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Alignment of standard treatment guidelines with medicine use indicators in a limited-resource setting: findings and implications

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Abstract

Background Standard treatment guidelines (STGs) are a critical public health tool for promoting rational use of medicines. No studies have evaluated alignment of STGs with medicine use indicators especially in low and-middle-income countries (LMICs) with disproportionate burden of disease and irrational medicine use.
Objective To determine the level of alignment of Namibia's STGs with WHO medicine use indicators.
Methods A descriptive policy analysis of alignment of Namibia's STGs and WHO medicine use indicators. Thirty-two conditions/diseases prevalent and managed at primary healthcare level were included in the study of alignment of the STGs with two WHO medicine use indicators in terms of average number of medicines/condition (polypharmacy, WHO target <2) and antibiotic prescribing (WHO target <30%) after adjusting for estimated encounters per condition. Data were analyzed using (SPSSv24 software, IBM Corporation, NY) to determine frequencies, percentages and means.
Key findings Of the 32 conditions/diseases studied, 41% had three or more medicines per condition indicated in the STGs. The weighted minimum and maximum average number of medicines/condition/encounter in the STGs were 2.62 and 2.78 respectively. Antibiotics were indicated for 72% (weighted per encounter = 75%) of the 32 conditions. Conditions/diseases of the urogenital system had the highest antibiotics indicated in the STGs (100%); respiratory (80%); ENT (80%); gastrointestinal (33%) before weighting conditions for estimated patient encounters, while ENT conditions had the highest antibiotics (32%) after weighting.
Conclusions Alignment of Namibia STGs and medicine use targets is sub-optimal. The STGs have a high indication of antibiotics and polypharmacy. Misalignment is the main contributor to sub-optimal medicine use indicators with respect to average number of medicines and antibiotics. Countries should review their STGs and align with medicine use indicators to enhance rational medicine use and fight antimicrobial resistance. This article provides guidance for aligning STGs with medicine use indicators.
Keywords antimicrobial resistance; indicators; low-and-middle income countries; medicine use; standard treatment guidelines (STGs)

Introduction

The continued failure of many countries to meet the World Health Organization (WHO) targets for rational medicine use is a public health threat in low- and middle-income as well as developed countries. Yet, rational prescribing is a key step to rational use of medicines, especially antibiotics, to combat antimicrobial resistance (AMR) globally. WHO estimates inappropriate medicine use at 50%,[1] that is 50% of all medicines are prescribed, dispensed or sold inappropriately and that 50% of patients fail to take their medicines correctly, and overprescribing in low- and middle-income countries (LMICs) at 6.1 drugs,[1] with uncritical use of antibiotics contributing to emergence of the global AMR epidemic[2] and wastage of limited resources.[3,4] Irrational medicine use means prescribing medicines that may not be appropriate to the clinical needs of the patients in

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doses that do not meet their own individual requirements or not prescribed for an adequate period of time and or not at the lowest cost to the patients and their communities.[5] Overprescribing refers to prescribing for a patient more than two medicines for a given disease/condition, considering WHO recommendation of <2 medicines.

Several studies in limited-resource settings show the average number of medicines per outpatient prescription (polypharmacy), ranging from 2.2 in Ethiopia, 2.3 in Pakistan, 2.9 in Namibia to a high 5.8 in Nigeria,[6-9] all of which are above the WHO target of <2.[10,11].

The percentage of outpatient prescriptions with an antibiotic has also been reported higher than the WHO target of <30% with studies in LMICs showing elevated antibiotic prescribing from 39.6 to 85% in Sudan, Pakistan, Namibia, South Africa, WHO African region and Ethiopia.[6-8,10-15] Yet antibiotics may not be necessary for some conditions like upper respiratory tract infections which are mainly viral in nature but antibiotic prescribing in these conditions as high as 45% has been reported.[16] This irrational use of medicines is a concern to public health, threat of exacerbating AMR and burdensome in already constrained LMICs.

Standard treatment guidelines (STGs) are a WHO strategy for rational use of medicines (i.e. 'patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community').[1,17-20] STGs guide healthcare workers to rationally and consistently prescribe medicines.

