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# QUALITY OF ANTIBIOTICS PRESCRIBED IN SELECTED OUTPATIENTS HEALTHCARE FACILITIES IN PAPUA NEW GUINEA

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*Running title: Antibiotics prescribing in PNG*

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**ABSTRACT:**
The study was conducted to evaluate compliance of antibiotics prescribing in three selected outpatients healthcare facilities in Papua New Guinea (PNG), to the country specific Standard Treatment Guidelines (STG) and to identify factors influencing prescribing pattern. The study was carried out in the Losuia Health Centre (LHC), Alotau Provincial Hospital and Port Moresby General Hospital (PMGH) outpatient departments. The study sample involved 300 participants at each setting. Oral amoxicillin products, chloramphenicol and co-trimoxazole made up approximately 70% of the antibiotics prescribed to 637/1090 of patients. Almost one-quarter (24.4%) of prescriptions for antibiotics were non-compliant selections. At the LHC approximately 20% of both dosage and duration errors occurred. Overall non-compliant prescribing for children was approximately 50% but significantly more compliant at PMGH (P= 0.0058) contrasting with the other settings. At the LHC only 30.6% of antibiotic prescriptions for children were compliant with STG requirements and fulfilled PNG regulatory requirements. With respect to the STGs, Community Health Workers (68.0%) and Nurse Officers made more non-compliant antibiotic selections. High levels of antibiotic prescribing combined with high levels of non-compliant antibiotic prescribing as compared to PNG-STGs, were identified in this study. This is a disturbing finding as it raises many questions related to quality assurance of health care interventions in PNG. The data also raises a clinical concern for the high level of oral chloramphenicol prescribed in out-patient settings.

**Keywords**: Antibiotics, Resistance, Prescribing, Developing Country, Compliance, Standard Treatment Guidelines

## INTRODUCTION:

Globally, antibiotics are one of the most frequently prescribed drug groups and there are reported concerns about the continuous indiscriminate and excessive use of antimicrobial agents including antibiotics, that promote the emergence of resistant organisms [1, 2]. Appropriate antibiotic prescribing is the first step for optimum antibiotic use and has the potential impact of reducing resistant micro-organisms [3]. In Papua New Guinea (PNG), the prescribing of antibiotics is performed by non-medical staff including Community Health Workers (CHWs), Nursing officers (NOs) and Health Extension Officers (HEOs) in health centres and mainly by medically trained staff at district and referral hospitals. Irregularly updated Standard Treatment Guidelines (STGs) have been available to these prescriber groups for decades [4]. In PNG, healthcare is primarily provided by the public sector with limited private facilities available in larger towns. Aid-posts provide basic care and health centres provide out-patient and limited in-patient care. Recently, the World Health Organization (WHO) released a report detailing the prevalence of antimicrobial resistance worldwide [5]. This indicated that antibacterial drugs have been prescribed/ used worldwide for several decades including extensive misuse. In the WHO Western Pacific region which includes Papua New Guinea (PNG), no specific resistance data were reported by the WHO for pathogens in PNG [5].

Resistance to selected antibiotics has been reported in PNG over the past 15 years. For example, Duke in 2000, found high levels of resistance to commonly prescribed antibiotics [6]. The report also indicated that a notable factor causing child mortality in PNG was the severity of sepsis arising from Gram-negative bacteria which were resistant to standard antibiotics [6]. Manning et al. in 2011 reported that for children with acute bacterial meningitis, all of the Haemophilus influenzae isolates were resistant to chloramphenicol [7]. An outbreak of nosocomial infection of Klebsiella pneumonia in hospitalised neonates in PNG showed resistance to cefalosporins which increased from 25% to 73% over 13 months with a patient mortality rate of 40% [8].

A recent study of outpatient antibiotic use in children based on the Integrated Management of Childhood Illness (IMCI) guidelines showed 54% of cases were treated with antibiotics and 40% of these were treated in a manner not compliant with the STGs. In addition, 29% received antibiotics when they were not recommended and 11% did not receive them when they should have [9].

In addition to reported high levels of antibiotic resistance and inappropriate use in PNG, anti-infectives including amoxicillin tablets, although not expired, were found upon laboratory analysis to contain less than their minimum specified active ingredient [10]. Furthermore, when unexpired antibiotic collected from community pharmacies in PNG were analysed, one batch of amoxicillin tablets was sub-standard and another counterfeit [11].

Purchasing and ensuring the ready availability of antibiotics of reliable quality, followed by optimum antibiotic prescribing according to STGs, can reduce the prevalence of resistant micro-organisms generated by excessive use [12]. Inappropriate prescribing of antibiotics has been identified in many health facilities in other developing countries [13-15]. High levels of antibiotic prescribing were also linked to specific health problems. For example, in Bangkok, Thailand, 63% of patients with upper respiratory tract infections were prescribed an antibiotic. Although patients were more likely to be prescribed antibiotics for bacterial conditions, 60% of those with likely viral conditions were prescribed antibiotics [16, 17]. In Indonesia, 90% of the 273 cases of fever of unknown origin were prescribed antibiotics, despite antibiotics not being recommended for this diagnosis [18].

This study aimed to evaluate prospectively, compliance of antibiotics prescribing in three selected outpatient healthcare facilities in PNG, to the STGs and to identify factors influencing prescribing quality in these settings.

