

Article

Validity of World Health Organisation prescribing indicators in Namibia's primary healthcare: findings and implications

Q. NIAZ¹, B. GODMAN^{2,3,4}, A. MASSELE⁵, S. CAMPBELL^{6,7}, A. KURDI^{3,8}, H.R. KAGOYA⁹, and D. KIBUULE¹

¹Department of Pharmacy Practice and Policy, Faculty of Health Sciences, University of Namibia, Windhoek, Namibia, ²Division of Clinical Pharmacology, Karolinska Institute, Karolinska University Hospital Huddinge, SE-141 86, Stockholm, Sweden, ³Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0RE, United Kingdom, ⁴Department of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Ga-Rankuwa, Pretoria, South Africa, ⁵Department of Biomedical Sciences, Faculty of Medicine, University of Botswana, Gaborone, Botswana, ⁶Centre for Primary Care, Division of Population Health, Health Services Research and Primary Care, University of Manchester, Manchester, M13 9PL, UK, ⁷NIHR Greater Manchester Primary Care Patient Safety Translational Research Centre, Institute of Population Health, University of Manchester, Manchester, M13 9PL, ⁸Department of Pharmacology, College of Pharmacy, Hawler Medical University, Erbil, Iraq, and ⁹Monitoring and Evaluation Unit, Management Sciences for Health, Windhoek-Namibia

Address reprint requests to: Brian Godman, Division of Clinical Pharmacology, Karolinska Institute, Karolinska University Hospital Huddinge, SE-141 86, Stockholm, Sweden. Email: Brian.Godman@ki.se Tel: +46 8 58581068; Fax: +46 8 59581070. Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0RE, UK. E-mail: brian.godman@strath.ac.uk.

Editorial Decision 21 June 2018; Accepted 26 July 2018

Abstract

Objective: World Health Organization/International Network of Rational use of Drugs (WHO/INRUD) indicators are widely used to assess medicine use. However, there is limited evidence on their validity in Namibia's primary health care (PHC) to assess the quality of prescribing. Consequently, our aim was to address this.

Design, setting, participants and interventions: An analytical cross-sectional survey design was used to examine and validate WHO/INRUD indicators in out-patient units of two PHC facilities and one hospital in Namibia from 1 February 2015 to 31 July 2015. The validity of the indicators was determined using two-by-two tables against compliance to the Namibian standard treatment guidelines (NSTG). The receiver operator characteristics for the WHO/INRUD indicators were plotted to determine their accuracy as predictors of compliance to agreed standards. A multivariate logistic model was constructed to independently determine the prediction of each indicator.

Main outcomes and results: Out of 1243 prescriptions; compliance to NSTG prescribing in ambulatory care was sub-optimal (target was >80%). Three of the four WHO/INRUD indicators did not meet Namibian or WHO targets: antibiotic prescribing, average number of medicines per prescription and generic prescribing. The majority of the indicators had low sensitivity and/or specificity. All WHO/INRUD indicators had poor accuracy in predicting rational prescribing. The antibiotic prescribing indicator was the only covariate that was a significant independent risk factor for compliance to NSTGs.

Conclusion: WHO/INRUD indicators showed poor accuracy in assessing prescribing practices in ambulatory care in Namibia. There is need for appropriate models and/or criteria to optimize medicine use in ambulatory care in the future.

Key words: INRUD criteria, Namibia, prescribing indicators, primary healthcare, validity

Introduction

The World Health Organisation (WHO) estimates the global burden of inappropriate prescribing of medicines to be over 50% [1, 2]. This is important especially in low and middle income countries (LMICs) which have the highest burden of non-communicable and infectious diseases. Moreover, the cost of medicines can account for up to 70% of total healthcare costs in LMICs, with a significant proportion out-of-pocket [2–4]. Consequently, it is very important to optimize medicine use in these settings. In Namibia, over 45% of the adult population currently live with hypertension [5], with cardiovascular diseases (CVD) currently accounting for 21% of annual deaths [6]. There are also high rates of infectious disease in Namibia leading at times to excessive and over use of antibiotics [7, 8]. As a result, there is a need for robust systems and indicators to monitor and guide medicine use to enhance appropriate prescribing.

The WHO/International Network for Rational Use of Drugs (WHO/INRUD) prescribing indicator framework was developed as an objective measure for evaluating the appropriateness of medicine use [2, 9, 10]. These indicators are currently seen as proxies for assessing the quality of prescribing as currently no international standards have been empirically developed [2]. This is a concern as these indicators are widely integrated into health management information systems (HMIS) across countries [2, 11, 12], and no indicator directly measures rational prescribing according to the WHO definition [13].

Namibia's public healthcare is based on a primary health care (PHC) system, funded mainly by the government. Currently, the WHO/INRUD indicators are integrated into the Namibian health system at all levels of healthcare [14]. The current prescribing targets and rates for the five key indicators are [2, 9, 14–17]:

- Average number of medicines per encounter—WHO Target; Namibia target <2, acceptable—2.5; currently in Namibia: 1.6–3.1. However, a high number of medicines per prescription may not necessarily mean irrational prescribing as seen in patients with chronic diseases or multimorbidities [9, 18].
- % of encounters with an antibiotic prescribed—WHO Target <30%, Namibia target <25%, acceptable—35%; currently in Namibia: 56–80%. It is difficult to assess whether these targets represent quality prescribing without knowing the presenting infections, which could be viral in origin as typically seen with upper respiratory tract infections (URTIs) [19] or the extent of underlying infectious diseases such as HIV and TB.
- % of encounters with an injection: WHO Target <20%, Namibia target <10%, acceptable—15%; safe medication use in Namibia 44%–50%.
- % of medicines prescribed by International non-proprietary name (INN)—WHO Target 100%, Namibia target—100%, acceptable—80%; currently, in Namibia: 74–80%. However, 100% may be difficult to achieve with substitution discouraged in a small group of medicines including those for epilepsy

[20, 21], and where there are concerns with the quality of generics [22, 23].