Countries spend significant resources in developing and/or updating STGs, and enforcing health workers' compliance to the STGs. Furthermore, countries spend their limited resources reporting on patient care and health facility performance indicators through health management information systems and pharmacy management information systems (PMIS). PMIS especially is used for monitoring medicines use and health workers' compliance to STGs, for example in Namibia. Feedback reports are generated for use at all levels of health care and policy implementation to improve public health care. Failure to meet targets of the indicators such as rational medicine use (RMU) is often attributed to limited compliance of health workers to STGs, especially in LMICs where implementation of such guidelines is limited by scarce resources for training health workers and routine supportive supervision for mentoring and performance monitoring.

Three medicine use indicators are routinely reported on as measures of polypharmacy (target <2 medicines), antibiotics use (target <30% prescriptions with antibiotics) and prescribing of generic medicines (target 100%).[10-11,15,21] The three indicators are an approximate measure of compliance with STGs. LMICs have strived to implement STGs with hope to improve these indicators; but many especially in Africa have not achieved WHO targets.[15]

Unfortunately, no country has evaluated STGs to determine whether the number of medicines and antibiotics indicated per condition/disease (weighted for estimated patient encounters) are aligned to the globally accepted WHO targets of <2 medicines/prescription and <30% prescriptions with antibiotics. The question is 'can a country meet WHO medicine use indicator targets if health workers prescribe medicines as indicated in the STGs?' Or could STGs be contributing to irrational medicine use? The authors studied alignment of STGs, a medicine use policy guideline, with the WHO medicine use indicators, considering that if STGs are aligned with WHO targets and if prescribers judiciously comply with the STGs, the extent of achievement of WHO targets in practice is likely. If medicines indicated per condition in STGs are already outside the WHO targets, it is unlikely that countries like Namibia implementing the STGs will meet the targets. The rationale of policy guideline (STGs) to practice and expected result is anticipated.

An assessment of effectiveness of STGs on medicine use indicators in Namibia found that implementation of STGs in the period 2012–2015 did not improve the national trends of medicine use indicators overall,[8] this is worrisome. A post-STG assessment reported limited compliance of prescribers to the STGs.[22] But compliance to STGs may not be the only factor for non-achievement of the indicator targets and more needs to be done to improve rational prescribing in public health care.

This study evaluated Namibia's STGs[23] to determine average number of medicines that are indicated for conditions/diseases managed at PHC level and whether antibiotics were indicated for the conditions/diseases. The findings will provide insights for Ministries of Health especially in LMICs to critically review and update their STGs to enhance RMU in public health care. Namibia's STGs are due for updating after 8 years since the first edition was launched in 2011. The findings will be a critical addition to considerations during development/revision of STGs. The study provides a tool that countries can adapt to validate their STGs and align with medicine use indicators. To the WHO, the findings will be useful for reviewing RMU indicator targets to make them realistic for the prevailing conditions and medicine use globally.

Methods

A descriptive policy analysis that evaluated alignment of Namibia's STGs and WHO medicine use indicators for diseases/conditions/diagnosis commonly managed at PHC level. Namibia's Ministry of Health and Social Services (MoHSS) launched the first comprehensive STGs in 2011,[22] intended to serve as the main reference for prescribing and dispensing medicines for common conditions/diseases in Namibia. The STGs are organised in seven sections, which are subdivided into 29 chapters according to diseases/conditions/body systems.

Design and implementation of Namibia's standard treatment guidelines

The study is based on Namibia's comprehensive STGs[23] implemented since 2011. The STGs were developed through extensive consultations at all levels in public and private health care and review of content by consultants.[23] An assessment conducted in 2013 showed that all health facilities had at least a copy of the STGs.[22] This study analyses the medicines indicated in the STGs for respective conditions/diseases. Thirty-two conditions/diseases commonly

encountered at PHC level categorised under five body systems, that is respiratory; ear, nose and throat (ENT); gastrointestinal; oral and dental diseases/disorders; and urogenital system were studied. Studies have reported these conditions/diseases as common in PHC.[24-26] The conditions were included in the study if they are among the most prevalent at PHC facilities in Namibia.