**METHODOLOGY:**

A prospective study was carried out at Losuia Health Centre (LHC), Alotau Provincial Hospital (APH) and Port Moresby General Hospital (PMGH) in PNG. All outpatients with written antibiotic prescription orders including the diagnosis written by the prescriber were obtained from each patient's health book and, where necessary, from patient interviews. The health workers at each setting were informed of the study but not its specific objectives. The study was approved by the Human Research Ethics Committee of Curtin University (PH-10-2010), the Milne Bay Province Medical Research Advisory Committee for LHC and APH and the PMGH Executive Committee for PMGH. Only patients who gave consent to participate in the study were included.

At LHC, the interviews were undertaken by a CHW who spoke to the patients using their local dialect and the researcher recorded the answers. At APH, the interview was undertaken by the researcher with assistance from the pharmacist and pharmacy technician. At PMGH, patient interviews were carried out at the hospital pharmacy when patients came to collect their medicines. The interview was undertaken by the researcher with assistance from the pharmacists and pharmacy technicians.

Data recording:

A data recording sheet was developed and used to collect data for each antibiotic prescribed in the health facilities. The data recording sheet collected the participant's prescription details and included: patient's date of birth/age, weight, gender, and date attending clinic, name of healthcare location, current diagnosis, all current medicines prescribed (name, dose, frequency, duration, total number supplied), prescriber category, injections given including total number supplied. The quantity and antibiotic supplied and the prescriber level restrictions were recorded. Data on current and relevant previous diagnoses and medications prescribed were recorded from a health booklet which was kept by each patient. A participant of thirteen (13) years or less was classified as a child.

The Pidgin-English language is the language widely spoken in PNG and was used for oral communication throughout the study while English was used as appropriate.

At LHC, patients were referred to see either a NO, or a CHW. The complicated cases were referred to the HEO. If the case was serious, the patient was referred to APH for further investigation. This hospital was not easily accessible as it involved 10-12 hours of travel by boat or 30 minutes by air subject to scheduling and funds. Either service was only available approximately once a week. At APH and PMGH, patients were referred to see either a NO, HEO or Medical Officer (MO). The complicated cases were referred to the Specialist Medical Officer (SMO) or the Senior Specialist Medical Officer (SSMO). The diagnosis and prescribed medicines were written into the patient's health book by the prescriber, which the patient kept. The patient then proceeded to the Pharmacy for the supply of medicines. After receiving their medicines, the patient was then asked to see the researcher where consent was sought.

Selection of subjects:

The study sites were chosen for convenience to appropriately represent the tiered levels of health care delivery in PNG. Consecutive outpatients seeking medicines during the two-week study period at each site were screened and if eligible, were invited to participate in the study. Subjects were deemed eligible provided they carried with them their health book and consented to participate in the study. However, eligible subjects were excluded if they were too ill to be interviewed, could not communicate or there was insufficient time for the consultation. In the case of children, their parent or guardian was interviewed.

Analysis of data:

Compliance of each antibiotic prescription with the relevant PNG STGs current at the time of the study was assessed. The STGs consisted of the Manual of Family Planning for Doctors, HEOs and Nurses in PNG [20]; Standard Management of Sexually Transmitted Infections and Genital Conditions [21]; Standard Treatment Guidelines for Children in PNG [22]; and, Standard Treatment for Common Illnesses of Adults in PNG [23]. The criteria were based on the antibiotic selection, dosage, frequency and duration as specified in the STGs in respect to the diagnosis written by the prescriber. Furthermore, "Overall compliance" was defined as compliance with the previous four criteria plus the category of the prescription item complying with legislative prescriber level restrictions for non-medical prescribers as defined in the Medical and Dental Catalogue (MDC) [24] and for the quantity of each antibiotic dispensed (issued to the patient or guardian). The diagnosis used was that recorded by the prescriber in the patient's health book which was viewed at the time of the interview. The antibiotic prescribed and the number dispensed were checked against the prescribed duration stated in the STGs.

Allocation of prescribing compliance was made by the researcher where no doubt existed and this was reviewed by two experts. Where doubt regarding the allocation occurred, a consensus decision was made by the researcher and the two independent experts. Where the antibiotic selected was deemed inappropriate with the STGs, dosage, frequency and duration were not determined. Data from the recording sheets were entered into an Excel® spread sheet. Prescribed antibiotics were classified according to the ATC codes [25]. Disease states were classified according to the diseases stated in the STGs with reference to the Australian Medicines Handbook [26].

Simple descriptive statistics were used to summarise the data with respect to prescribing patterns, and the numbers and proportions of prescriptions which were classified as compliant within each age group and setting. A Generalised Estimating Equation (GEE) was used to identify any significant differences in compliance between the different compliance criteria, and between settings and age-groups. This particular model was used instead of the logistic regression model, because it took into account the correlations between observations on the same participant. Results of the analysis are reported similarly to a logistic regression, with odds ratios relative to some reference category, their 95% confidence intervals, and p-values. Analyses were performed using the statistical software program SAS version 9.2 (SAS Institute Inc, Cary, USA, 2008), and a p-value<0.05 was taken to indicate a statistically significant association in all tests.

**RESULTS**:

The data reported in this paper have been derived from a separate and expanded analysis of overall prescribing investigated at the three out-patient locations [19]. Antibiotics included in this study were: antibacterials (penicillins, other antibacterials, cefalosporins and other reserved antibiotics) listed in the MDC [24] with reference to the Australian Medicines Handbook [26] and excluding antituberculosis, antileprosy drugs, antifungals, antivirals, antiretrovirals, antiprotozoals, antimalarials and anthelmintics. The scope was also informed from the WHO ATC lists of antibiotics [25]. The overall prescribing parameters for antibiotics at the three locations, relative to overall prescribing, are summarised in Table 1.