- Compliance to Essential Medicine Lists—WHO Target—100%. In Namibia—compliance to Standard Treatment Guidelines currently at 15.4%–44.6% depending on the region; acceptable >80%.

The task to reliably measure the quality of prescribing in PHCs should compare with robust methodologies that have been used in other circumstances to assess the quality of care including the Integrated Management of Childhood Illness (IMCI) project, the Adult Primary Care Assessment Tool (PACT) and the quality indicators that have been developed for antibiotic prescribing [24–29].

Consequently, the aim of this study was to appraise the applicability of current WHO/INRUD prescribing indicators in assessing the quality of prescribing in PHC settings in Namibia. Subsequently, use the findings if pertinent to suggest the development of different indicators to guide future prescribing. This includes compliance to Namibian Standard Treatment Guidelines (NSTG) [30]. The NSTG, which include treatment guidance for patients in both hospital and ambulatory care including community infectious diseases, are seen as appropriate for assessing the quality of prescribing based on the WHO definition of rational medicine use [12]. This is because STGs in LMICs are typically based on the principles of rational use of medicines and adapted from WHO recommendations. We are aware that different treatment guidance documents exist in Namibia, which can give conflicting advice [31]. Adopting the NSTG as the gold standard helps to address such concerns.

Methods

Study design and setting

A cross-sectional design was undertaken to determine the quality of medicine prescribing among public healthcare facilities in Namibia [9]. Prescribing habits of physicians in out-patient departments (OPD), stratified by WHO/INRUD prescribing indicators, were assessed against compliance with current NSTG [30].

The study was conducted in three OPD settings among public health facilities in Khomas region, one of the fourteen regions of Namibia that houses Windhoek, the capital city, with a cosmopolitan population [32]. The health facilities were selected based on the level of healthcare provided, which included a clinic, health center and hospital settings, in line with WHO recommendations [9]. These facilities were purposively selected because of their large and diverse patient populations and, close proximity to each other. In addition, reflective of the situation across Namibia.

Study subjects and procedure

Patients at the OPD units were stratified by the level of care facility to include two PHC facilities—Khomasdal Clinic (KMDC) and Katutura Health Centre (KHC), and one hospital—Intermediate

Hospital Katutura (IHK). The Khomasdal clinic was purposely selected out of the 10 clinics in the Khomas region based on its proximity and demographic and service similarity to KHC and IHK. All patients receiving OPD care at the selected health facilities were included in the study. The sample size of 1243 for patient prescriptions was determined using the Kish Leslie method [33]. This estimation was based on an earlier study where compliance to STGs was 26%, giving a $P = 0.26$ [17]; with β power set at 80%, $\alpha = 0.05$ with a critical value of 1.96 for a two-tailed test.

To evaluate current prescribing practices, we evaluated the most recent prescription in the patients' health passport—that is a prescription written on the day of the study visit that may include more than one medicine. The data collection tool (Annex) was pre-tested among 10 patients at the OPD at IHK, and subsequently refined to improve its robustness. Prescribing data was collected from the patient health passports by the research team led by QN and three trained and experienced data collectors using the standardized data abstraction tool.

Inclusion and exclusion criteria

We included all out-patient prescriptions generated from 1 February 2015 to 31 July 2015. We excluded prescriptions from inpatient settings and specialist OPDs where the medicine use patterns are more complex. We also excluded patients where the diagnosis was not supported by the signs and symptoms recorded in the patient's health passport and those on a follow-up visit or reattendance.

Measurement, analysis, validation and criterion development

The WHO/INRUD prescribing indicators were used as predictors for compliance to the NSTG as the principal outcome measure. We determined the level of compliance and prescribing indicators in the OPD setting. The sensitivity and specificity of each WHO/INRUD prescribing indicator, e.g. the average number of medicines, % prescriptions with antibiotics or injections and % of medicines prescribed by INN, was assessed as predictors for compliance to the NSTG to determine their validity. The association of the other covariates such as the level of health facility, patient demographics, medication prescribed, primary diagnosis and/or comorbidities, were also assessed against the WHO/INRUD prescribing indicators.

Quantitative data analysis was undertaken using SPSS Version 23. The WHO/INRUD prescribing indicators were determined using descriptive statistics of frequencies. The specificity and sensitivity of the prescribing indicators were determined by constructing two-by-two tables for each indicator. A plot of the sensitivity against the (1-specificity) was constructed to generate receiver operator characteristic (ROC) for each prescribing indicator. The area under the curve (AUC) for the ROC was subsequently determined to derive the optimal specificity and sensitivity of the prescribing indicators in determining compliance to the NSTG.

The accuracy of the indicator in predicting compliance to the NSTG was classified according to the AUC point system: 0.90–1 = excellent, 0.80–0.90 = good, 0.70–0.80 = fair; 0.60–0.70 = poor and 0.50–0.59 = fail. An indicator with an AUC value greater than 0.5 does not rely on chance, and can discriminate between prescriptions that are compliant or non-compliant to the NSTG [34]. Consequently, the AUC cut-off was set at 0.6 for a valid prescribing indicator. A level of AUC ≥ 0.6 is considered to be of satisfactory accuracy in evaluating the sensitivity and specificity of the indicator [34].

Compliance to the NSTG was determined using a correctness score sheet derived from a panel incorporating three experts—one clinical pharmacist, one consultant physician and QN from the research team. The association between the prescribing indicators and the compliance level was determined using bivariate analysis with the Chi-squared test. A multivariate logistic regression analysis was used to determine the odds ratios for each prescribing indicator in predicting compliance to NSTG prescribing. A student's t -test and/or ANOVA were used to determine associations between continuous variables. In this study, the level of significance (α) was set at $P = 0.05$ at a 95% confidence interval.

