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An analysis of policies for cotrimoxazole, amoxicillin and azithromycin use in Namibia’s public sector: findings and therapeutic implications

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(Accepted for publication International Journal of Clinical Practice – please keep CONFIDENTIAL).

Abstract

**Background:** Despite Namibia’s robust medicine use systems and policies, antibiotic use indicators remain suboptimal. Recent medicine use surveys rank cotrimoxazole, amoxicillin and azithromycin (CAA) among the most used medicines. However there is rising resistance to CAA (55.9% - 96.7 %). Unfortunately to date there have been limited studies evaluating policies to improve antibiotic use in Namibia. **Aim:** To evaluate public sector pharmaceutical policies and guidelines influencing the therapeutic use of CAA antibiotics in Namibia. **Methods:** Evaluate Namibia’s pharmaceutical policies and guidelines for CAA use through quantitative text analysis. The main outcome variables are existence of antibiotic policies, therapeutic indications per antibiotic and the type/level of health care facility allowed to use the antibiotic. **Results:** Policies for antibiotic use were limited with only the draft Namibia Medicines Policy having a statement on antibiotic use. Several essential antibiotics had no therapeutic indications mentioned in the guidelines. 29 antibiotics were listed for 69 therapeutic indications; CAA (49.3%) antibiotics and ATC J01C/J01D (48%) having the highest indications per antibiotic. For CAA antibiotics, this suggested use was mainly for acute respiratory infections (n=22, 37.2%). Published policies (58.6 % - 17/29) recommended antibiotics for use at the primary health care (PHC) level, with CAA antibiotics recommended mostly for respiratory tract infections and genitourinary infections. **Conclusions:** Policy and guidelines for antibiotic use in Namibia are not comprehensive and are skewed towards PHCs. Existing policies promote the wide use of
CAA antibiotics, which may inadvertently result in their inappropriate use enhancing resistance rates. This calls for the development of more comprehensive antibiotic guidelines and essential medicine lists in tandem with local antimicrobial resistance patterns. In addition, educational initiatives among all key stakeholder groups.

What’s known
- There is considerable overuse of common antibiotics across countries particularly in primary health care centres leading to increasing resistance rate
- There are ongoing developments to improve the use of antibiotics across countries including general and specific guidelines treatment guidelines, essential medicine lists and quality indicators for antibiotics. In addition growing surveillance of antibiotic resistance patterns to guide the empiric use of antibiotics
- However there can be concerns that the various groups producing prescribing guidance are not co-ordinated

What’s new
- Novel way for low and middle income countries to assess utilization of common antibiotics against treatment guidelines, quality indicators and essential medicine lists especially where there are concerns with antibiotic resistance patterns
- There appeared to be no co-ordination in Namibia between the various government bodies producing treatment guidelines, essential medicine lists and monitoring resistance patterns. As a result, continued high use of common antibiotics across multiple conditions exacerbating resistance rates
- Several antibiotics were also listed in essential medicine lists but not included in any guidelines. This has implications for their misuse, which needs to be addressed

KEY WORDS: Antibiotic use, policies, cotrimoxazole, amoxicillin, azithromycin, Namibia

Introduction

Inappropriate use of antibiotics increases antibiotic resistance leading to increases in morbidity, mortality and costs of treatment [1-5]. This is not helped by the fact that in most sub-Saharan countries, antibiotic treatment policies are not up-to-date, and there can be high rates of self-purchasing of antibiotics, leading to increased antimicrobial resistance to essential antibiotics [6-11]. This has had a devastating impact on public health in the sub-Saharan Africa [12-16]. However, effective policies including education of all key stakeholder groups, prescribing restrictions as well as indicators have enhanced the appropriate use of antibiotics [14, 17-20].

In Namibia, despite the scale-up of medicine use systems and policies [Table 1; 12,21-30], antibiotic use and policy compliance indicators in the public health sector remain suboptimal [6, 31-33]. As a result, there has been growing resistance to essential antimicrobials used among public health facilities in Namibia and sub-Saharan Africa; with a similar situation for antimalarials. These include chloroquine [34,35], cotrimoxazole [36-42], sulphadoxine/pyrimethamine [2] and ampicillin [43-46]. Reports from the Namibia’s National Institute of Pathology (NIP) have also indicated increasing incidence of antibiotic resistance to first-line antibiotics particularly cotrimoxazole, azithromycin and amoxicillin (CAA), ranging
between 55.9% - 96.7% [36,39,47,48]. Despite the heightening resistance to CAA in Namibia, ABC analyses on expenditure of medicines and medicine use surveys at public health facilities in Namibia continue to rank CAA antibiotics among the top 15 expenditure items or top three antibiotics [6,21,32,49].