Table 1 Antibiotic prescription data according to patient, drug and age group at each outpatient location and their proportion of all drug prescribing; P-values are obtained from Chi-square tests, unless otherwise specified.

| Variable | Subgroup | LHC (%) N=356 | APH (%) N=318 | PMGH (%) N=416 | Total N =1090 | P-value |
|---|---|---|---|---|---|---|
| Antibiotics prescribed(patient based) | | 219/356 (61.5) | 185/318 (58.2) | 233/416 (56.0) | 637/1090 (58.4) | 0.2999 |
| Antibiotics prescribed (drug based) | | 279/828 (33.7) | 202/696 (29.0) | 278/971 (28.6) | 759/2495 (30.4) | 0.0496* |
| Antibiotic injections+ (patient based) | | 42/219 (19.2) | 5/185 (2.7) | 11/233 (4.7) | 58/637 (9.1) | <0.0001 |
| Gender (frequency of antibiotic prescribing) | Female | 106/192 (55.2) | 89/178 (50.0) | 112/202 (55.4) | 307/572 (53.7) | 0.4958 |
| | Male | 113/164 (68.9) | 96/140 (68.6) | 121/214 (56.5) | 330/518 (63.7) | 0.0174 |
| Age group (frequency of antibiotic prescribing) | Adult | 120/216 (55.6) | 103/212 (48.6) | 164/320 (51.2) | 387/748 (51.7) | 0.3438 |
| | Child | 99/139 (71.2) | 82/106 (77.4) | 69/96 (71.9) | 250/341 (73.3) | 0.5224 |

*p-value calculated using a GEE model. +Based on numbers of patients prescribed antibiotics
The p-values compare the distributions of these demographic variables across locations. Age group was missing for one record at LHC

The proportions of females who were prescribed antibiotics were similar across locations, but it appeared that a smaller proportion of males at PMGH received them compared to the other sites. Overall, a significantly greater proportion of males received antibiotics compared to females (330/578 [63.7%] vs 307/572 [53.7%]; p=0.0008). While there was no significant difference across sites in the prescriptions for adults or children separately, it appeared that, overall, a significantly higher proportion of children received antibiotics than adults (250/341 [73.3%] v 387/748 [51.7%]; p<0.0001).

Over 70% of children were prescribed an antibiotic at each consultation. Approximately 10% of all antibiotic prescriptions included more than one antibiotic. Patients not prescribed any drugs were not included in the study.

Table 2 Disease classifications for patients prescribed antibiotics

| Diseases^ | Frequency* | (%) |
|---|---|---|
| 15.4 Acute soft tissue injuries | 126 | 16.30 |
| 5.5 Malaria | 116 | 15.00 |
| 19Asthma, COPD | 110 | 14.23 |
| 19.5Cough | 75 | 9.70 |
| 5.1 Bacterial infections | 38 | 4.92 |
| 12.1 Dyspepsia, reflux & peptic ulcers | 38 | 4.92 |
| 19.1 Bronchiolitis | 38 | 4.92 |
| Others | 232 | 30.01 |
| Total | 773 | 100.00 |

*Subjects may have more than one diagnosis; ^Disease classifications based on the STGs with reference to the Australian Medicines Handbook classification [26]

The most common disease classifications for patients who were prescribed antibiotics at all locations are reported in Table 2. Possibly, owing to a lack of resources for health care staff to be able to differentiate the cause of a fever, or because patients were living in remote areas where antimalarials and antibiotics were prescribed together on many occasions. The match between the diagnosis and antibiotic prescribing varied widely with location. For example, at APH every upper respiratory tract infection diagnosis was prescribed amoxicillin, at PMGH scabies treatment included oral antibiotics and simple cough/fever was routinely managed with antibiotics.

Most prescribed antibiotics during the period of this study were amoxicillin oral products, followed by chloramphenicol, which was consistently prescribed at all locations (Table 3). Notably, three antibiotics made up approximately 70% of all antibiotics prescribed. Most antibiotics were for oral administration, with some antibiotic injections especially at LHC; very few antibiotic ear or eye drops or ointments were prescribed. The compliance of antibiotic prescribing overall and at each location is reported in Table 4 based upon each prescribing parameter assessed.

Table 3 Number of antibiotic items grouped according to antibiotic class prescribed at each location

| Antibiotics | LHC (%) | APH (%) | PMGH (%) | Total (%) | P-value |
|---|---|---|---|---|---|
| Amoxicillin products | 104 (37.3) | 104 (51.5) | 147 (52.9) | 355 (46.8) | <0.0001 |
| Chloramphenicol | 40 (14.3) | 25 (12.4) | 30 (10.8) | 95 (12.5) | |
| Co-trimoxazole | 49 (17.6) | 24 (11.9) | 22 (7.9) | 95 (12.5) | |
| Metronidazole | 32 (11.5) | 11 (5.5) | 17 (6.1) | 60 (7.9) | |
| Penicillin | 35 (12.5) | 7 (3.5) | 11 (4.0) | 53 (7.0) | |
| Cloxacillin | 8 (2.9) | 18 (8.9) | 23 (8.3) | 49 (6.5) | |
| Doxycycline | 5 (1.8) | 2 (1.0) | 9 (3.2) | 16 (2.1) | |
| Erythromycin | 1 (0.4) | 7 (3.5) | 6 (2.2) | 14 (1.8) | |
| Others | 5 (1.8) | 4 (2.0) | 13 (4.8) | 22 (2.8) | |
| Total | 279 (36.8) | 202 (26.6) | 278 (36.6) | 759 (100.0) | |

