSS 24.

The collected data were filled in the data collection tool. Of note, data were collected after IREC approval from Kabarak University and the National Commission for science, technology, and innovation (NACOSTI).

All the data was cleaned and coded using Excel before being transferred and analysed in the Statistical Package for Social Sciences (SPSS for Windows, version 24). Frequencies were run to identify coding and data entry errors. Plausibility checks were carried out, and inconsistent data were compared with the original raw data, and data were cleaned appropriately. The researcher coded all the data; hence interobserver variation was avoided.

A preliminary investigation of the data was undertaken using the contingency frequency tables. Several Chi-square tests were undertaken to identify the association between potential explanatory factors. These Chi-square tests were used to identify the association between the antibiotic prescription and the demographic and the clinical factors. In addition, Chi-square tests were used to find any significant difference between percentages of prescriptions in public and the faith-based hospital, and the level of education of prescribers. Subsequently, binary logistic regression was run for significant variables to calculate their effect on antibiotic prescription. The confidence interval was 95% and p value of <0.05 was considered significant.

6. Results and discussion

Table1. Demographic characteristics of the under-fives (N=385)

		n	**%**
Age (months)	0-11	66	17.1
	12-23	127	32.9
	24-35	92	23.8
	36-47	47	12.2
	48-58	53	13.7
Gender	Male	237	61.6
	Female	148	38.4
	Close to the hospital	252	65.5

Proximity to hospital*	Far from the hospital	133	34.5
Hospital type	Faith-based(Mission)	232	60.2
	Public	153	39.8

*Living within 10 km from the hospital.

Most patients were under-three years of age (< 36 months), and three-fifths of them were male. Two third of all URTI cases were living within 10 km from the respective hospital.

Table 2: Prevalence of antibiotic prescription for URTI among Under-fives

Variable		**With antibiotics n (%)**	**No antibiotics n (%)**	**p-value**
Treatment for URTI		271 (70.4)	114(29.6)	0.00
Diagnosis	Tonsillitis in URTI	59 (96.7)	2 (3.2)	0.00
	URTI without tonsillitis	212(65.4)	112 (34.6)	
Duration of symptoms	<7 days	219 (70.1)	93 (29.9)	0.68
	>7 days	8 (61.5)	5 (38.5)	
	Not reported	44 (73.3)	16 (26.7)	
Body temperature	No fever (<38C)	125(65.8)	65 (34.2)	0.33
	Fever(≥ 38)	21(75)	7 (25)	

The overall prevalence of antibiotic prescription for URTI was 70.4%. Considering only patients who had URTI with signs of tonsillitis, the prevalence was even higher, 96.7%. This percentage was significantly elevated compared to 65.4% of antibiotics prescribed for patients who had URTI without signs and symptoms of tonsillitis (p-value 0 .00). Most patients had symptoms for less than seven days. However, the duration of symptoms was not associated with antibiotic prescriptions. For the cases where the temperature was reported, 87% had no fever, and there was no significant difference in antibiotic prescribing for patients with fever and those with no fever (75% versus 65.7%, p: 0.33).

Table 3: Tonsillitis and McIsaac score

		Age		Total cases
		<3 years	≥3 years	
Temperature	<38	30	16	46

≥38	10	5	15
Total tonsillitis cases	40 (65%)	21 (35%)	61

Forty patients out of the 61 (65.5%) with tonsillitis were under-three (low risk of bacterial tonsillitis and therefore note eligible for the McIsaac score). Of the remaining 35% that qualified for the McIsaac score, 5 (8% of the 61 cases) had a score of 3 (age=1, fever=1, and inflamed tonsils=1) that could warrant a throat swab and a consideration of antibiotic, not a routine antibiotic prescription.

Table 4: Binary Logistic regression analysis for potential determinants of antibiotic prescription

Variables	**(Antibiotic Rx%)**	**OR**	**lower**	**Upper**	**Sig**
Facility	Public (77.1%)	1.74	1.09	2.77	.019
	Faith-based (65.9%)				
Patients' Age (year)	<3 (68.7%)	1.36	.81	2.28	.24
	≥3 (75%)				
Patients' Gender	Male (70.5%)	.98	.62	1.54	.96
	Female (70.3%)				
Proximity to the Hospital*	Near the hospital (74.6%)	1.77	1.12	2.77	0.01
	Far from the hosp (62.4%)				
Diagnosis	URTI with tonsillitis(96.7%)	21.2	4.52	99.33	0.00
	URTI without tonsillitis(65.4%)				
Clinician cadre	CO (77.5%)	15.9	6.98	36.2	0.00
	MO(23.5%)				

*proximity means within 10 km from the hospital.