One of the factors driving increased prescribing of antibiotics in Namibia is the burden of infectious diseases particularly HIV/AIDS [6,32,33,36,39], which may well aggravate resistance to essential antibiotics [12,14,50]. One area of concern are the primary health care (PHCs) centers [32,51-56] with gaps in laboratory diagnostics, education regarding appropriate antibiotic use and human capacity [5,6,31]. Among PHCs, the risk of antibiotic misuse is exacerbated by the high workload for health workers with limited training on antibiotic pharmacotherapy as recommended by WHO and Medicines and related Act of Namibia [57-61]. In addition, only one indicator HF 13 regarding the number of antibiotics per prescription is used to monitor antibiotic use in Namibia. This currently only applying among public facilities including PHCs, district hospitals including state hospitals, intermediate hospitals that serve as regional referral hospitals and state hospitals that serve as national referral hospitals [25-29,62].

**Aims**

Consequently, we sought to address this by developing and evaluating antibiotic use indicators at policy level in Namibia as the first step to improve future antibiotic use in ambulatory care in Namibia. Box 1 contains details of the current systems and policies in Namibia.

**Box1: Systems and policies for medicine use in Namibia**

**Pharmaceutical Systems in Namibia:**

- Pharmaceutical Management information system (PMIS): A system implemented in all hospital and public health facility for reporting on performance and monitoring human resources for pharmacy and medicine indicators. This is implemented by the Ministry of Health and Social Services – Pharmaceutical division
- Electronic data base system: including the electronic dispensing tool, the stock card Dashboard, the TB manager and the Rx solution to collect monthly data on the use of medicines at public health facility
- System for access to essential medicines: An updated Namibia essential medicine list provides for the level of use of various medicines which all accessed free at public health facilities

**Policies:**

- Namibia Medicine policy: provide a frame work for access and availability to safe, efficacious and cost effective medicines to the population and the rational use of medicines.
- Pharmacy Act, 2004: provides for the education and qualifications as well as continued professional development of personnel involved in the use of medicines in Namibia
- Medicines and related substances act of 2003: provides for the control of the use, distribution and sale of medicines in Namibia and categorizes medicines in schedules
Materials and methods

**Medicine policy documents**

We searched the Ministry of Health and Social services (MoHSS) websites and government of Namibia websites for policy documents relating to pharmaceuticals that were developed between 1990 to 2015. The search strategy included the use of terms such as “policy, medicine, guideline, Act, laws, regulations and Namibia”. The most recent editions of all policy documents in the MoHSS database on Pharmaceutical services division were included in this study.

A total of seven policy documents were identified as up-to-date and pertinent pharmaceutical policy documents and were analyzed for content on antibiotic policy statements. The Namibia essential medicine list (Nemlist) [22] was used as the defining document for assessing antibiotic use in Namibia’s public health sector. The Nemlist is critical with implementing the national medicine policy through defining the range of essential medicines recommended for use at different levels of the public sector. The Nemlist is also a critical document to operationalize treatment policies and guidelines. The Namibian standard treatment guidelines (2011) [23], the national guidelines for management of HIV/AIDS (2015) [24], the national guidelines for management of tuberculosis (2015) [25], the guidelines for management of malaria (2011) [26] and for integrated management of childhood illnesses (2012) [27], were used as the principal documents from which indications for essential antibiotics in the Nemlist were reviewed.

The Pharmacy Act (2004) [29], the Medicines related substance Act (2003) [30], and the draft National medicine policy [28] were used as reference documents in the analysis. These Acts of parliament that regulate the use of medicines and pharmacy professionals were used to identify laws supporting the judicious use of antibiotics in the health care sector of Namibia. Both Acts and the national medicine policy provide an overarching legal frame work for policies on medicine use including antibiotic in Namibia.