Table 4: Compliance of prescribed antibiotics at Alotau Provincial Hospital (APH) Losuia Health Centre (LHC) and Port Moresby General Hospital (PMGH) including each indicator assessed and relevant interactions

| Variable | Compliant n/N (%) | Odds Ratio | 95% CI | p-value |
|---|---|---|---|---|
| (A) Compliance | | | | |
| Dosage | 516/574 (89.9) | 17.20 | 7.51 - 39.38 | <0.0001 |
| Duration | 521/574 (90.8) | 13.46 | 6.25 - 28.98 | <0.0001 |
| Selection | 574/759 (75.6) | 1 | | |
| Dosage APH | 131/136 (96.3) | 0.43 | 0.15 - 1.27 | 0.1261 |
| Dosage LHC | 185/235 (78.7) | 0.07 | 0.03 - 0.18 | <0.0001 |

| | | | | |
|---|---|---|---|---|
| Dosage PMGH | 200/203 (98.5) | 1 | | |
| Duration APH | 130/136 (95.6) | 0.47 | 0.17 - 1.25 | 0.1296 |
| Duration LHC | 192/235 (81.7) | 0.11 | 0.05 - 0.25 | <0.0001 |
| Duration PMGH | 199/203 (98.0) | 1 | | |
| Selection APH | 136/202 (67.3) | 0.77 | 0.51 - 1.16 | 0.2068 |
| Selection LHC | 235/279 (84.2) | 1.98 | 1.27 - 3.09 | 0.0028 |
| Selection PMGH | 203/278 (73.0) | 1 | | |
| (B) Compliant Selection | | | | |
| Location | | | | |
| APH | 136/202 (67.3) | 0.21 | 0.09 - 0.48 | 0.0002 |
| LHC | 235/279 (84.2) | 1.08 | 0.43 - 2.72 | 0.8664 |
| PMGH | 203/278 (73.0) | 1 | | |
| Location & Age | | | | |
| APH Adult | 82/115 (71.3) | 1.56 | 0.84 - 2.90 | 0.1563 |
| APH Child | 54/87 (62.1) | 1 | | |
| LHC Adult | 128/158 (81.0) | 0.48 | 0.23 - 1.01 | 0.0535 |
| LHC Child | 107/121 (88.4) | 1 | | |
| PMGH Adult | 135/201 (67.2) | 0.25 | 0.12 - 0.53 | 0.0003 |
| PMGH Child | 68/77 (88.3) | 1 | | |
| (C) Compliant Dosage | | | | |
| Location | | | | |
| APH | 131/136 (96.3) | 0.44 | 0.10 - 1.92 | 0.2737 |
| LHC | 185/235 (78.7) | 0.06 | 0.02 - 0.20 | <0.0001 |
| PMGH | 200/203 (98.5) | 1 | | |
| Age group | | | | |
| Adult | 335/345 (97.1) | 8.68 | 4.17 - 18.04 | <0.0001 |
| Child | 181/229 (79.0) | 1 | | |
| (D) Compliant Duration | | | | |
| Location | | | | |
| APH | 130/136 (95.6) | 0.43 | 0.12 - 1.56 | 0.1973 |
| LHC | 192/235 (81.7) | 0.09 | 0.03 - 0.26 | <0.0001 |
| PMGH | 199/203 (98.0) | 1 | | |
| Age group | | | | |
| Adult | 314/345 (91.0) | 0.87 | 0.47 - 1.63 | 0.6627 |
| Child | 207/229 (90.4) | 1 | | |
| (E) Compliant on all criteria concurrently | | | | |
| Location | | | | |
| APH | 125/202 (61.9) | 0.27 | 0.13 - 0.55 | 0.0003 |
| LHC | 155/279 (55.6) | 0.21 | 0.10 - 0.40 | <0.0001 |
| PMGH | 195/278 (70.1) | 1 | | |
| Location & Age | | | | |
| APH Adult | 77/115 (67.0) | 1.68 | 0.92 - 3.05 | 0.0894 |
| APH Child | 48/87 (55.2) | 1 | | |
| LHC Adult | 98/158 (62.0) | 1.66 | 1.01 - 2.75 | 0.0470 |
| LHC Child | 57/121 (47.1) | 1 | | |
| PMGH Adult | 132/201 (65.7) | 0.40 | 0.21 - 0.77 | 0.0058 |
| PMGH Child | 63/77 (81.8) | 1 | | |
| (F) Compliant on all criteria, plus satisfying prescriber rules | | | | |
| Location | | | | |
| APH | 116/202 (57.4) | 0.36 | 0.18 - 0.70 | 0.0029 |
| LHC | 109/279 (39.1) | 0.16 | 0.08 - 0.30 | <0.0001 |
| PMGH | 175/278 (63.0) | 1 | | |
| Location & Age | | | | |
| APH Adult | 72/115 (62.6) | 1.66 | 0.92 - 2.99 | 0.0941 |

| | | | | |
|---|---|---|---|---|
| APH Child | 44/87 (50.6) | 1 | | |
| LHC Adult | 72/158 (45.6) | 1.67 | 0.98 - 2.83 | 0.0584 |
| LHC Child | 37/121 (30.6) | 1 | | |
| PMGH Adult | 118/201 (58.7) | 0.48 | 0.27 - 0.88 | 0.0180 |
| PMGH Child | 57/77 (74.0) | 1 | | |

The frequency of administration was also assessed but the data were not included in Table 4 since overall 98.6 % of prescription items had a compliant frequency, the lowest being 97.0% at LHC.