Table 1 Bivariate analysis of factors associated with the compliance to NSTG prescribing

Characteristics	Compliance to NSTG			
	Yes (%)	No (%)	P-value	Cramer-V
Facility level				
Hospital	491 (70.5)	205 (29.5)		
PHC	416 (76.1)	131 (23.9)	0.030*	0.062
Prescriber type				
Medical officer	785 (72.4)	300 (27.6)		
Nurse	112 (77.2)	36 (22.8)	0.198	0.036
Patient gender				
Female	505 (73.1)	186 (26.9)		
Male	402 (72.8)	150 (27.2)	0.919	0.003
Patient age				
Adult (≥ 16 years)	701 (74.6)	239 (25.4)		
Child (<16 years)	206 (68)	97 (32)	0.025*	0.064
Antimicrobial used				
Yes	565 (65.5)	298 (34.5)		
No	342 (90)	38 (10)	0.000*	0.254
Analgesic used				
Yes	512 (72)	199 (28)		
No	395 (74.2)	137 (25.8)	0.380	0.025
Trained on STG				
Yes	291 (72.2)	112 (27.8)		
No	616 (73.3)	224 (26.7)	0.676	0.012
Resp diagnosis				
Yes	226 (70.4)	95 (29.6)		
No	676 (73.8)	240 (26.2)	0.239	0.033
CVS diagnosis				
Yes	17 (81)	4 (19)		
No	890 (72.8)	332 (27.2)	0.406	0.024
GIT diagnosis				
Yes	25 (75.8)	8 (24.2)		
No	882 (72.9)	328 (27.1)	0.712	0.010
Comorbidity				
Yes	106 (75.2)	35 (24.8)		
No	801 (72.7)	301 (27.3)	0.531	0.018
Antibiotic prescribed				
Yes	483 (63.6)	276 (36.4)		
No	424 (87.6)	60 (12.4)	0.000*	0.263
Generic prescribing				
>80%	346 (76)	109 (24)		
<80%	559 (71.1)	227 (28.9)	0.062	0.053
Injection prescribing				
Yes	105 (78.4)	29 (21.6)		
No	802 (72.3)	307 (27.7)	0.137	0.042
# medicine prescribed				
<3 medicines	656 (74.9)	220 (25.1)	0.019*	0.067
>3 medicines	251 (68.4)	116 (31.6)		

Resp = respiratory; CVS = cardiovascular, GIT = gastrointestinal tract; * = ($P < 0.05$)-Statistically significant—Pearson Chi-square Test-.

Ethics

Permission to conduct the research was granted by the University of Namibia (UNAM) and the Ministry of Health and Social Services (MoHSS). Specific patient and prescriber identifiers such as the names and ID numbers were not collected but rather a specific numbering was assigned to each study participant for purposes of identification.

Results

We will first discuss compliance to the NSTG and factors involved before discussing the characteristics of the prescriptions, in line with the principal objectives.

Level of compliance to the NSTG

Overall, out of the 1243 prescriptions (one each from 1243 patients), the majority (73%) complied with the NSTG through the appropriate choice of medicine(s) or treatment for the diagnosis indicated. Compliance to treatment suggestions in the NSTG was significantly higher at PHC facilities (76.1%) than at the hospital (70.5%, $P = 0.03$) (Table 1).

Factors associated with compliance to the NSTG by treatment indication

Compliance with the NSTG was significantly associated ($P < 0.05$) with the health facility level and type ($P = 0.03$), the patients' age

Table 2 Bivariate analysis: validating prescribing indicator against compliance to NSTG

	NSTG Compliant		Totals (%)	P-value	Cramer-V
	Yes (%)	No (%)			
Antibiotic indicator					
Positive (759)	483 (53.3) ^a	276 (82.1)	759 (61.1)	0.000*	0.263
Negative (484)	424 (46.7)	60 (17.9) ^b	484 (38.9)		
Injection indicator					
Positive (759)	105 (11.6) ^a	29 (8.6)	134 (10.8)	0.137	0.042
Negative (484)	802 (88.4%)	307 (91.4) ^b	1109 (89.2)		
Generic indicator					
Positive (759)	346 (38.2) ^a	109 (32.4)	455 (36.7)	0.60	0.053
Negative (484)	559 (61.8%)	227 (67.6) ^b	1109 (63.3)		
Average medicines					
<3 medicines (759)	656 (72.3) ^a	220 (65.5)	876 (70.5)	0.019*	0.067
>3 medicines (484)	251 (27.7)	116 (34.5) ^b	367 (29.5)		

^a = sensitivity; ^b = Specificity; * = significant association— $P < 0.005$.