**Methods**

Quantitative policy analysis methods were used to evaluate pharmaceutical policy indicators for antibiotic use [63]. A document analysis design was subsequently used to analyse the content of the identified policies for antibiotic use in Namibia’s public health care. The Nemlist was used as the defining document for the analysis of antibiotic use in Namibia by the health care facility level, for vital, essential and necessary medicines (VEN) classification of medicines [22] and formulations. The treatment guidelines were subsequently used as asserting documents for content analysis on the use of Nemlist antibiotics by indication and prescriber.
The search strategy included the use of search terms as “infection, inflammation, itis, and acute, chronic, bacterial, viral, fungal, and protozoa and/or parasitic” to identify indications for antibiotics and/or CAA. Searched terms including “antibiotic, cotrimoxazole, amoxicillin, azithromycin, and antinfectives” were used to identify the antibiotics within the treatment guidelines and analyse the indications. The medicine regulations and laws were used as reference documents, and were reviewed for policy statements on antibiotic use. The main outcome variables were policy statements on antibiotic use, indications per antibiotic on the essential medicines list and factors associated with antibiotic use. The data were abstracted on a developed form and entered into SPSS v21 software for quantitative analysis.

**Ethical considerations**
The study has no ethical implications as no human subjects were interviewed or recruited in this study. The study adopted a policy document analysis approach where secondary data was used from policy documents which are all accessible for use by the public. All extracts from the policy documents have been referenced.

**Results**

**Policy indicators for antibiotic use**
Only the HF-13 indicator is currently used to measure antibiotic use in Namibia [49] at the health facility level. Five policy indicators for measuring effective and safe antibiotic use were developed based approaches by Brown [64] and evaluated (Table 1). These indicators assessed the implementation of antibiotic policies across sectors. They were developed based on access, availability and use of antibiotics as described by the Namibian medicine policy statements for the general use of medicines. These indicators focus on both access and availability of antibiotic policy documents at the National level and their implementation at the points of access of antibiotics.

<table>
<thead>
<tr>
<th>Policy indicator</th>
<th>Thresh hold</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Availability and access to key antibiotic policy documents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of policy documents with policies on antibiotic use</td>
<td>100%</td>
<td>1/7</td>
</tr>
<tr>
<td>Available of a comprehensive antibiotic policy</td>
<td>100%</td>
<td>_</td>
</tr>
<tr>
<td># Antibiotic policy statements in the National Medicines Policy</td>
<td>100%</td>
<td>_</td>
</tr>
<tr>
<td>#Antibiotic treatment documents: guideline, formulary</td>
<td>100%</td>
<td>_</td>
</tr>
<tr>
<td>Availability of an antibiogram / surveillance policy</td>
<td>100%</td>
<td>_</td>
</tr>
<tr>
<td><strong># of indications per antibiotic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average # of indications per ATC class J01C and J01D</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Average # of indications per top ABC antibiotics</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td># of antibiotics by body systems (empiric therapy)</td>
<td>50%</td>
<td>9/11(75%)</td>
</tr>
<tr>
<td>% antibiotics in Nemlist with indications in STG</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

**Levels of use of an antibiotic**
% of antibiotics for use at PHC level 50% 100%
% of with restricted use by specialist 50% 100%
% of antibiotics used for prophylaxis therapy 50% 2
% of antibiotics indicated for URTI 10%

**Current antibiotic policies in Namibia**

A total seven policy documents were reviewed for policies on antibiotic use. The majority were treatment guidelines 42.9% (3/7), with only the draft National Medicine Policy 14.3% (1/7) having a policy statement on antibiotic use; “*The need for rational use holds good for all medicines, but it is especially necessary in certain situations, e.g.: i. the use of antibiotics, where reckless use will promote the development of antimicrobial resistance*”. Currently, Namibia has no policy document specific to antibiotic use; no medicines or antibiotic formulary and no antibiograms to guide antibiotic use. A total of 29 antibiotics are included in Namibia’s essential medicine list; 3 of which have no indications in the standard treatment guidelines (Figure 1). Overall, the treatment guidelines include 69 indications for antibiotic use.

The Medicines and related substances control Act, 2003 categorizes most antibiotics as prescription only medicines and categorizes them as schedule 2 medicines. Cotrimoxazole, amoxicillin and azithromycin are classified as essential and vital and cotrimoxazole as essential.