The odds of being prescribed an antibiotic for URTI were 1.74(95%CI 1.09-2.77) times higher in the public facility compared to the faith-based facility. The age of the patients and their gender did not influence the odds of antibiotic prescription. However, the proximity to the hospital increased the odds of being prescribed an antibiotic. OR 1.77(95%CI 1.22-2.77). Also, for patients with tonsillitis, the odds of antibiotic prescription were high, OR 21(95%CI 4.52-99.3), and lastly, clinical officers were more likely to prescribe an antibiotic compared to medical officers, OR 15.9(95%CI 6.98-36.2).

Discussion

The purpose of this study was to profile the pattern of antibiotic prescriptions for URTI in under-fives in outpatient clinics in Tharaka-Nithi County.

Prevalence of antibiotic prescription for URTI

Overall, this study found that the prevalence of antibiotic prescription for URTI in the outpatient clinic was high at 70.4%, compared to reported WHO figures of 30%(Ofori-Asenso, Brhlikova, and Pollock 2016), and 20% of the European surveillance network(Williams et al. 2018). The high prevalence was associated with the level of education of the prescriber, proximity to the hospital, public facility, and the diagnosis of tonsillitis.

The high percentage of antibiotic prescriptions in this study was slightly lower than previous studies conducted in other places. In 2019, a study conducted in nine private primary healthcare clinics in Nairobi reported a prevalence of antibiotic prescription for URTI of 97.3% (Kleczka et al. 2019) with another second study conducted in four not-for-profit outreach clinics reporting a high antibiotic prescription prevalence of 79.7% (Mekuria et al. 2019). Similarly, another study in Namibia found similar results with up to 78% of URTI patients being managed with an antibiotic in a public health centre (Kunda and Haoses-Gorases 2015). The findings of high prevalence in the group of private clinics in Nairobi could be explained by the financial incentive in the private sector, as Mekuria et al. reported. Our study was conducted at a mission and a public hospital, where prescription incentives might be non-monetary and which might explain the slightly lower prevalence compared to the previous studies.

In regards to tonsillitis treatment, the study established that there were significant differences between the percentages of antibiotic prescription for tonsillitis versus other URTI. The difference in treatment might be explained by the misconception that most cases of tonsillitis are of bacterial aetiology hence requiring antibiotic treatment. Furthermore, the misconstrued aetiology of tonsillitis is recognised as one explanation for variation in treatment, which was supported by the fact that only 8% of the total of 61 patients with tonsillitis had a modified Centor score (McIsaac) of 3. The rest of the patients had less than 3 points or were less than three years old. Studies have shown that being less than three years old makes the bacterial aetiology less likely and therefore, cannot be calculated by this scoring system (Shulman et al. 2012). Several studies have established similar findings of higher antibiotic prescriptions for tonsillitis compared to other URTI symptoms (M et al., 2018, McKay et al., 2016b). In some studies, the use of antibiotics for tonsillitis was ongoing even in the under-three years old, where the streptococcal aetiology is less likely. (Aabenhus et al. 2017). Similarly, in the United kingdom, William had the same findings, where 71.6% of children were given an antibiotic despite having a threshold of less than 20% in Europe (Williams et al. 2018).

The high prevalence of antibiotic prescription for URTI is not surprising; instead, it indicates the practice is taking place in developed and developing economies. However, the difference established is that fewer antibiotics are described in developed countries. The postulated explanation in the prevalence difference of antibiotics prescription could be due to the restrictions in antibiotic prescription in developed countries and the level of education of prescribers in their outpatient clinics (Ternhag et al., 2014).

These poor prescription habits in Low and middle-income countries would be associated with poor policies in the restriction of antibiotic use and the knowledge of primary care providers (Zhang et al. 2017).

Factors associated with antibiotic prescriptions

Private versus Public hospital

This study found that patients in the public hospital were more likely to be prescribed antibiotics than in the private faith-based hospital. The difference in prescription practice in the two hospitals could be explained by the fact that clinicians team in the public outpatient clinics was constituted mainly of COs compared to those in the mission hospital where it was constituted of some MOs. Similar differences have been reported in Malaysia(Bp et al. 2013).

Another potential reason could be the fact that under-fives receive free treatment in public hospitals in Kenya. Free access to health care services may increase the possibility of a return visit to the hospital, which may push clinicians to prescribe antibiotics in the second visit. Additionally, the workload in public hospitals is higher compared to the mission or private hospitals (Calbo et al. 2013 & Manyisa and van Aswegen 2017), and this has been associated with a high risk of antibiotic prescription for URTI in outpatient settings(Calbo et al. 2013; Manyisa and van Aswegen 2017). This finding contrasts with the data from Malta that showed no difference in public versus private settings for antibiotic prescription by the general practitioners (Saliba-Gustafsson et al. 2019).