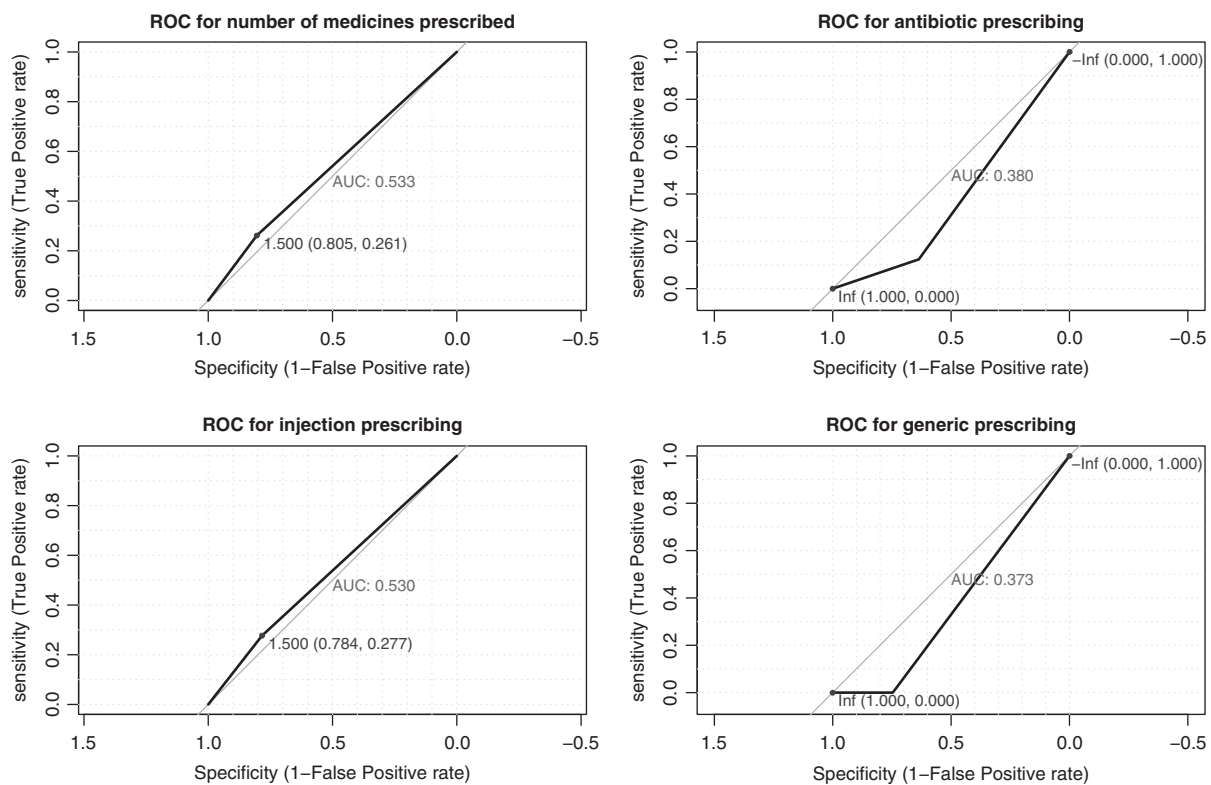


Figure 1. Receiver Operator Characteristics (ROC) curves for prescribing indicators in Namibia.

($P = 0.025$), the prescribing of antimicrobial/antibiotics ($P < 0.001$) and the average number of medicines per prescription ($P = 0.019$) (Table 2). There was no significant association ($P > 0.05$) between compliance to the NSTG and prescriber cadre, patient gender, prescribing by INN and the presence of analgesics or antihistamines on the prescription (Table 1). There was also no association between the level of INN prescribing, the use of injections and prescriber type with compliance to the NSTG (Table 1).

Validity of the prescribing indicators against compliance to the NSTG

The sensitivity rates of the WHO/INRUD indicators ranged from 11.6% to 72.3% (Table 2). The average number of medicines per prescription had an acceptable sensitivity (72.3%, $P = 0.019$). The specificity of the WHO/INRUD indicators ranged from 17.9% to 91.4% (Table 2). The injection prescribing indicator had an acceptable specificity of 91.43% ($P = 0.137$) (Table 2).

ROC for the WHO/INRUD indicators against compliance to NSTG

The ROC test yield failed accuracy for three indicators: Injection prescribing (AUC = 0.49; 95%CI: 0.45–0.52, $P = 0.421$), average number of medicines per prescription (AUC = 0.46; 95%CI: 0.43–0.5, $P = 0.045$), generic prescribing (AUC = 0.51; 95%CI: 0.48–0.55, $P = 0.46$). The antibiotic prescribing indicator had a poor accuracy (AUC = 0.49; 95%CI: 0.61–0.68, $P = 0.001$) (Fig. 1).

Multivariate logistic model for factors associated with compliance to the NSTG

A logistic regression analysis was conducted to predict compliance to the NSTG for 1240 patients based on the health facility level, prescriber cadre category, patient demographics, diagnosis by body system and the category of medication prescribed as predictors (Table 3). Three prescription records were excluded from the logistic regression analysis due to one or more missing characteristics. A test of the full model against a constant only model was statistically significant, indicating that the predictors as a set reliably distinguished between compliance and non-compliance to the NSTG prescribing in the PHCs ($\chi^2 = 147.2$, $P < 0.001$ with $df = 34$). Nagelkerke's R^2 of 0.163 indicated a relationship between prediction and grouping by compliance to NSTGs. Prediction success overall was 73.4% (96.6% for compliance to the NSTG and 11.3% for non-compliance). The Wald criterion demonstrated that only prescribing of an antibiotic and/or antimicrobial ($P < 0.001$) made a significant contribution to the prediction.

The WHO/INRUD indicators including the average number of medicines per prescription, INN prescribing rates and the extent of injection prescribing, were not significant predictors for compliance to the NSTG. In addition, patient's demographics, prescriber cadre category, diagnosis and the health facility level were also not a significant predictor for compliance to the NSTG. One covariate—antibiotic/ antimicrobial prescribing (OR=0.2, 95%CI: 0.20–0.48)—was identified as an independent risk factor for compliance to the NSTG (Table 3). Prescribing of an antibiotic decreases compliance to the NSTG by 80%.