Clarithromycin is indicated for two infections in the treatment guideline but not listed in the essential medicine list. HIV/AIDS and TB treatment policies provide for the use of cotrimoxazole as preventive therapy (CPT) in all HIV positive children and lifelong use in adults unless there are contraindications. Treatment polices in the HIV/AIDS treatment guidelines however recommend that the use of CPT in adults can be discontinued if two consecutive CD+4 counts are consistently above 350 cells/mm$^3$.

**Patterns of indications for antibiotic use by treatment policies guidelines**

The majority of the antibiotics in the treatment policies and guidelines are β-lactam antibiotics (48.0%) - ATC class J01C and J01D and for use at the PHC level (58.6%). There is a significantly higher number of antibiotics indicated for treatment of oral/dental infections ($p < 0.001$), CNS infections ($p < 0.041$), HIV/AIDS related illnesses ($p = 0.005$) and the management of eye and ear infections. Both parenteral and oral forms of antibiotics are indicated or use at the PHC level (Table 2).
Table 2: Characteristics of antibiotics in the treatment guidelines (n = 29)

<table>
<thead>
<tr>
<th>ATC class of the antibiotic</th>
<th>Number (%)</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$p$ – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>J01 A</td>
<td>1(3.4)</td>
<td>7</td>
<td>14.310</td>
<td>0.046</td>
</tr>
<tr>
<td>J01 B</td>
<td>1(3.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 C</td>
<td>9(31)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 D</td>
<td>5(17.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 E</td>
<td>1(3.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 F</td>
<td>4(13.8)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 G</td>
<td>3(10.3)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 M</td>
<td>2(6.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01 X</td>
<td>3(10.3)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic formulation</th>
<th>Number (%)</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$p$ – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>12 (41.4)</td>
<td>2</td>
<td>3.38</td>
<td>0.185</td>
</tr>
<tr>
<td>Parenteral</td>
<td>12 (41.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral and parenteral</td>
<td>5(17.2)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indicated for use at PHC</th>
<th>Number (%)</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$p$ – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>12 (41.4)</td>
<td>2</td>
<td>7.103</td>
<td>0.000</td>
</tr>
<tr>
<td>No</td>
<td>14(48.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>3(10.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ATC class of CAA antibiotics</th>
<th>Number (%)</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$p$ – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>3(10.7)</td>
<td>2</td>
<td>18.241</td>
<td>0.000</td>
</tr>
<tr>
<td>No</td>
<td>26(37.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotics indicated by policy</th>
<th>Number (%)</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$p$ – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential medicine list</td>
<td>28(96.6)</td>
<td>2</td>
<td>25.138</td>
<td>0.000</td>
</tr>
<tr>
<td>Treatment guidelines</td>
<td>28(96.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaria policy</td>
<td>2(6.9)</td>
<td>2</td>
<td>21.552</td>
<td>0.000</td>
</tr>
<tr>
<td>HIV treatment guideline</td>
<td>4(13.8)</td>
<td>2</td>
<td>15.207</td>
<td>0.000</td>
</tr>
<tr>
<td>Tuberculosis guideline</td>
<td>2(6.8)</td>
<td>2</td>
<td>21.552</td>
<td>0.000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% Antibiotics per infection</th>
<th>Number (%)</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$p$ – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory infection</td>
<td>15(51.7)</td>
<td>1</td>
<td>0.034</td>
<td>0.853</td>
</tr>
<tr>
<td>Genitourinary infection</td>
<td>12(41.4)</td>
<td>1</td>
<td>0.862</td>
<td>0.353</td>
</tr>
<tr>
<td>Musculoskeletal disorders</td>
<td>14(48.3)</td>
<td>1</td>
<td>0.034</td>
<td>0.853</td>
</tr>
<tr>
<td>Oral and dental infections</td>
<td>3(10.3)</td>
<td>1</td>
<td>18.241</td>
<td>0.000</td>
</tr>
<tr>
<td>CNS infections</td>
<td>9(31.0)</td>
<td>1</td>
<td>4.172</td>
<td>0.041</td>
</tr>
<tr>
<td>HIV disorders</td>
<td>7(24.1)</td>
<td>1</td>
<td>7.759</td>
<td>0.005</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>10(34.5)</td>
<td>1</td>
<td>2.793</td>
<td>0.095</td>
</tr>
<tr>
<td>Prophylaxis in Malnutrition</td>
<td>5(17.5%)</td>
<td>1</td>
<td>12.448</td>
<td>0.000</td>
</tr>
<tr>
<td>Ear and Eye infections</td>
<td>8(6.9)</td>
<td>1</td>
<td>5.828</td>
<td>0.016</td>
</tr>
<tr>
<td>Obstetric infections</td>
<td>2(6.9)</td>
<td>1</td>
<td>21.552</td>
<td>0.016</td>
</tr>
<tr>
<td>Septicaemia/ Malaria</td>
<td>10(34.5)</td>
<td>2</td>
<td>2.793</td>
<td>0.095</td>
</tr>
</tbody>
</table>