Clinicians' level of education of the prescriber

The odds of a CO to prescribe an antibiotic for URTI was 15.9 times higher than the MO. This high prescription could be linked to the difference in the levels of education and the associated clinical confidence. Similarly, in Malaysia, COs were found to prescribe more than MOs (Bp et al. 2013). McKay et al. in their systematic review found that 'front-line' general practitioners such as family physicians and emergency physicians, in developed countries were more likely to prescribe antibiotics than paediatricians or internal medicine practitioners. The review attributed this form of prescription to the workload of the 'front-line practitioners and the type of training (McKay et al. 2016b). These two reasons could be considered in our study, whereby clinical officers attend to more patients compared to medical officers in the outpatient clinics.

Proximity to the hospital

Living close to the hospital was significantly associated with an antibiotic prescription. It is assumed that patients who live close to the facility are more likely to be reassured and advised to return to the facility if symptoms persist instead of prescribing antibiotics. The hospital proximity was a determinant of antibiotic prescription in a study conducted by Ternhag in Sweden. He explained that it was because of easy follow-up visits (Ternhag et al., 2014). Therefore, it appears that, if patients can easily return the clinic, the odds of being prescribed an antibiotic increase.

Patients' Age

Contrary to other studies, age was not used to influence the decision of antibiotic prescription for URTI in this study. This study was different from another study conducted in England where older children had more antibiotic prescriptions than the younger ones (Williams et al. 2018). In contrast, one study in Italy found that the proportion of antibiotic prescriptions was decreasing with age with older children having fewer antibiotic prescriptions (Resi 2003).

Fever and Antibiotic prescription

Despite the recommendation against antibiotic prescription, several studies reported in the McKay et al. review demonstrated that fever was a determinant of antibiotic prescription for URTI (McKay et al. 2016b). However, this study did not find an association between fever and antibiotic prescription. Most patients had no fever, but they were given antibiotic prescriptions. In cases of tonsillitis, a fever could increase the Centor score and therefore, the likelihood of antibiotic prescription. However, in this study, only 8% of patients had a score of 3 because they had a fever with inflamed tonsils, and they were more than three years old. This finding contrasts with a study conducted in Malta and other places where the fever was a predictor of antibiotic

prescription for URTI (Saliba-Gustafsson et al. 2019) M et al., 2018). Therefore, in this study, other factors apart from fever could be the main contributors to the prescription of antibiotics.

7. Recommendations

Policy recommendations:

i. There is an urgent need to reinforce the regulation for antibiotic prescribing and dispensing in rural hospitals.
ii. Clinicians' training needs to clarify the management of common viral infections and the contraindication of antibiotic prescription in the context of antimicrobial resistance. This training needs to continue with ongoing medical educations in their facilities for updates.
iii. There is a need to balance the number of patients that each clinician should see per day for them to have enough time for patient's education in the clinic.
iv. Hospitals need to initiate and sustain antimicrobial stewardship programs and clarify the guidelines on antibiotic use.

Recommendations for further research

i. A study on the prevalence of antibiotic prescription for URTI in children with moderately elevated C-reactive protein.
ii. A study on the antibiotic prescription for tonsillitis with negative throat swab for group A streptococcal infection in children.
iii. A study on the effectiveness of continuing medical education on prescribing practices.
iv. A study on the impact of an antimicrobial stewardship program in a rural hospital on antibiotic prescription.

8. Conclusion

Antibiotic prescribing for URTI was 70,4% in this part of central Kenya, which is higher than the 30% recommended by WHO and 20% from the European guidelines for URTI. The public hospital had higher prescribing practices than the faith-based hospital. The factors that were associated with higher antibiotic prescribing were: the suspicion of tonsillitis, the level of education of the prescriber and the patients' living in the proximity of the hospital. There is a need to implement evidence-based intervention in hospitals to mitigate inappropriate antibiotic prescriptions. Further studies can consider assessing the antibiotic use in the community, and the extend of antimicrobial resistance in the hospitals of the region.

References

Aabenhus, Rune, Malene Plejdrup Hansen, Laura Trolle Saust, and Lars Bjerrum. 2017. "Characterisation of Antibiotic Prescriptions for Acute Respiratory Tract Infections in Danish General Practice: A Retrospective Registry Based Cohort Study." *Npj Primary Care Respiratory Medicine* 27(1):1–6.

Anon. n.d. "Health Matters: Antimicrobial Resistance." *GOV.UK*. Retrieved February 25, 2020 (https://www.gov.uk/government/publications/health-matters-antimicrobial-resistance/health-matters-antimicrobial-resistance).

Bell, Brian G., Francois Schellevis, Ellen Stobberingh, Herman Goossens, and Mike Pringle. 2014. "A Systematic Review and Meta-Analysis of the Effects of Antibiotic Consumption on Antibiotic Resistance." *BMC Infectious Diseases* 14:13.