Table 3 Multivariate logistic model for compliance to NSTG prescribing

Covariates	OR (95% CI)	P-value
Facility level		
Hospital	0.7 (0.5, 1.1)	
PHC	1.0	0.114
Prescriber cadre		
Medical	0.7 (0.5, 1.1)	0.127
Nursing	1.0	
Completed STG training		
Yes	1.1 (0.8, 1.6)	0.534
No	1.0	
Patient's gender		
Female	1.1 (0.8, 1.4)	0.677
Male	1.0	
Patient's age (years)		
Adult (≥ 16 years)	0.9 (0.6,1.2)	0.403
Child (< 16 years)	1.0	
Antibiotic prescribed		
Yes	0.2 (0.2,0.48)	0.000*
No	1.0	
Injectable prescribed		
Yes	1.5 (0.9,2.4)	
No	1.0	0.122
Number medicines prescribed		
< 3	1.1 (0.8, 1.4)	0.714
> 3	1.0	
% generic medicines prescribed		
Yes	1.2 (0.9,1.6)	0.309
No	1.0	
Diagnosis by system		
Gastrointestinal	1.2 (0.7,2.0)	0.439
Musculoskeletal	1.5 (0.9,2.5)	0.094
Cardiovascular	0.4 (0.1,1.2)	0.110
Central nervous system	0.7 (0.2,2.3)	0.503
Obstetrics and gynaecology	0.7 (0.2,2.1)	0.478
HEENT	1.5 (0.9,2.4)	0.117
Lower Respiratory Tract	1.5 (0.5,4.8)	0.495
Genital Urinary Tract	1.1 (0.6,2.1)	0.721
Fever	0.9 (0.3,2.3)	0.821
Non specific diagnosis	1.0	
Comorbidity		
Yes	1.3 (0.8,2.0)	0.247
No	1.0	
Treatment prescribed		0.182
Antimicrobial	1.0	
GIT medication	0.6 (0.3, 1.0)	0.053
Decongestants	0.3 (0.1,1.1)	0.069
Antihistamines	0.6 (0.2,1.7)	0.350
Cardiovascular	3.5 (0.9,12.7)	0.063
Psychiatric	2.4 (0.6,9.9)	0.222
Emollients	1.2 (0.2,6.0)	0.821
Non-pharmacotherapy	1.1 (0.5,2.6)	0.845
Endocrine medicines	4.0 (0.4,38.5)	0.226
Rehydration salts	0.6 (0.3,1.2)	0.113
Anti-asthmatic agents	0.6 (0.1,3.8)	0.618
Analgesics/antoinflammatory	1.1 (0.8,1.7)	0.501
Constant	8.1	0.000

Characteristics of patient prescriptions at OPD units

The majority of prescriptions were initiated at the OPD of the hospital (56%; $P < 0.001$), by physicians (87.3%; $P < 0.001$), for females (55.6%; $P < 0.008$) and adults (≥ 18 years—73.4%).

Table 4 shows the bivariate analysis of the WHO/INRUD indicators. The antibiotic prescribing indicator was significantly higher among nurse prescribers, children, prescriptions with an antimicrobial, a respiratory diagnosis and patients with comorbidities. Antibiotic prescribing was lower with a diagnosis of a cardiovascular or gastrointestinal condition. Other areas of interest included INN prescribing associated with the health facility ($P < 0.001$), the type of prescriber ($P = 0.033$), co-medication with an analgesic ($P < 0.001$) and prescriber training on STGs ($P < 0.001$).

WHO/INRUD prescribing indicators at the primary healthcare facilities

Three thousand, seven hundred and fifty-nine medicines were prescribed among the 1243 prescriptions. The average number of medicines per prescription was 3.02 ± 1.14 (IQR = 2–4). This was highest at the hospital level (3.15 ± 1.197) compared to the clinic (2.93 ± 1.142) and health center (2.85 ± 1.017) ($P = 0.004$). 63%

of medicines were prescribed by INN and more than two thirds of the prescriptions included an antibiotic—69% ($P = 0.059$). The percentage of prescriptions with $\geq 80\%$ of medicines prescribed by INN was 36.6% ($n = 382/1241$). Injection prescribing was 10.8% ($n = 134/1243$), highest at the hospital 12.8%.

Discussion

The majority of the prescribing indicators according to the WHO/INRUD criteria were sub-optimal among these facilities in Namibia (Table 4). However, 70% of prescriptions in this study had three or less medicines prescribed, with an average of 3.12 ± 1.14 medicines per prescription. This is similar to other African countries [2]. 3759 medicines (63.9%) were prescribed by INN, which is also similar to other African countries [2] although lower than Ethiopia at 98.7% [35] and Botswana at 79% [36]. This needs to be addressed to avoid patient confusion if different branded generics with different names are dispensed on each occasion, with the drive towards lowering