*NPar Chi-square test
**Treatment policy indications per antibiotic**

Out of the 29 essential antibiotics, amoxicillin, azithromycin and metronidazole have the most indications per antibiotic, three antibiotics have no indications in the treatment guidelines and cotrimoxazole is the main antibiotic used in HIV/AIDS for preventive therapy (Figure 1). Phenoxymethylpenicillin, a limited spectrum penicillin, is indicated for infections other than pharyngitis / tonsillitis. CAA antibiotics are indicated for approximately half of the indications.

**Figure 1: Number of treatment indications per antibiotic (n = 69)**
Factors associated with indications for CAA antibiotics

Treatment policies indicated the prescribing of CAA antibiotics for the treatment of respiratory, musculoskeletal, gastrointestinal and genitourinary infections. Policies recommend the use of CAA antibiotics for a wide range of systemic conditions, prophylaxis in HIV/AIDS, malnutrition (Table 3).

Treatment policies are more likely to indicate the use CAA antibiotics at the PHC rather than hospital level [OR 35.75(95% CI; 4.21–303.42), \( p < 0.001 \)].

### Table 3: Indication for CAA antibiotics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean indications (± SD)</th>
<th>F</th>
<th>95%CI</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory infection</td>
<td>6±5.29</td>
<td>0.92±1.197</td>
<td>31.7</td>
<td>2.769 – 7.384</td>
</tr>
<tr>
<td>Genitourinary infection</td>
<td>2±3.464</td>
<td>1±1.356</td>
<td>11.83</td>
<td>-1.014 – 3.014</td>
</tr>
<tr>
<td>Musculoskeletal infection</td>
<td>2.33±2.51</td>
<td>1.27±2.09</td>
<td>0.122</td>
<td>-1.593 – 3.721</td>
</tr>
<tr>
<td>Oral/Dental infections</td>
<td>1.00±1.732</td>
<td>.15±.613</td>
<td>10.053</td>
<td>-0.098 – 1.791</td>
</tr>
<tr>
<td>CNS infection</td>
<td>.33±.577</td>
<td>.31±.471</td>
<td>0.028</td>
<td>-0.574 – 0.625</td>
</tr>
<tr>
<td>HIV/AIDS infections</td>
<td>.67±.577</td>
<td>.31±.679</td>
<td>0.039</td>
<td>-0.482 - 1.2</td>
</tr>
<tr>
<td>Gastrointestinal infections</td>
<td>.67±.577</td>
<td>.54±1.104</td>
<td>0.409</td>
<td>-1.215 – 1.472</td>
</tr>
<tr>
<td>Malnutrition therapy</td>
<td>.33±.577</td>
<td>.15±.368</td>
<td>1.451</td>
<td>-0.305- 0.664</td>
</tr>
<tr>
<td>Ear and eye infection</td>
<td>1.00±1.000</td>
<td>.31±.618</td>
<td>0.620</td>
<td>-1.216 – 1.510</td>
</tr>
<tr>
<td>Obstetrics and Gynaecology infections</td>
<td>0.00±0.00</td>
<td>.08±.272</td>
<td>1.108</td>
<td>-0.404 – 0.250</td>
</tr>
<tr>
<td>Septicaemia/Malaria</td>
<td>0.00±0.00</td>
<td>0.42±0.578</td>
<td>15.187</td>
<td>1.717 – 16.027</td>
</tr>
</tbody>
</table>

NB: Levene's Test for Equality of Variances; CI = 95% Confidence interval

The standards in the STGs criteria for use of CAA antibiotics

Azithromycin and amoxicillin are selectively indicated for treatment of 90% of respiratory tract infections in the STGs; including upper respiratory infections that are commonly of a viral aetiology [61] and to manage secondary bacterial infections [23]. Cotrimoxazole is recommended for prophylaxis against PCP and other types of pneumonia in HIV/AIDS patients.