Overall almost one quarter of antibiotic prescription items were non-compliant to antibiotic selections (Table 4A). These included 44 (23.8%) when no antibiotics should have been selected for the diagnosis and 46 (24.6%) where a specific antibiotic was indicated in the guidelines but a different one was selected. It is notable that prescribing of compliant dosages and durations were significantly better than antibiotic selections. Considering the interaction of location with these parameters (Table 4A), using PMGH as the reference, LHC had significantly more compliant selections. LHC data highlighted different prescribing issues with significantly lower compliant dosages and durations of treatment, when compared with PMGH. The analysis in section (A) of Table 4 is based on 1907 records (one record for each type of compliance: (759+574+574) while the other sections of the table are based on either 759 records or the 574 records where drug selection was compliant.

It is noted that, when selection ("Compliant Selection" Table 4B) is based on the 759 antibiotic prescription records, and after adjustment for age-group, APH stands out as significantly less compliant (P = 0.002) compared to LHC and PMGH. After adjustment for differences in compliant selections between location, compliant selections for children were significantly higher (p = 0.0003) than for adults at PMGH. With respect to compliant dosage (Table 4C) overall adults received significantly (8.68 fold; P < 0.0001) more compliant dosing and LHC was significantly less compliant P < 0.0001) than PMGH. APH was not significantly different from PMGH with regard to dosing (96.3% compliant vs 98.5%). It is notable that, after adjustment for differences between settings, dosages for children were significantly less compliant than for adults (p < 0.0001).

In terms of compliant duration times of antibiotic treatments (Table 4D) it is evident that LHC prescribed significantly less compliant antibiotic durations than the other settings, however overall durations for adults and children were similar.

When considering compliance when all three criteria were combined (Table 4E), so that non-compliance on any one (or more) criteria rendered prescribing of the antibiotic non-compliant, both APH (P = 0.0003) and LHC (P < 0.0001) performed significantly poorer than PMGH in overall prescribing compliance. It is notable that only 155/279 of antibiotics prescribed at LHC were compliant overall. Evaluating the interaction of setting and age identified that only 57/121 of antibiotic prescriptions for children at LHC were compliant. There was an interaction between location and age-group where antibiotic prescribing for children was significantly more compliant than for adults at PMGH whereas the opposite appeared to be true at LHC and no significant difference in age groups occurred at APH.

The non-compliance of antibiotic prescribing when additional factors (prescriber level restrictions and number dispensed) were assessed at each location is also shown in Table 4F. These other factors were whether the non-medical prescriber was authorised to prescribe particular medicines according to the prescriber restrictions defined in the MDC [24], and whether the antibiotic and/or quantity dispensed were correct. This latter criterion included no supply (stock not available), or an undersupply or oversupply according to the dosage and duration prescribed; including these regulatory requirements identified, only 109/279 of antibiotics prescribed at LHC met all STG prescribing and PNG regulatory requirements. When based on PMGH it performed 6.25 times more poorly in meeting these requirements. It is notable that the interaction of setting and age found only 37/121 of antibiotic prescriptions at LHC met all STG and PNG regulatory requirements. It is also evident that PMGH provided significantly more compliant antibiotic prescriptions for children than LHC (P < 0.001) or at APH (P= 0.0029).

Data in Table 5 shows the level of compliant prescribing with respect to prescriber category. Medically qualified prescribers made more non-compliant drug selections with respect to the STGs but their dosages, frequencies and treatment durations closely followed the STGs. Non-medical prescribers made more non-compliant drug dosage and duration errors.

Table 5: Overall compliance of prescribing antibiotics by prescriber category. P-value from Chi-square

| Prescribers | Non-compliant (%) | Compliant (%) | Total (%) | P-value |
|---|---|---|---|---|
| CHW | 53 (68.0) | 25 (32.0) | 78 (10.3) | <0.0001 |
| DT/RDO/DO | 1 (7.7) | 12 (92.3) | 13 (1.7) | |
| RHEO/HEO | 61 (49.6) | 62 (50.4) | 123 (16.2) | |
| RMO/MO/SMO | 154 (39.3) | 238 (60.7) | 392 (51.6) | |
| NO | 85 (55.6) | 68 (44.4) | 153 (20.2) | |
| Total | 354 (46.6) | 405 (53.4) | 759 (100.0) | |

Legend: Inapp = Inappropriate; App = Appropriate; CHW = Community Health Worker; DT = Dental Therapist; RDO = Resident Dental Officer; DO = Dental Officer; NO = Nursing Officer; RHEO = Resident Health Extension Officer; HEO = Health Extension Officer; RMO = Resident Medical Officer; MO = Medical Officer; SMO = Senior/Specialist Medical Officer

**DISCUSSION:**

This study reports specific data in PNG on the compliance of antibiotic prescribing for adults and children from outpatient healthcare facilities, related to official health department guidelines. High levels of non-compliant prescribing occurred with all prescriber groups with the exception of dentists (but they were responsible for very few prescriptions). Most prescribing was performed by nurse officers and medical doctors. Overall in this study, 58.4% (637/1090) of patients who were prescribed drugs received an antibiotic independent of location. This percentage is higher than the 54% reported in a cohort of children outpatients in a recent PNG study [9]. It is also higher than the WHO/INRUD prescribing indicators, which from the period 1982-2006 was just below 50% [27]. Prescribed antibiotics constituted 759/2495 of all drugs prescribed over all the studied locations. Although the prescribing of antibiotics in this study was high, it was also noted that at LHC, there were overall few patients diagnosed with chronic diseases. The diagnoses were usually for acute conditions. However, many more patients with chronic diseases were included in the total cohort at PMGH with only a small non-significant decrease in antibiotic prescribing. It is possible that high antibiotic prescribing could be influenced by poor accessibility since many families are obligated to walk for several hours, even up to a day, to attend their health care facilities. This makes it difficult for them to easily return for another consultation if their condition deteriorates. It is unknown whether some were prescribed as a precautionary supply since no evidence to support this possibility was available from the patient's health booklet.