Table 4 Bivariate analysis of factors associated with the WHO/INRUD indicators

Characteristics	Prescription has an antibiotic prescribed			No. medicines per prescription			Prescription has an Injection			% INN prescribing/ prescription		
	Yes (%)	No (%)	P-value	<3 (%)	>3 (%)	P-value	Yes (%)	No (%)	P-value	$\geq 80\%$	<80%	P-value
Facility level												
Hospital	409 (58.8)	287 (41.2)		456 (65.5)	240 (34.5)		89 (12.8)	607 (87.2)		145 (20.9)	549 (79.1)	
PHC	350 (64)	197 (36)	0.069	420 (76.8)	127 (23.2)	0.000	45 (8.2)	502 (91.8)	0.01	310 (56.7)	237 (43.3)	0.000
Prescriber type												
Medical officer	646 (59.5)	439 (40.5)		764 (70.4)	321 (29.6)		121 (11.2)	964 (88.8)		385 (35.5)	698 (64.5)	
Nurse	113 (71.5)	45 (28.5)	0.004	112 (70.9)	46 (29.1)	0.903	13 (8.2)	145 (91.8)	0.268	70 (44.3)	88 (55.7)	0.033
Patient gender												
Female	424 (61.4)	267 (38.6)		483 (69.9)	208 (30.1)		76 (11)	615 (89)		257 (37.2)	433 (62.8)	
Male	335 (60.7)	217 (39.3)	0.815	393 (71.2)	159 (28.8)	0.618	58 (10.5)	494 (89.5)	0.781	198 (35.9)	353 (64.1)	0.634
Patient age												
Adult (≥ 16 years)	499 (53.1)	441 (46.9)		666 (70.9)	274 (29.1)		119 (12.7)	821 (87.3)		348 (37.1)	591 (62.9)	
Child (<16 years)	260 (85.8)	43 (14.2)	0.000	210 (69.3)	93 (30.7)	0.609	15 (5)	288 (95)	0.000	107 (35.4)	195 (64.6)	0.609
Antimicrobial used												
Yes	753 (87.3)	110 (12.7)		570 (66)	293 (34)		86 (10)	777 (90)		319 (37)	544 (63)	
No	6 (1.6)	374 (98.4)	0.000	306 (80.5)	74 (19.5)	0.000	48 (12.6)	332 (87.4)	0.163	136 (36)	242 (64)	0.740
Analgesic used												
Yes	433 (60.9)	278 (39.1)		540 (75.9)	171 (24.1)		83 (11.7)	628 (88.3)		225 (31.6)	486 (68.4)	
No	326 (61.3)	206 (38.7)	0.895	336 (63.2)	196 (36.8)	0.000	51 (9.6)	481 (90.4)	0.240	230 (43.4)	300 (56.6)	0.000
Trained on STG												
Yes	231 (57.3)	172 (42.7)		251 (62.3)	152 (37.7)		53 (13.2)	350 (86.8)	0.062	87 (21.6)	316 (78.4)	
No	528 (62.9)	312 (37.1)	0.061	625 (74.4)	215 (25.6)	0.000	81 (9.6)	759 (90.4)		368 (43.9)	470 (56.1)	0.000
Resp diagnosis												
Yes	267 (83.2)	54 (16.8)		220 (68.5)	101 (31.5)		21 (6.5)	300 (93.5)		119 (37.1)	202 (62.9)	
No	490 (53.5)	426 (46.5)	0.000	651 (71.1)	265 (28.9)	0.392	113 (12.3)	803 (87.7)	0.004	334 (36.5)	580 (63.5)	0.866
CVS diagnosis												
Yes	2 (9.5)	19 (90.5)		16 (76.2)	5 (23.8)		1 (4.8)	20 (95.2)		6 (28.6)	15 (71.4)	
No	757 (61.9)	465 (38.1)	0.000	876 (70.5)	362 (29.6)	0.563	133 (10.9)	1089 (89.1)	0.370	449 (36.8)	771 (63.2)	0.438
GIT diagnosis												
Yes	14 (42.4)	19 (57.6)		25 (75.8)	8 (24.2)		1 (3)	32 (97)		13 (40.6)	19 (59.4)	
No	745 (61.1)	465 (38.4)	0.026	851 (70.3)	359 (29.5)	0.500	133 (11)	1077 (89)	0.146	442 (36.6)	767 (63.4)	0.638
Comorbidity												
Yes	99 (70.2)	42 (29.8)		70 (49.6)	71 (50.4)		10 (7.1)	131 (92.9)		48 (34)	93 (66)	
No	660 (59.9)	442 (40.1)	0.018	806 (73.1)	296 (26.9)	0.000	124 (11.3)	978 (88.7)	0.134	407 (37)	693 (63)	0.493

* = ($P < 0.05$)—Statistically significant—Pearson Chi-squared Test; INN International non-proprietary name.

Resp, respiratory; CVS, cardiovascular; GIT, gastrointestinal tract.

generic prices through increased competition [20], and patients are unsure whether they are taking the same medicine [37]. There are also concerns with the use of injections especially in hospital (Table 1). This will be investigated further to ensure injections are not given unnecessarily in the future.

Encouragingly, the majority (73%) of prescriptions were compliant to NSTG recommendations (Table 2). This rate is an improvement on a previous study conducted among public facilities in Namibia [17], and compares favourably with a recent study among PHCs in Botswana where there were concerns with antibiotic prescribing [36]. This high compliance rate in Namibia also compares favourably with developing countries where compliance rates to STGs have ranged from 30% to 50% [10, 38]. One possible reason why our study found a higher compliance rate may be due to the fact that we excluded prescriptions where the diagnosis was not supported by the recorded signs and symptoms. Having said this, our compliance rate is lower than the compliance level set at 85% by MSH [39] and there are concerns that antibiotic prescribing remains sub-optimal at most facilities (Table 4). Consequently STG compliance was seen as sub-optimal, although relatively similar across health facilities.

Overall, all the WHO/INRUD indicators had a poor to fail rating with the AUC of the ROC (Fig. 1). In addition, all the indicators showed sub-optimal sensitivity and specificity. This raises doubts about the appropriateness of the current WHO/ INRUD criteria to assess the quality of prescribing in countries with high rates of both infectious and non-infectious diseases such as Namibia and other sub-Saharan African countries. This is because our findings suggest a poor performance or accuracy of the WHO/ INRUD indicators in evaluating appropriate medicine use in ambulatory care in Namibia. A multivariate logistic regression showed that only the antibiotic prescribing indicator independently predicted compliance to the NSTG ($p < 0.001$) (Table 3). These findings, together with the recent findings from PHCs in Botswana [36], are a major concern as the WHO/INRUD indicators are still widely used in Namibia and globally to monitor and report on medicine use.

Consequently, there is a need to review the use of WHO/INRUD indicators in differing levels of care, patient populations, and health sector disease states, and update these building on OMCI, PACT and other projects. This means developing new indicators that more accurately assess the quality of prescribing with their validity and reliability robustly tested using agreed methodologies [40, 41]. Possible indicators surrounding antibiotic use could include target ratios for broad to narrow-spectrum penicillins, cephalosporins and macrolides, as well as target percentage goals for combination penicillins vs. amoxicillin and for the fluorquinolones, as these have all been identified as areas of concern to increase AMR rates and adverse drug reactions [28, 29, 42, 43]. There could also be target BP rates for patients with CVD given current high prevalence rates in Namibia and concerns with adherence [44], as well as HbA1c levels in patients with type 2 diabetes, similar to initiatives in the UK [45, 46]. Prescribing targets could also be established for INN prescribing to further improve rates, with greater education around INN prescribing starting in medical school to again mirror activities in the UK with its high voluntary INN prescribing rate [46]. Potential next steps will include organizing meetings with key stakeholder groups to develop and refine potential indicators using robust methodologies to better assess the quality of prescribing in the future among PHCs in Namibia.