Discussion

Despite the existence of guidelines for antibiotic use in various treatment guidelines in Namibia including HIV/AIDS, malaria, and tuberculosis as well as the integrated management of childhood illnesses in Namibia [22-27] (Table 1), Namibia has no comprehensive antibiotic policy, antibiotic guidelines, antibiotic formulary or antibiograms. These strategies provide the evidence based for the appropriate use of antibiotics [10, 45, 60, 65,66]. Previous studies in Namibia on antibiotic use have recommended the development of guidelines specific to antibiotics in both the private and public sectors [6,31-33]. Unfortunately to date, only the draft
National medicine policy has a policy statement on antibiotics which is mentioned in a passive way [29].

Approximately half of the antibiotics indicated in the treatment policies are of ATC classes J01 D and J01C (β-lactam) and / or CAA antibiotics (Table 2 and Figure 1). Medicine use surveys across all sectors in Namibia have implicated the overuse of penicillins and macrolides particularly for upper respiratory tract infections (URTIs) and common community acquired diseases [6,33]. The rate of antibiotic utilisation was estimated at 78% for all URTIs and 48% for all other infections in the public sector despite their origin [6,33]. The Pharmaceutical Management Information System (PMIS) data indicates that only two regions in Namibia currently meet the HF-13 indicator for antibiotic use [49]. National and regional ABC analyses that categorize medicine consumption by expenditure in Namibia continue to indicate CAA and β-lactam antibiotics among the most used medicines [32,49,62]. We also found that phenoxyethylpenicillin, an ATC J01C antibiotic, is indicated for several infections despite its narrow spectrum against GAȕHS that causes tonsillitis and pharyngitis. Studies conducted in Greece [67,68] , Libya [69] , Egypt [69] and Nigeria [70-72] report rates of penicillin use between 15.5 % - 54% with amoxicillin, co-Amoxiclav®, ampicillin and cloxacillin the most used penicillins. Macrolides use is estimated at14.5 %, which includes the use of azithromycin, erythromycin and clarithromycin. The medicine policies in Namibia may be influencing the high use of CAA antibiotics at health facilities as the medicines that are highly used are the medicines with the highest number of indications per antibiotic and used at all levels and all prescribers as well as in prophylactic programmes [Table 1; Figure 1; 6]. The over use of CAA antibiotics due to policy indications may cause selective pressure for antimicrobial resistance, and irrational practices may exacerbate the problem [2,4,6,12]. Sensitivity reports have reported a rising resistance to CAA ranging between 58 – 95.6% [4, 31]. This needs to be addressed to enhance the effectiveness of these important antibiotics. This includes addressing suboptimal adherence to good prescribing practices that have been reported in medicine use surveys in Namibia and addressing poor indicators of good antibiotic prescribing such as number of antibiotics per prescription, which is currently seen as to high in Namibia across all sectors [6,32,33,49].

In addition, three antibiotics (10%) on the essential medicine list have no indications in the treatment guidelines (Figure 1). Two antibiotics contained in treatment guidelines – clarithromycin and dapsone - are not listed on the essential medicines list. The lack of concurrence between the essential medicines list and the treatment guidelines may lead to inappropriate use and limited access of antibiotics. This needs to be resolved.

In Namibia, there are also currently two committees for the essential medicines list and treatment guidelines, which work in parallel. This may lead to policy duplication or omissions, both potentially causing negative consequences on access and therapeutic outcomes [22, 23]. This again needs to be looked at to improve future antibiotic use.