Data collection

Data were retrospectively extracted from Namibia's STGs into a specially structured excel database in September–October 2019. The database captured sections of the STGs, chapters, subsections, condition/disease, level at which the condition/disease is managed, all medicines indicated for that condition/disease captured as medicine1, medicine2 and medicine3 until all listed medicines/indications were captured. Medicines were listed as applicable for management of the condition/disease at PHC level of a clinic, health center or hospital (PHC) and whether the condition/disease was referred to hospital or specialist level of management. Every condition included in the analysis was validated by a team that constituted a pharmacist and physician as to whether management of that condition can be initiated and completed at a PHC facility as per the STG and the Namibia Essential Medicines List (Nemlist).[27] Conditions indicated for management at PHC level or those whose medicines were classified in the Nemlist as available at PHC level were classified as PHC level conditions for this study. Conditions categorised as mild, moderate or severe were captured as such as they had applicable medicines listed. Where indicated for adults and children, these were also captured as separate conditions as they had specific medicines listed. Where more than one treatment option was indicated and for first or second line therapy, these were also captured as conditions to enable listing of the medicines indicated. For the included conditions, duplicates were checked to only include conditions with mild states managed at PHC. Only those conditions for which medicines were indicated were captured from the STGs. Where a condition targeted in this study had cross-reference to another chapter in the STGs, the applicable data were extracted from the referenced chapter.

Additional variables were created for minimum and maximum number of medicines indicated for a condition/disease, whether or not an antibiotic was indicated for the management of that condition/disease. Minimum number of medicines indicated meant the least number of medicines that could be prescribed for that condition/disease if no other ailments were diagnosed. Maximum number of medicines/condition meant the number of medicines that could be prescribed including additional conditions/diseases listed, for example addition of an antibiotic only in case of secondary infection, that is they were conditional additions to the basic medicines indicated for that condition/disease. Only conditions/diseases managed at PHC level were included in this study.

Data analysis

Data were exported from the Excel database and analysed in SPSSv24 to generate frequencies, percentages of the minimum and maximum number of medicines/condition, frequency and percentage of conditions/diseases with antibiotics indicated, and average number of medicines for each category of condition/disease, that is diseases of the respiratory system; ENT; gastrointestinal; oral and dental diseases/disorders; and urogenital system. In order to facilitate comparisons of STGs and WHO medicine use indicators, the average number of medicines and antibiotics per condition were weighted against the expected number of encounters for each of the disease conditions in order to estimate the overall rates (Table 1).[28-32] A study based in Namibia by Niaz *et al*.[33] was used as a benchmark to estimate proportion of prescriptions (patients encounters) with given number of medicines. In Niaz *et al*. study that included 1243 prescriptions, he estimated the encounters with 1 medicine (7.0%), 2 medicines (26.5%), 3 medicines (37.0%), 4 medicines (18.7%), 5 medicines (8.8%), 6 medicines (1.5%) and 7 medicines (0.5%). This was used to weight the average number of medicines per condition indicated in the STG to align it to the actual encounters in practice (unweighted average) in Table 1. The proportions of patient encounters were adjusted based on the occurrence of number of medicines in our study. Thereafter, each disease condition was weighted against prevalence of the disease conditions in PHC after weighting patient encounters to obtain the overall (weighted) average number of medicines per condition.

Ethics

The Human Research Ethics Committee (HREC) of the University of Namibia (UNAM) and the Research and Ethics Board of the MoHSS (26 February 2019) approved this study. The need for informed consent was waived as the study used secondary data and no human subjects were recruited in this study. The study used Namibia's published STGs and other documents accessible to the public. All extracts from the documents have been referenced.

Results

A total of 139 conditions/diseases with medicines indicated in the STGs were captured into the study database. Of these, 65 (47%) conditions/diseases did not have level of management indicated in the STGs. After validation based on the set inclusion/exclusion criteria, 32 (23%) conditions/diseases overall were selected for study (Figure 1, Table 2). The majority of the 32 condition/diseases were of the ENT (31% (n = 10)), gastrointestinal (28% (n = 9)) and urogenital (22% (n = 7)) systems.

Number of medicines indicated in the standard treatment guidelines/condition

Overall, 59% (n = 19) of the 32 conditions/diseases had one or two medicine(s) indicated/condition as the minimum number of medicines while 41% had three or more medicines/condition. Forty-one per cent (n = 13) of the 32 conditions/diseases had a maximum of two medicines/condition listed in the STGs while 59% had three to six medicines/condition indicated (Table 1). The minimum and maximum average number of medicines/condition in the STGs (unweighted) was 2.3 and 2.8

Table 1 A summary of conditions/diseases and medicines indicated in the Namibia Standard Treatment Guidelines of 2011 for management of conditions/diseases at primary healthcare level