Studies in other developing countries have shown similar results. In Yemen [28], antibiotics were prescribed in 51.0% of patient encounters and 23.8% of the total number of prescribed drugs in public hospital outpatients. A higher percentage (65.0%) of antibiotic use was recorded in the health care facilities in Ghana [29]. A pilot study carried out in three health centres in Cambodia, showed that the percentage of antibiotics prescribed ranged from 10.0% to 66.0% [30]. A Jordanian Hospital outpatient department found that the average percentage of prescriptions involving antibiotics was 35.6% from 187,822 prescriptions surveyed [31]. In South Ethiopia, the percentage of encounters in which an antibiotic was prescribed was 58.1% [32]; in Khartoum State (Sudan) 81.3% of prescriptions involved an antibiotic [33], and in India 37% of prescriptions were antibiotics [15].

The leading causes of outpatient visits reported in 2007-2008 in PNG were: malaria, skin diseases, simple cough, pneumonia, diarrhoea, other respiratory diseases, and accidents [34]. Similar findings were evident in this study (Table 2). It is notable that malaria treatment often included antibiotics, which was not in accordance with the STGs. It is notable that upper respiratory tract infections and simple cough almost always resulted in antibiotics being prescribed. Prescribing antibiotics for conditions for which there is no clinical benefit contributes to the development of antibiotic resistance [35, 36].

No determination can be made from the study data as to the appropriateness of the diagnosis or the selection of antibiotic relating to the health condition of the presenting patient. However, prescriber knowledge/consideration whether the patient is suffering the effects of a bacterial infection, the probable micro-organism involved and the sensitivity of the micro-organism to the antibiotic selected is essential, especially in the absence of pathology facilities in many remote health centres in PNG. Amoxicillin products, chloramphenicol and co-trimoxazole made up approximately 70% of all antibiotics prescribed (Table 3). However, antibiotic selection that was STG non-compliant occurred in one quarter of prescriptions, more frequently written by medical doctors. The reasons for this are unknown but could include a lack of prescriber awareness of the current STGs or because prescribers were aware of unpublished resistance data and/or prescribing was based on personal experience of clinical failures from STG listed antibiotic choices.

The high use of chloramphenicol in PNG is a concern. It is usually reserved for severe typhoid/paratyphoid fever where other antibiotics are unsuitable. It may be used in patients allergic to penicillins or cefalosporins in selected cases such as meningitis, brain abscess, or acute epiglottitis and in rickettsial infections where tetracyclines are unsuitable. Its use in PNG was not for these infections. It can however, cause serious adverse reactions. Its use requires ongoing patient monitoring, which would be difficult to perform in most outpatient settings in PNG.

The level of non-compliant prescribing as assessed against official STGs (Table 4) approximates 40%. However, when the PNG prescriber restriction criteria, correctness of the antibiotic dispensed and the quantity supplied were included in the assessment to consider compliance of antibiotic prescribing against official PNG guidelines, the level increased to approximately 50%. This high level of non-compliant prescribing raises concerns about the use or appropriateness of the STGs, the quality of dispensing and raises questions about the capacity of the supply chain management system that relies heavily on the official STGs and Essential Medicines Lists (EMLs) in PNG. Additionally, the poor ability of some non-medical prescriber categories to correctly calculate children's dosages and antibiotic durations is of concern. The reasons for dispensing inaccuracy may depend on antibiotic stock shortages and competency, as well as satisfying patient requests. It is notable there were occasions when the quantity supplied to the patient considerably exceeded that prescribed, as well as others that involved undersupply.

Prescriber factors:

In PNG, apart from medical and dental officers, HEOs, NOs, CHWs, and Dental Therapists are permitted to prescribe defined medicines (including antibiotics) for patients. Therefore, as seen in this study, most of the prescribing of antibiotics at LHC was undertaken by CHWs (33.3%) and NOs (48.0%), while MOs performed most of the prescribing at APH (67.6%) and PMGH (92.3%).

The data in Table 5 showed that 39.3% of prescribing by medical prescribers was non-compliant which was mainly associated with antibiotic selection. Overall, non-medical prescribers showed even higher levels of non-compliant prescribing with respect to STGs.

Further studies need to be undertaken to determine the reasons for this, but Cabana et al. outlined a range of factors that could affect prescribers' compliance with STGs [37]. Some possibilities would be lack of: awareness, familiarity, agreement, self-efficacy, support, and a reminder system.

A study by Stark et al. [38] acknowledged the contributions of nurses in the delivery of health care in rural areas of low-income countries with 50-80% of all healthcare professionals being nurses. Nurses performed roles including prescribing medications for which they may or may not have had adequate training, often in the absence of legislation and regulation [39]. This situation is reflected in PNG where much of the antibiotic prescribing at LHC which is a rural health centre was undertaken by nurses (48.0%). LHC, as is similar to all other regional health centres in PNG, is staffed only by non-medical prescribers.