Bp, Kho, Ong Cm, Tan Ft, and Wee Cy. 2013. "Antibiotic Prescribing for Upper Respiratory Tract Infections in Sarawak District Hospitals." *The Medical Journal of Malaysia* 68(2):136–40.

Calbo, Esther, Luis Álvarez-Rocha, Francisco Gudiol, and Juan Pasquau. 2013. "A Review of the Factors Influencing Antimicrobial Prescribing." *Enfermedades Infecciosas y Microbiología Clínica* 31:12–15.

Kjærgaard, Jesper, Marilena Anastasaki, Marianne Stubbe Østergaard, Elvira Isaeva, Azamat Akylbekov, Nhat Quynh Nguyen, Susanne Reventlow, Christos Lionis, Talant Sooronbaev, Le An Pham, Rebecca Nantanda, James W. Stout, and Anja Poulsen. 2019. "Diagnosis and Treatment of Acute Respiratory Illness in Children under Five in Primary Care in Low-, Middle-, and High-Income Countries: A Descriptive FRESH AIR Study." *PLoS ONE* 14(11).

Kleczka, Bernadette, Pratap Kumar, Mercy Karimi Njeru, Anita Musiega, Phoebe Wekesa, Grace Rabut, and Michael Marx. 2019. "Using Rubber Stamps and Mobile Phones to Help Understand and Change Antibiotic Prescribing Behaviour in Private Sector Primary Healthcare Clinics in Kenya." *BMJ Global Health* 4(5).

Kunda, Mwape, and Lischen Haoses-Gorases. 2015. "An Investigation of Antibiotic Prescribing in Patients with Upper Respiratory Tract Infections (URTIs) at Katutura Health Centre, Windhoek, Namibia." *Single Cell Biology* 04(04).

M, Manne, Deshpande A, Hu B, Patel A, Taksler Gb, Misra-Hebert Ad, Jolly Se, Brateanu A, Bales Rw, and Rothberg Mb. 2018. "Provider Variation in Antibiotic Prescribing and Outcomes of Respiratory Tract Infections." *Southern Medical Journal* 111(4):235–42.

Manyisa, Zodwa M., and Elsie J. van Aswegen. 2017. "Factors Affecting Working Conditions in Public Hospitals: A Literature Review." *International Journal of Africa Nursing Sciences* 6:28–38.

McKay, Rachel, Allison Mah, Michael R. Law, Kimberlyn McGrail, and David M. Patrick. 2016a. "Systematic Review of Factors Associated with Antibiotic Prescribing for Respiratory Tract Infections." *Antimicrobial Agents and Chemotherapy* 60(7):4106–18.

Mekuria, Legese A., Tobias FR de Wit, Nicole Spieker, Ramona Koech, Robert Nyarango, Stanley Ndwiga, Christine J. Fenenga, Alice Ogink, Constance Schultsz, and Anja van't Hoog. 2019. "Analysing Data from the Digital Healthcare Exchange Platform for Surveillance of Antibiotic Prescriptions in Primary Care in Urban Kenya: A Mixed-Methods Study" edited by E. Rutebemberwa. *PLOS ONE* 14(9):e0222651.

Ofori-Asenso, Richard, Petra Brhlikova, and Allyson M. Pollock. 2016. "Prescribing Indicators at Primary Health Care Centers within the WHO African Region: A Systematic Analysis (1995-2015)." *BMC Public Health* 16(1).

Resi, D. 2003. "Antibiotic Prescriptions in Children." *Journal of Antimicrobial Chemotherapy* 52(2):282–86.

Saliba-Gustafsson, Erika A., Alexandra Dunberger Hampton, Peter Zarb, Nicola Orsini, Michael A. Borg, and Cecilia Stålsby Lundborg. 2019. "Factors Associated with Antibiotic Prescribing in Patients with Acute Respiratory Tract Complaints in Malta: A 1-Year Repeated Cross-Sectional Surveillance Study." *BMJ Open* 9(12).

Shulman, S. T., A. L. Bisno, H. W. Clegg, M. A. Gerber, E. L. Kaplan, G. Lee, J. M. Martin, and C. Van Beneden. 2012. "Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America." *Clinical Infectious Diseases* 55(10):e86–102.

Williams, Megan Rose, Giles Greene, Gurudutt Naik, Kathryn Hughes, Christopher C. Butler, and Alastair D. Hay. 2018. "Antibiotic Prescribing Quality for Children in Primary Care: An Observational Study." *The British Journal of General Practice* 68(667):e90–96.

Zhang, Zhitong, Yanhong Hu, Guanyang Zou, Mei Lin, Jun Zeng, Simin Deng, Rony Zachariah, John Walley, Joseph D. Tucker, and Xiaolin Wei. 2017. "Antibiotic Prescribing for Upper Respiratory Infections among Children in Rural China: A Cross-Sectional Study of Outpatient Prescriptions." *Global Health Action* 10(1):1287334.