STG chapter & description	Respiratory system	Ear, nose & throat system	Gastrointestinal system	Oral & dental diseases & disorders	Urogenital system	Combined
Number of conditions[†]	5	10	9	1	7	32
Minimum number of medicines/condition [n (%weighted by encounters)]						
One (1)	1 (13%)	3 (9%)	2 (8%)	ND	1 (10%)	7 (7%)
Two (2)	3 (51%)	4 (33%)	2 (30%)	1 (100%)	2 (38%)	12 (27%)
Three (3)	ND	2 (47%)	3 (41%)	ND	4 (52%)	9 (38%)
Four (4)	1 (36%)	ND	2 (21%)	ND	ND	3 (19%)
Five (5)	ND	1 (11%)	ND	ND	ND	1 (9%)
Minimum average #medicines/condition in STG	2.2	2.2	2.6	2.0	2.4	2.3
Unweighted average per patient encounter (Minimum average #medicines/condition)	2.59	2.71	2.78	2.0	2.42	2.92
Weighted average per patient encounter (minimum average #medicines/condition)	0.52	1.08	0.55	0.10	0.36	2.62
Maximum number of medicines/condition [# (%weighted by encounters)]						
One (1)	ND	2 (10%)	2 (8%)	ND	1 (8%)	5 (7%)
Two (2)	3 (32%)	2 (37%)	1 (30%)	ND	2 (30%)	8 (27%)
Three (3)	1 (45%)	5 (51%)	3 (41%)	ND	3 (41%)	12 (37%)
Four (4)	1 (23%)	ND	3 (21%)	ND	1 (21%)	4 (19%)
Five (5)	ND	ND	ND	ND	ND	1 (9%)
Six (6)	ND	1 (2%)	ND	1 (100)	ND	2 (1%)
Maximum average #medicines/condition in STG	2.6	2.7	2.8	6.0	2.7	2.8
Unweighted average per patient encounter (Maximum average #medicines/condition)	2.91	2.49	2.75	6.0	2.75	2.99
Weighted average per patient encounter (Maximum average #medicines /condition)	0.52	1.00	0.55	0.30	0.41	2.78
Approximate burden of condition per PHC patient encounter (%)	20[‡]	40[§]	20[¶]	5[††]	15[‡‡]	
Unweighted percent of conditions with antibiotic(s) indicated in Namibia's STGs (%)	80	80	33	100	100	72
Weighted percent of conditions with antibiotic(s) indicated in Namibia's STGs (%)	16	32	7	5	15	75

ND, No data.

[†]A count of conditions managed at primary healthcare level with medicines indicated in Namibia's STGs.

[‡]World Health Organization (2004) 'Respiratory Care in Primary Care Services: a survey in 9 countries', http://whqlibdoc.who.int/hq/2004/WHO_HTM_TB_2004.333.pdf. Accessed on 19/01/2020

[§]Renati, S. and Linder, J. A. (2016) 'Necessity of office visits for acute respiratory infections in primary care', Family Practice, 33(3), pp. 312–317. https://doi.org/10.1093/fampra/cmw019.

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[††]World Health Organization (2018) Fact sheets/Detail/Oral health https://www.who.int/news-room/fact-sheets/detail/oral-health Accessed on 20/01/2020

[‡‡]Vasudevan, R. (2014) 'Urinary Tract Infection: An Overview of the Infection and the Associated Risk Factors', Journal of Microbiology & Experimentation. https://doi.org/10.15406/jmen.2014.01.00008.

(weighted average for estimated patient encounters = 2.62 and 2.78) respectively (Table 1).

Antibiotics indicated for management of common PHC conditions

Majority (75%) of the 32 conditions/diseases had at least one antibiotic indicated for their management at PHC level. Unweighted conditions/diseases of the urogenital system had the highest indication of antibiotics (100%) while condition/diseases of the respiratory, ENT and gastrointestinal systems equally had high antibiotics indicated at 80%, 80% and 33% respectively (Table 1). After weighting the conditions for estimated patient encounters, conditions of the ENT had the highest indication of antibiotics (32%; Figure 2).