Antibiotic resistance:

Antibiotic resistance can develop more quickly in scenarios where widespread unsupervised access to antibiotics and lack of compliance with STGs is common [5]. Although emphasis internationally is still being placed on the development of updated STGs, which need to reflect current resistance patterns, it is clear that as found in this study it is the lack of adherence to current STGs that is the underlying issue that also needs to be addressed [40]. This is problematic in PNG where the STGs are not updated for many years. Although we strongly support the development and provision of STGs to prescribers they are only a useful tool for prescribers when they contain up to date information. It would seem that although dire warnings of the end of the usefulness of antibiotics have been issued, the methods (prescriber education and information dissemination) still being proposed in 2013 to solve the problem are the same methods that have consistently failed over the past thirty years [41]. There seems little point in educating prescribers to follow STGs that are out of date and lead to treatment failures.

A recent study of antibiotic use in children in outpatient settings in selected locations in PNG also found high rates of non-compliance with STGs but the rates of return visits for mild pneumonia were similar irrespective of an appropriate or inappropriate antibiotic prescription [9]. This finding needs careful follow-up of patients in several settings to enable patient outcomes to be fully evaluated. These data may also point to the STGs not providing appropriate information.

Limitations:

This study has evaluated the compliance of antibiotic prescribing to official STGs at three sites which represent the main tiers of health care delivery in PNG. We would not consider there would be marked differences at other sites. Data were collected over two week periods but there is no reason to believe these were different from any other period. Drug supplies are delivered every two months and the study was approximately mid-way between deliveries. It is possible that more antibiotic shortages could occur towards the end of a two-month delivery cycle possibly influencing prescribing selections.

## CONCLUSIONS:

These results demonstrate unacceptably high levels of antibiotic prescribing and of non-compliant antibiotic prescribing in selected health care provider settings in PNG. Medical prescribers made more non-compliant antibiotic selections while non-medical prescribers made more non-compliant dosage and duration errors. Overall non-compliant antibiotic prescribing was higher in children than adults mainly because of the inability of some non-medical prescribers to calculate dosages with respect to weight. It is important that interventions are performed to reduce antibiotic prescribing and improve the level of dosage and duration prescribing. This can be achieved when regularly updated STGs are available and are monitored. STGs should include antibiotic selections that have documented defined levels of resistance. Resistance patterns in PNG healthcare settings for current antibiotics should be published on an annual basis. The high level of prescribing of oral chloramphenicol in outpatient settings requires review by clinical microbiologists.

## REFERENCES:


1. Hariharan H, Sharma S, Chikweto A, Matthew V, DeAllie C. Antimicrobial drug resistance as determined by the E-test in Campylobacter jejuni, C. coli, and C. lari isolates from the ceca of broiler and layer chickens in Grenada. Comparative immunology, microbiology and infectious diseases. 2009;32(1):21-8.
2. Krivoy N, Abed El-Ahal W, Bar-Lavie Y, Haddad S. Antibiotic prescription and cost patterns in a general intensive care unit. Pharmacy Practice (Internet). 2007;5(2):67-73.
3. Akande T, Ologe M, Medubi G. Antibiotic prescription pattern and cost at University of Ilorin teaching hospital, Ilorin, Nigeria. International Journal of Tropical Medicine. 2009;4(2):50-4.
4. Joshua IB, Passmore PR, Sunderland BV. An evaluation of the essential medicines list, standard treatment guidelines and prescribing restrictions, as an integrated strategy to enhance quality, efficacy and safety of and improve access to essential