The main limitation of the study was that it was carried out in only one region of Namibia and with a limited number of health

facilities. In addition the study was of a cross-sectional design carried over a 6-month-period, which have their own limitations. However, we believe our findings are robust based on the chosen site and their representational characteristics providing future guidance to improve medicine use in Namibia and wider.

Conclusion

All the four WHO/INRUD indicators had low validity in predicting the quality of prescribing as outlined in the NSTG. In addition, prescribing according to the WHO indicators at health facilities in Namibia were sub-optimal. This needs to be addressed. Any developed indicators have to meaningfully assess the quality of prescribing in Namibia since only the antibiotic prescribing indicator among the WHO/INRUD indicators was an independent covariate for assessing the appropriateness of prescribing based on the NSTG. These are projects for the future.

Supplementary material

Supplementary material is available at *International Journal for Quality in Health Care* online.

Acknowledgements

The authors would like to acknowledge prescribers and pharmacists at the study sites for facilitating the data collection.

Authors contributions

N.Q., H.R.K. and D.K. designed the study and collected data. N.Q., D.K., B.G., S.C. and A.B. analysed the data. N.Q. and D.K. were responsible for the data validation. N.Q. and D.K. wrote the initial draft. B.G., A.M., S.C., A.B., H.R.K. and D.K. refined successive drafts. All the authors approved the final manuscript. B.G. is the guarantor.

References

1. WHO. The World Medicines Situation. 2004. Available at URL: <http://apps.who.int/medicinedocs/en/d/Js6160e/>.
2. Ofori-Asenso R, Brhlikova P, Pollock AM. Prescribing indicators at primary health care centers within the WHO African region: a systematic analysis (1995–2015). *BMC Public Health* 2016;16:724.
3. Ofori-Asenso R, Agyeman AA. Irrational use of medicines—a summary of key concepts. *Pharmacy* 2016;4:35.
4. Cameron A, Ewen M, Ross-Degnan D *et al.* Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet* 2009;373:240–9.
5. Ndishishi A. 'Namibia Demographic and Health Survey 2013.' Namibia Demographic and Health Survey 2013. Windhoek: Ministry of Health and Social Services. Available at URL: <http://catalog.ihns.org/index.php/catalog/5873/study-description>.
6. WHO. Global Health Observatory. Raised blood pressure. 2014. Available at URL: http://www.who.int/gho/ncd/risk_factors/blood_pressure_prevalence_text/en/.
7. Kameera F, Cockran M, Mubita M *et al.* The potential effect of using the Cockcroft–Gault method on Tenofovir-associated renal impairment reports and on clinical decisions regarding Tenofovir use in individual patients: implications for the future. *J Infect Dis Prev Med* 2017;5:170.
8. Nakwatumbah S, Kibuule D, Godman B *et al.* Compliance to guidelines for the prescribing of antibiotics in acute infections at Namibia's national referral hospital: a pilot study and the implications. *Expert Rev Anti Infect Ther* 2017;15:713–21.