Discussion

The study assessed the level alignment of Namibia's Standard Treatment Guidelines with medicine use targets in terms of

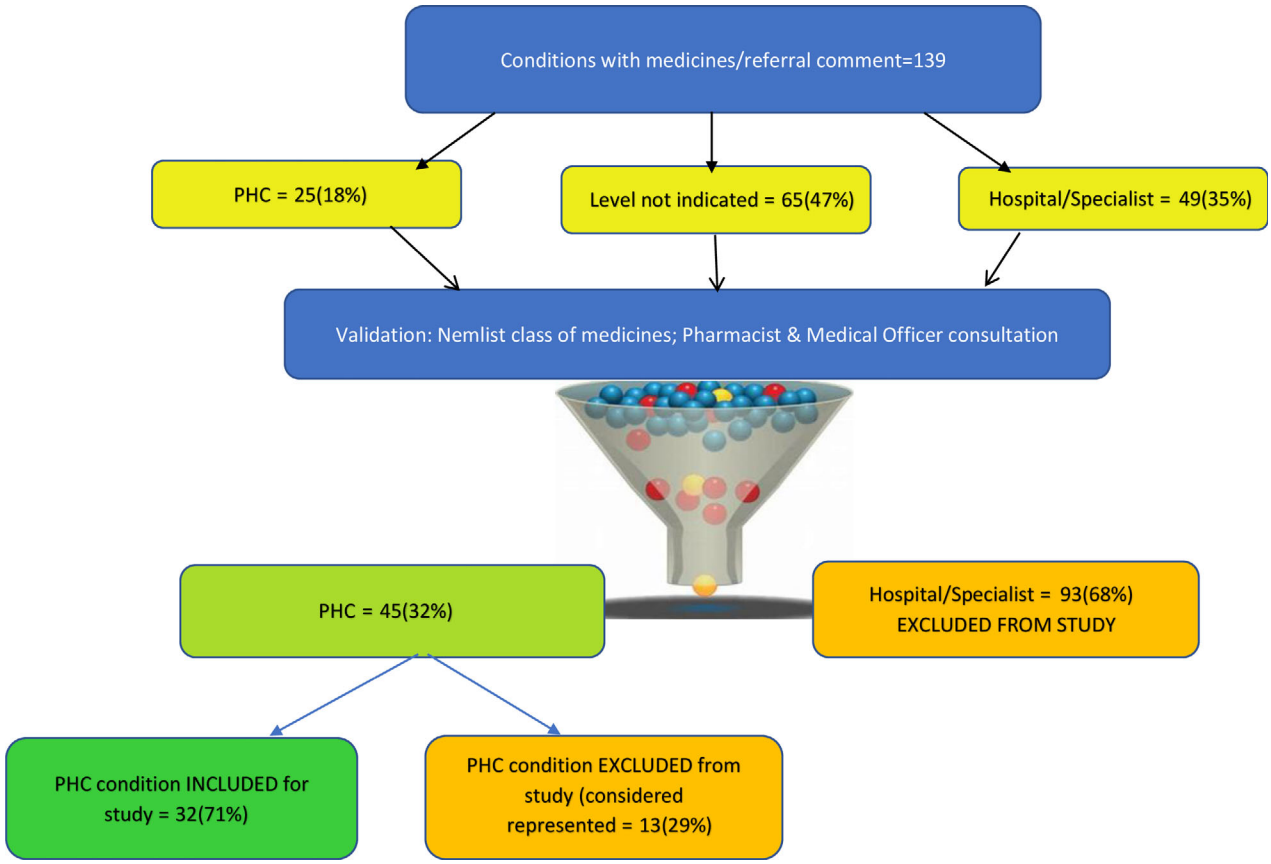

Figure 1 Selection of conditions for study on alignment of Namibia's Standard Treatment Guidelines with Medicine Use Indicators, October 2019.