This study found that medicine policies indicate all the CAA antibiotics for use at all levels of health care in Namibia including primary health care (Table 1) for both curative and preventative programmes. In primary health care, cotrimoxazole is indicated for HIV/AIDS related infections and amoxicillin in presumptive prophylaxis in malnutrition. Overall, CAA antibiotics are indicated for use in 75% (9/11) of indications by body systems with the respiratory,
genitourinary and musculoskeletal disorders systems have the most indications for CAA antibiotics. The wide number of indications of CAA antibiotics by level of health care and disease is a risk factor for overuse and the development of AMR [52,56,60,68,73-75], with misuse linked to limited prescriber and diagnostic capacity as well as pressure from patients [43,51,52,54, 61]. In Namibia, with the current human resource issues, nurses are the main prescribers at the lower levels of care, e.g. PHCs, where antibiotic prescribing is mainly empiric. In addition, compliance to STGs is estimated to be between 48 – 75% [23,32,33]. Whilst this appears similar to public health settings studies across countries, this needs to be improved [13,15,43,67,76].

In Lesotho [7] 57.8% of the antibiotics prescriptions did not comply with the National standard treatment guidelines. A study by Shiva et al. [15] reported that 69.6% of the prescribers do not comply with guidelines and formularies on the basis of right antibiotic indication, dose and duration. This may be due to issues of lack of knowledge regarding appropriate antibiotic prescribing with physicians in a recent systematic review requesting educational input to improve their prescribing [43].

Medicine policies and guidelines in Namibia currently indicate the use of CAA antibiotics for most respiratory; urogenital; musculoskeletal and gastrointestinal infections; disease conditions that are highly prevalent at PHCs in Namibia [Table 3; 22-27]. The study by Kunda [37] indicates high use of antibiotics in URTIs of up to 78% in Namibia, which needs to be addressed given the high percentage of URTIs that are viral in origin. Cotrimoxazole is indicated for management of bloody diarrhea. However the NIP antibiogram shows up to 90% resistance levels of most bacteria common in respiratory and urinary tract infections such as S. aureus, S. pneumoniae and E.coli to amoxicillin and cotrimoxazole [47]. Consequently, there is a need to revise the guidelines as well as instigate policies that reduce resistance rates to these effective antibiotics. The latter potentially including extensive educational initiatives including patients.

**Conclusions and recommendations**

Policy indicators for antibiotic use are suboptimal in Namibia and may be an important driver in the current overuse of CAA antibiotics in Namibia. Overall, Namibia currently lacks a comprehensive antibiotic policy and up-to-date guidelines, formulary and antibiograms. This may negatively impact on evidence based empiric therapy at all levels of care, which is a concern given current high resistance rates to CAA antibiotics.

There are also concerns with the lack of coherence between the Nemlist and STGs, with some of the antibiotics listed in the EML having no indications in STGs. Treatment guidelines also currently have a high number of indications per antibiotics for CAA and ATC class J01C antibiotics. This needs to be urgently addressed. Medicine policies in Namibia are an important factor that currently promotes the wide use of CAA antibiotics by level of health care and by disease. Alongside this, current antibiotic indications are not in tandem with NIP resistance reports and may lead to the loss of sensitivity to essential antibiotics such as CAA antibiotics.

Consequently, it is recommended that the authorities in Namibia urgently develop a comprehensive antibiotic policy, including the harmonization of policy documents, to improve
antibiotic use at all levels of health care, particularly at PHCs where human resource capacity is currently a problem. The antibiotic guidelines should be revised to parallel local resistance patterns. As a result, we recommend the development of a compressive antibiotic guideline, based on annual antibiograms, and with agreed quality indicators to improve future antibiotic use. This alongside additional education for all key stakeholder groups, especially PHC personnel, to improve future antibiotic prescribing.

We also believe our methodology of combining an analysis of current policy documents including formularies, antibiotic prescribing behavior and resistance patterns is applicable to other lower and middle income countries as they strive to improve their antibiotic use. We will be monitoring developments in Namibia in the future as part of continuing research activities in this critical area.

Acknowledgements
We acknowledge the MoHSS - Namibia and Management sciences for Health Namibia that made copies for this review available. The authors would also like to acknowledge Prof. T. Rennie the associate Dean of the School of Pharmacy for editing the manuscript prior to submission

Conflict of interest and funding
The authors hereby declare that they have no conflicts of interest to disclose. This study did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sectors for undertaking this research. However, the write up of this publication was in part supported by a VR-Link grant (Vetenskapsrådet) from Swedish Research Council (VR-Link 2013-6710)

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