9. WHO. How to investigate drug use in health facilities: Selected drug use indicators. Available at URL: <http://apps.who.int/medicinedocs/en/d/Js2289e/>.
10. Holloway KA, Ivanovska V, Wagner AK *et al*. Have we improved use of medicines in developing and transitional countries and do we know how to? Two decades of evidence. *Trop Med Int Health* 2013;18:656–64.
11. Kumar R, Indira K, Rizvi A *et al*. Antibiotic prescribing practices in primary and secondary health care facilities in Uttar Pradesh, India. *J Clin Pharm Ther* 2008;33:625–34.
12. Ogwal-Okeng JW, Obua C, Waako P *et al*. A comparison of prescribing practices between public and private sector physicians in Uganda. *East Afr Med J* 2004;Suppl:S12–6.
13. WHO. The Rational Use of Drugs- Report of the Conference of Experts Nairobi. Available at URL: <http://apps.who.int/medicinedocs/documents/s17054e/s17054e.pdf>
14. MoHSS. National Pharmacy Management Information Systems (PMIS) Feedback report Apr - Sep 2015 National Pharmacy Management Information Systems (PMIS) Feedback report. Windhoek
15. Lates JA, Shiyandja N. Third National Survey on the Use of Drugs in Namibia's Public Health Institutions, Including Monitoring the Implementation of the National Drug Policy. Windhoek: Ministry of Health and Social Services, Namibia. 2001. Available at URL: <http://www.google.co.uk/url?sa=t&crct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKewiHmbv3zvPRAhVLL8AKHdWzCisQFggaMAA&url=http%3A%2F%2Farchives.who.int%2Fficium%2Fficium2004%2Fresources%2Fppt%2FAD022.ppt&usq=AFQjCNFrQn8kAWtrmzGNF9UXTEewUj0TVQ&bvm=bv.146094739,d.d2s>.
16. Kunda M. An investigation of antibiotic prescribing in patients with upper respiratory tract infections (URTIs) at Katutura Health Centre. Windhoek: University of Namibia. 2014. Available at URL: <http://repository.unam.na/handle/11070/843>.
17. Akpabio E, Sagwa E, Mazibuko G *et al*. (2014). Assessment of Compliance of Outpatient Prescribing with the Namibia Standard Treatment Guidelines in Public Sector Health Facilities, (March). Windhoek: MSH-Namibia
18. Osborne CA, Batty GM, Maskrey V *et al*. Development of prescribing indicators for elderly medical inpatients. *Br J Clin Pharmacol* 1997;43:91–7.
19. Dyar OJ, Beovic B, Vlahovic-Palcevski V *et al*. How can we improve antibiotic prescribing in primary care? *Expert Rev Anti Infect Ther* 2016;14:403–13.
20. Godman B, Baker A, Leporowski A *et al*. Initiatives to increase the prescribing of low cost generics; the case of Scotland in the international context. *Med Res Arch* 2017;3:1–36.
21. MHRA UK. Antiepileptic drugs: new advice on switching between different manufacturers' products for a particular drug. Available at URL: <https://www.gov.uk/drug-safety-update/antiepileptic-drugs-new-advice-on-switching-between-different-manufacturers-products-for-a-particular-drug>.
22. Fadare JO, Adeoti AO, Desalu OO *et al*. The prescribing of generic medicines in Nigeria: knowledge, perceptions and attitudes of physicians. *Expert Rev Pharmacoecon Outcomes Res* 2016;16:639–50.
23. Khan B, Godman B, Babar A *et al*. Assessment of active pharmaceutical ingredients in the registration procedures in Pakistan: implications for the future. *GABI J* 2016;5:154–63.
24. Yin J, Wei X, Li H *et al*. Assessing the impact of general practitioner team service on perceived quality of care among patients with non-communicable diseases in China: a natural experimental study. *Int J Qual Health Care* 2016;28:554–60.
25. Mansoor GF, Chikvaizde P, Varkey S *et al*. Quality of child healthcare at primary healthcare facilities: a national assessment of the Integrated Management of Childhood Illnesses in Afghanistan. *Int J Qual Health Care* 2017;29:55–62.
26. Larson E, Vail D, Mbaruku GM *et al*. Beyond utilization: measuring effective coverage of obstetric care along the quality cascade. *Int J Qual Health Care* 2017;29:104–10.
27. Edward A, Dam K, Chege J *et al*. Measuring pediatric quality of care in rural clinics—a multi-country assessment-Cambodia, Guatemala, Zambia and Kenya. *Int J Qual Health Care* 2016;28:586–93.
28. de Bie S, Kaguelidou F, Verhamme KM *et al*. Using Prescription Patterns in Primary Care to Derive New Quality Indicators for Childhood Community Antibiotic Prescribing. *Pediatr Infect Dis J* 2016;35:1317–23.
29. WHO. Antimicrobial Medicines Consumption (AMC) Network. 2017. Available at URL: <http://www.euro.who.int/en/publications/abstracts/antimicrobial-medicines-consumption-amc-network-amc-data-20112014-2017>.
30. MoHSS. *Namibia Standard Treatment Guidelines (NSTG)*. Windhoek, Namibia: Ministry of Health and Social Services, 2012.
31. Kibuule D, Mubita M, Naikaku E *et al*. An analysis of policies for cotrimoxazole, amoxicillin and azithromycin use in Namibia's public sector: findings and therapeutic implications. *Int J Clin Pract* 2017;71.
32. Namibia Statistics Agency. Namibia 2011 Population & Housing Census - Main Report. Windhoek. Available at URL: http://nsa.org.na/microdata1/index.php/catalog/19/related_materials.
33. Kish And Leslie Sample Size Formula. Available at URL: <http://www.pdfdocuments2.com/k/28/kishand-leslie-sample-size-formula.pdf>.
34. Park SH, Goo JM, Jo CH. Receiver operating characteristic (ROC) curve: practical review for radiologists. *Korean J Radiol* 2004;5:11–8.
35. Desalegn AA. Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: a cross-sectional study. *BMC Health Serv Res* 2013;13:170.
36. Mashalla Y, Setlhare V, Masele A *et al*. Assessment of prescribing practices at the primary healthcare facilities in Botswana with an emphasis on antibiotics: findings and implications. *Int J Clin Pract* 2017;71.
37. Olsson E, Wallach-Kildemoes H, Ahmed B *et al*. The influence of generic substitution on the content of patient-pharmacist communication in Swedish community pharmacies. *Int J Pharm Pract* 2017;25:274–81.
38. Ntšekhe M, Hoohlo-Khotle N, Tlali M *et al*. Antibiotic Prescribing Patterns at Six Hospitals in Lesotho. Available at URL: <http://apps.who.int/medicinedocs/en/d/Js21028en/>.
39. Management Sciences for Health. *MDS-3: Managing Access to Medicines and Health Technologies*. Arlington VA: Management Sciences for Health, 2012. <http://apps.who.int/medicinedocs/documents/s19577en/s19577en.pdf>.
40. Campbell SM, Braspenning J, Hutchinson A *et al*. Research methods used in developing and applying quality indicators in primary care. *BMJ* 2003;326:816–19.
41. Campbell SM, Kontopantelis E, Hannon KL *et al*. Framework and indicator testing protocol for developing and piloting quality indicators for the UK Quality and Outcomes Framework. *BMC Fam Pract* 2011;12:85.
42. Coenen S, Ferech M, Haaijer-Ruskamp FM *et al*. European Surveillance of Antimicrobial Consumption (ESAC): quality indicators for outpatient antibiotic use in Europe. *Qual Saf Health Care* 2007;16:440–5.
43. Adriaenssens N, Coenen S, Tonkin-Crine S *et al*. European Surveillance of Antimicrobial Consumption (ESAC): disease-specific quality indicators for outpatient antibiotic prescribing. *BMJ Qual Saf* 2011;20:764–72.
44. Nashilongo MM, Singu B, Kalemeera F *et al*. Assessing adherence to anti-hypertensive therapy in primary health care in Namibia: findings and implications. *Cardiovasc Drugs Ther* 2017;31:565–78.
45. Carey IM, Nightingale CM, DeWilde S *et al*. Blood pressure recording bias during a period when the Quality and Outcomes Framework was introduced. *J Hum Hypertens* 2009;23:764–70.
46. Godman B, Bishop I, Finlayson AE *et al*. Reforms and initiatives in Scotland in recent years to encourage the prescribing of generic drugs, their influence and implications for other countries. *Expert Rev Pharmacoecon Outcomes Res* 2013;13:469–8.