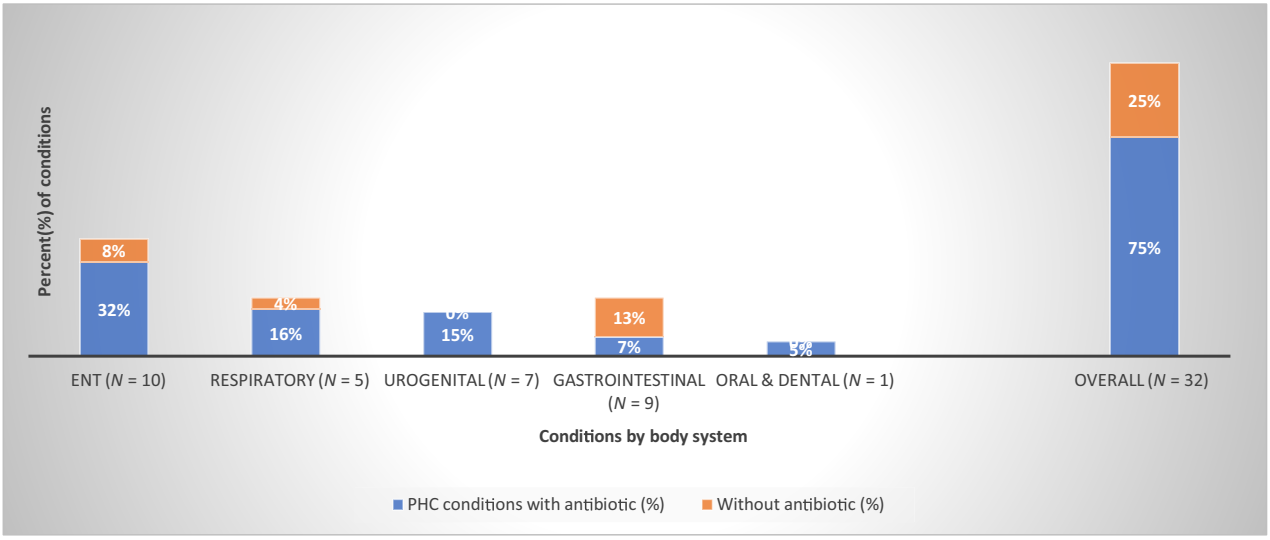

Figure 2 Weighted percentage of common Primary healthcare (PHC) conditions with antibiotic(s) indicated in Namibia's Standard Treatment Guidelines (STGs).

two medicine use indicators: polypharmacy and antibiotic prescribing for the most prevalent conditions/diseases at PHC level. Two assumptions were made in making comparisons between medicine use metrics in the STGs and the WHO targets. First, we assumed the ideal, that is, judicious compliance to the STGs when prescribing at PHC facilities. This was to validate the hypothesis whether the STGs would indeed promote rational medicine use if followed judiciously.

Second, we estimated the average number of medicine and antibiotics per condition/prescription in the STGs after we adjusted based on estimated patient encounters and prevalence of the conditions in PHC (Table 1). This facilitated comparisons based on the same denominator of average number of medicines or antibiotics per encounter.

The study found a minimum and maximum average of 2.3 and 2.8 medicines respectively indicated per condition in Namibia's STGs. After adjusting for the denominator, the minimum and maximum average number of medicines per encounter in the STGs were 2.63 and 2.79 respectively. This is above the WHO and the MoHSS PMIS target of 2 medicines per encounter.[34] Thus, for the 32 most prevalent conditions in PHC, the STGs may inherently promote irrational use of medicines or rather the medicines use targets may require to be adjusted to accurately reflect correct treatment regimens. Moreover, a recent study by Niaz *et al*.[10] suggests poor validity of WHO medicine use indicators, indicating poor specificity and sensitivity. This misalignment between the STGs and WHO medicine use indicators may promote irrational medicine use or indicators with low sensitivity and specificity may misinform decision and efforts to improve medicine use. Nevertheless, unnecessary use of medicines remains high among LMICs with most (>95%) patients receiving medicines.[35-39].

An 8-year review of PMIS medicine use indicators in Namibia found average medicines/outpatient prescription at 2.9.[8] This high rate of polypharmacy may be due to a number of factors, including non-compliance to STGs as well misalignment of STGs and the WHO medicine metrics in cases of high compliance. Prescribers' compliance to STGs was reportedly as low as 26.2% by strict criteria and 55.1% by loose criteria.[22] Limited compliance to STGs has been documented in other LMICs like Lesotho 42.8% and South Africa 45.1%.[40,41] The weighted average number of medicines/condition indicated in the STGs per encounter is similar to 2.9 (range: 2.3–3.1) reported from an 8-year review[8] and MoHSS PMIS quarterly feedback reports in Namibia,[21] and other LMICs like 2.2 and 2.3 in Ethiopia and Sudan.[6,13] Some studies in LMICs have reported even higher average number of medicines/prescription: Botswana 2.8, Namibia 2.98 and 3.14 for adults and children respectively, Pakistan 3.4, Ghana 4.1 and WHO African region 3.1.[11,15,33,42,43] This could be due to various factors, particularly non-compliance as well as misalignment of the STGs and WHO medicine use indicators in these countries, among other factors.