medicines in Papua New Guinea. Health policy and planning. 2015:czv083.
5. WHO. Antimicrobial resistance: global report on surveillance: World Health Organization; 2014.
6. Duke T. Antibiotic-resistant bacteria sepsis in Papua New Guinea. PNG Medical Journal. 2000;43(1-2):82-90.
7. Manning L, Laman M, Greenhill AR, Michael A, Siba P, Mueller I, Davis TME. Increasing chloramphenicol resistance in streptococcus pneumoniae Isolates from Papua New Guinean children with acute bacterial Meningitis. Antimicrobial Agents and Chemotherapy. 2011;55(9):4454-6.
8. Lithgow AE, Kilalang C. Outbreak of nosocomial sepsis in the Special Care Nursery at Port Moresby General Hospital due to multiresistant Klebsiella pneumoniae: high impact on mortality. PNG Medical Journal. 2009;52(1-2):28-34.
9. Senn N, Rarau P, Salib M, Manong D, Siba P, Rogerson S, Mueller I, Genton B. Use of antibiotics within the IMCI guidelines in outpatient settings in Papua New Guinean children: an observational and effectiveness study. PloS One. 2014;9(3):e90990.
10. Hetzel MW, Page-Sharp M, Bala N, Pulford J, Betuela I, Davis TM, Lavu EK. Quality of antimalarial drugs and antibiotics in Papua New Guinea: A survey of the health facility supply chain. PloS one. 2014;9(5):e96810.
11. Nair A, Strauch S, Lauwo J, Jähnke RW, Dressman J. Are counterfeit or substandard anti-infective products the cause of treatment failure in PNG? J Pharm Sci. 2011;100(11):5059-68.
12. Akande TM, Ologe M, Medubi GF. Antibiotic prescription pattern and cost at University of Ilorin teaching hospital, Ilorin, Nigeria. International Journal of Tropical Medicines. 2009;4(2):50-4.
13. Akande TM, Ologe MO. Prescription pattern in a secondary health facility in Ilorin, Nigeria. Annals of African Medicine. 2007;6(4):186-9.
14. Erah PO, Olumide GO, Okhamafe AO. Prescribing practices in two health care facilities in Warri, Southern Nigeria: A comparative study. Tropical Journal of Pharmaceutical Res.2003;2(1):175-82.
15. Torvi JR, Dambal S. Drug prescription pattern in paediatric outpatient clinic in a tertiary hospital. Pediatr Res. 2011;15(2):77-80.
16. Suttajit S. Care seeking and treatment for adults with URIs in congested communities in Bangkok: Where problems occur. Geneva: World Health Organization; 2004.
17. Suttajit S. Antibiotic prescribing in upper respiratory tract Infections: Patterns and predictors of physician prescribing in health centers in Bangkok. Geneva: World Health Organization; 2004.
18. Hartayu T, Asdie HAH, Suryawati S. Antibiotic use for patients with fever of unknown origin at Panti Rapih Hospital, Yogyakarta, Indonesia. Geneva: World health Organization; 2004.
19. Joshua IB, Passmore PR, Parsons R, Sunderland VB. Appropriateness of prescribing in selected healthcare facilities in Papua New Guinea. Health policy and planning. 2014;29(2):257-65.
20. DoH. Manual of Family Planning for Doctors, HEOs and Nurses in Papua New Guinea. In: Health, editor. 2nd Edition ed. Port Moresby: Depart of Health; 2008.
21. DoH. Standard Management of Sexually Transmitted Infections & Genital Conditions in Papua New Guinea. A manual for Health Workers. In: Health, editor. Port Moresby: Department of Health; 2006.
22. DoH. Standard Treatment for Common Illnesses of Children in Papua New Guinea. A manual for Nurses, Community Health Workers, Health Extension Officers and Doctors. In: Health, editor. 8 ed. Port Moresby: Department of Health; 2005.
23. DoH. Standard Treatment for Common illness of Adults in Papua New Guinea. A Manual for Nurses, Health Extension Officers and Doctors. In: Health, editor. 5 ed. Port Moresby: Depart of Health; 2003.
24. DoH. Papua New Guinea Medical and Dental Catalogue. In: Health, editor. 9th ed. Port Moresby: Depart of Health; 2002.
25. WHO. Anatomical, Therapeutic, Chemical Classification (ATC). WHO 1999 Model list by ATC-code [Internet]. 2002.
26. AMH. Australian Medicines Handbook (AMH). Adelaide: Newstyle Printing, Mile End, SA.; 2010. 929 p.
27. WHO. Medicines Use in Primary Care in Develping and Transitional Countries: Fact Book Summarising Results from Studies

reported between 1990 and 2006. Geneva WHO; 2009. Contract No.: WHO/EMP/Mar/2009.3.

28. Al-Shami AM, Izham MMI, Abdo-Rabbo A. Evaluation of the quality of prescriptions with antibiotics in the Government Hospitals of Yemen. J of Clinical and Diagnostic Research. 2011;5(4):808-12.
29. Bosu WK, Adjei OD. An audit of the antibiotic prescribing practices in the health care facilities of west district of Ghana. Journal of West African Medical. 2000;19(4):298-303.
30. Chareonkul C, Khun VL, Boonshuyar C. Rational drug use in Cambodia: study of three pilot health centers in Kampong Thom Province. The Southeast Asian Journal of Tropical Medicine and Public Health. 2002;33:418-24.
31. Al-Niemat SI, Bloukh DT, Al-Harasis MD, Al-Fanek AF, Salah RK. Drug use evaluation of antibiotics prescribed in a Jordanian hospital outpatient and emergency clinics using WHO prescribing indicators. Saudi Med Journal. 2008;29(5):743-8.
32. 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 services research. 2013;13(1):1.
33. Ahmed AM, Awad AI. Drug use practices at pediatric hospitals of Khartoum State, Sudan. Annals of Pharmacotherapy. 2010;44(12):1986-93.
34. DOH. National Health Plan 2011–2020: Transforming our health system towards Health Vision 2050. In: Health, editor. Port Moresby: Department of Health; 2010.
35. Ware J. Rational use of antibiotics for upper respiratory infections: an evidence-based approach. Clinical excellence for nurse practitioners: the international journal of NPACE. 2000;4(3):151-7.
36. Larrabee T. Prescribing practices that promote antibiotic resistance: strategies for change. Journal of pediatric nursing. 2002;17(2):126-32.
37. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud P-AC, Rubin HR. Why don't physicians follow clinical practice guidelines?: A framework for improvement. Jama. 1999;282(15):1458-65.
38. Stark R, Nair, N.V. & Omi, S. Nurse practitioners in developing countries: some ethical considerations. Nursing Ethics. 1999;6(4):273-7.
39. Miles K, Seitio O, McGilvray M. Nurse prescribing in low-resource settings: professional considerations. International Nursing Review 53, 290–296. 2006;53:290-6.
40. Radyowijati A, Haak H. Improving antibiotic use in low-income countries: an overview of evidence on determinants. Social science & medicine. 2003;57(4):733-44.

41. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, Vlieghe E, Hara GL, Gould IM, Goossens H. Antibiotic resistance—the need for global solutions. The Lancet infectious diseases. 2013;13(12):1057-98.