This is a concern given that WHO recommends 2 medicines/encounter. Few medicines imply less pill burden than if more, and sometimes unnecessary medicines, are prescribed per condition/encounter. Less medicines impact on patients' adherence and improve treatment outcomes.[44] Many conditions/diseases have three or more medicines indicated; this should be reviewed and aligned to the WHO target of 2 or rather indicators with a high number of medicines indicated per condition adjusted.

Our study found a high indication of antibiotics in the STGs with 72% of the conditions having an antibiotic and 75% after weighing based on estimated patient encounters. This is more than twice the WHO and MoHSS target of <30%.[10-11,15,34] Moreover, none of the five categories of conditions/diseases studied met the WHO and MoHSS target for both the weighted and unweighted (Figure 2 and Table 1). A high indication of antibiotics for the most prevalent conditions in PHC increases estimates of medicine use indicators or rather the WHO targets may not be valid in certain settings with high prevalence of infectious diseases.[10].

Our findings may partially explain why antibiotic prescribing was found at a high 48.1% and increased by 1.28% antibiotics/prescription/quarter in a Namibian study.[8] Studies in other LMICs have reported equally high antibiotic prescribing in India 45%, Botswana 42.7%, Pakistan 48.9%, Ghana 59.9%, WHO African region 46.8 % and South Africa 68.7%.[11,15,41-43,45] Notably, many countries have implemented STGs but still reported high antibiotic prescribing both in developed and developing countries.[46] Gong *et al*.[47] note that despite improvements in rational medicine use after implementing China's national essential medicines programme, irrational medicine use was still high and called for, among other interventions, review of clinical guidelines which could be one of the underlying causes. An

Table 2 List of the diseases/conditions studied

Body system	Disease/condition
Respiratory	Acute asthma attack, acute bronchitis, pulmonary and extra-pulmonary tuberculosis, pneumocystis jirovecii pneumonia (PCP), community-acquired pneumonia
Ear, nose and throat (ENT)	Otitis externa, acute otitis media – children, furuncle (Boil), nasal and sinus infection: infections of the external nose, common cold (coryza), acute sinusitis, nasal and sinus allergy – mild, epistaxis (nosebleed), acute tonsillitis and pharyngitis (sore throat), acute laryngotracheobronchitis (croup)
Gastrointestinal	Acute abdomen, abdominal Injuries – patient has no signs of acute abdomen or shock, anorectal disorders – constipation, diarrhoea without blood – moderate dehydration, dysentery and diarrhoea with blood and mucous, amoebiasis, gastro-oesophageal reflux disease and oesophagitis – mild to moderate GORD, gastritis and peptic ulcer disease, treatment for eradication of *Helicobacter pylori* – option 2: parasitic GIT infestations
Oral and dental diseases/disorders	Aphthous ulcer
Urogenital	Urethral discharge, genital ulcer disease (ulcers), genital ulcer disease (ulcers) – treatment for partner, vaginal discharge syndrome, lower abdominal pain syndrome, scrotal swelling – no sudden pain, trauma, hydrocele, etc., urinary tract infection (lower UTI) – option 1

Table 3 A checklist for aligning medicines/condition in the Standard Treatment Guidelines with WHO medicine use indicators

Section of STGs	Chapter	Subsection	Condition	Medicine1	Medicine2	Medicine3	Medicine4	Medicine5	Minimum† number of medicines	Maximum‡ number of medicines	Antibiotic(s) indicated Yes/No	Level of healthcare PHC/ Hospital/ Specialist	Remark§ Okay/Review to align with medicine use indicators

STG, standard treatment guidelines.
†A count of the main medicines indicated for management of the listed condition if no other ailments are diagnosed.
‡A count of all medicines that can be prescribed for the listed condition including medicines for additional conditions, for example addition of an antibiotic only in case of secondary infection.
§Remark: The validator will recommend if the medicines indicated are okay and within WHO medicine use indicator targets or recommend further review of medicines for the affected condition. Such review may include critical analysis of quality of evidence for the medicines indicated and where possible reduce number of medicines and or antibiotics for the named conditions

initiative of Medicines Utilization Research in Africa (MURIA) is a great development to stimulate research and act on recommendations for improving rational medicine use.[48].

Many studies focus on implementation of and prescribers' compliance to STGs such as in Kenya, India, Lesotho, Namibia and Botswana.[4,22,40,42,49-51] There is inopportunely little mention of evaluating STGs if they could be contributing to high antibiotic prescribing and polypharmacy. Even WHO recommends auditing prescriptions to determine compliance to antibiotic policy[52] but not highlighting need for alignment of STGs to medicine use indicator targets or revising targets to what is realistic. Yet, a study done in Namibia showed that WHO medicine use indicators were poor predictors of rational medicine prescribing[10].

Irrational medicine use contributes to high cost of health care, bigger burden in LMICs; adverse drug reactions, poor adherence and poor treatment outcomes.[44,51,53] Globally, irrational antibiotic prescribing is contributing to the AMR catastrophe and must be addressed from policy development (treatment guidelines), implementation, monitoring and evaluation to continuous quality improvement. With limited/no surveillance data on AMR and antibiotic consumption globally,[52] validating STGs' alignment to medicine use indicators is critical and urgent. WHO highlights validation of STGs as a key step.[52] The validation can be done through extensive peer review, field testing and critical rating of quality of evidence used for recommended medicines.[20,54] In addition, continuous evaluation of guidelines is key when revising based on clinical failure rates, AMR resistance patterns and compliance with STGs.[nn].

The findings of high antibiotic indication and more than three medicines/condition indicated necessitate validation of STGs as one of the steps in developing/updating to ensure that they are aligned to WHO medicine use indicators. Only then will effective implementation of such updated guidelines impact on rational medicine use.

The findings of this study should be interpreted considering the following limitations. Firstly, the study was based on Namibia's first comprehensive STGs implemented since 2011. Current practice in public health care may be different. Nonetheless, the data were found relevant for study as the STGs edition is still being implemented. The findings are therefore important for development of the second edition. Secondly, the study focused on five of the 29 chapters of the STGs. The chapters were selected based on management of conditions/diseases at PHC level. Thus, it omitted condition/diseases recommended for management at higher and specialist levels, as well as diseases like HIV/AIDS, a big burden whose management then was more at hospital level/designated facilities but currently is decentralised to PHC level. However, many of the opportunistic infections associated with HIV/AIDS are covered in the conditions/diseases that fall within the five body systems covered in this study. Thirdly, this is the first study in a limited-resource setting and possibly globally to assess alignment of STGs with medicine use indicators. The study used the STG metrics in this study as proxy measures of actual medicine use in outpatient departments and weighted number of

medicines with estimated patient encounters and prevalence of conditions to estimate overall average medicines per condition given that the study did not directly assess patient encounters. There was limited literature on the occurrence of the conditions in Namibia, and the prevalences were estimated based on global literature. The study provides evidence for a need to undertake similar studies and also provides a methodology and tool for easy adaptation. Fourthly, the study used the Nemlist 6th edition of 2016 in which some medicines were reclassified yet the study assessed alignment of the STGs 2011. Thus, some medicines indicated for PHC in the STGs may no longer be classified as such. Nonetheless, the extracted data were validated by technical experts to ensure that all conditions/diseases included for the study are accurately classified.

Conclusions and recommendations

There is suboptimal alignment between Namibia's STGs and WHO medicine use metrics in terms of number of medicines and antibiotics per condition/patient encounter. The weighted number of medicines and antibiotics per condition/encounter for common conditions/diseases at PHC level is high. Conditions with more than three medicines each need further review to include only the most efficacious medicines for management of such conditions. Rational prescribing with minimal medicines and antibiotics is critical for lessening pill burden that impacts on adherence and AMR.

The study recommends urgent alignment of STGs with medicine use indicators globally but especially in LMICs which have disproportionate burden of disease and irrational medicine use, yet with limited research to inform clinical and public health interventions. A structured checklist (Table 3) may be adapted to validate and align STGs to WHO medicine use indicators. WHO should consider reviewing targets for indicators of polypharmacy and antibiotic prescribing. It might be necessary to design guidelines for interpreting WHO targets as in some cases the higher number of medicines or antibiotics like in this study might not necessarily imply irrational use of medicines. MURIA should advocate for and support LMICS to review medicine use indicators in relation to the existing STGs, and use findings to inform updating of STGs. MURIA's objective of 'To investigate factors that may influence the appropriate use of medicines' should consider review of STGs to align with medicine use indicators as part of this objective.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors' contributions

KHR, MH, RT conceptualized and appraised the study through various stages. KHR extracted data from the STGs into the study database. KHR and DK validated the data. HRK analyzed data.

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