Impact of pharmacist-prescriber partnerships to track antibiotic prescribing in publicly funded primary care in the Cape Town metropole, South Africa: An implementation study

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Background. More than 80% of the South African (SA) population receive their care in publicly funded primary care clinics. The majority come from socioeconomically disadvantaged communities, and bear the greatest burden from infectious diseases. However, there are very limited published data on and evaluation of antibiotic prescribing linked to clinical indication. This is a major gap.
Objectives. To assess the impact of a pharmacist-prescriber partnership to track antibiotic prescribing in publicly funded primary healthcare clinics in the Cape Town metropole, SA.
Methods. We conducted a prospective observational study across five clinics where there was a dispensing pharmacist team. At each clinic, a prescriber-pharmacist team gathered prospective antibiotic prescribing data for 'acute cough', linked to clinical indication, and provided individual prescribing feedback through each clinic's WhatsApp messaging platform about their prescribing quality (antibiotic dose, duration, frequency).
Results. Eight out of every 10 patients (adults and children) were prescribed an antibiotic (n=457). In a third of patients, an antibiotic was prescribed for suspected 'community-acquired pneumonia'. The WhatsApp prescribing feedback was used in half of all visits. The proportion of pharmacy-dispensed antibiotics concordant with local guidelines in terms of prescribing quality was 95% (95% confidence interval 0.93 - 0.98), n=239). Against AWaRe (access/watch/reserve) guidance, 97% of antibiotics prescribed belonged to the 'access' group.
Conclusion. Although prescribing concordance with guidelines was good, a significant proportion of patients were prescribed an antibiotic for 'acute cough'. Our findings have filled a fundamental gap in the evidence base that will inform antibiotic stewardship innovations, guideline development and future interventions.

Keywords: antimicrobial stewardship; primary care, prescribing feedback

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South Africa (SA) has a high burden of infectious diseases complicated by the disproportionate impact of HIV and tuberculosis. Antibiotic resistance affects low- and middle-income countries disproportionately.[1] Respiratory tract infections such as acute cough form the bulk (>60%) of all antibiotic prescriptions in primary care.[2] Frontline clinicians (doctors, nurse prescribers) must make daily decisions about antibiotic treatment without knowing the exact cause of infection or whether patients require antibiotics. The decision to prescribe an antibiotic, for example, for acute cough, is a complex behaviour that requires bespoke interventions tailored to the context.

The evidence gap

This upper middle-income country is responding to the national threat from antibiotic resistance through its National Strategic Framework (2018 - 2024).[3,4] The Standard Treatment Guidelines and Essential Medicines List (EML) for SA (primary healthcare level) provide an evidence base for prescribing in primary care.[5] However, there is limited published research and evaluation of antibiotic prescribing in primary care, especially in the public sector, because of a lack of integrated pharmacy, laboratory and clinical information systems. This is a fundamental evidence gap. Where prescribing data are available, these data are retrospective, and antibiotic prescribing data are not linked to clinical indication.[4,6,7] There have been no studies that have systematically documented sequential patients with acute cough attending publicly funded primary care health facilities in SA. Prospective antibiotic prescribing data are key as a benchmark for future antibiotic stewardship interventions and guideline development, to optimise the quality of antibiotic prescribing and reduce the risk of antimicrobial resistance in primary care.[8]

Pharmacist-prescriber partnerships to optimise antibiotic prescribing

SA has made significant inroads into this gap by employing a multidisciplinary strategy in hospitals, where pharmacists and

clinicians are engaged in antibiotic stewardship partnerships to improve antibiotic prescribing.[9,10] However, this is needed in community settings, too.[4] This will become increasingly important in the country's transition to the anticipated National Health Insurance, where pharmacists are likely to expand their role in primary healthcare services to increase access, and point-of-care tests may be expanded into the community for common infection syndromes. There is good evidence from high-income countries (HICs) that a pharmacist-prescriber model effectively decreases antibiotic prescribing, and increases guideline-adherent prescribing in community settings.[11] However, evidence generated in HICs is not always applicable in a country like SA, which has markedly different patient populations, disease spectra, health systems and social and cultural determinants of health.[12] This study builds on exploratory work[12-14] to test this approach in the context of an upper middle-income country.

The aim of our study was to assess the implementation of a pharmacist-prescriber partnership (PPP) to track and optimise antibiotic prescribing for patients presenting with acute cough in publicly funded primary healthcare clinics (PHCs) in the Cape Town metropole, SA.

In order of priority, there were three study objectives. The first objective was to collect baseline observational data (demographic, clinical and prescribing data) of patients presenting with acute cough. The second objective was to to assess the proportion of antibiotics prescribed for acute cough that are concordant with local prescribing guidance when PHCs employ PPPs. The third objective was to measure the impact of PPPs on health outcomes (subsequent contacts with the health services or hospital admission within 7 days).

Methods

The Cape Town metropole is a peri-urban region of just under 300 km (188 miles) around Cape Town. It includes the suburbs of Khayelitsha and Mitchells Plain, with an estimated population of 4.5 million people. Based on census data,[15] most of the population are uninsured (77%) and rely on publicly funded healthcare in the region. Access to basic services such as water, sanitation and electricity is good (>85%), but unemployment is high (>40%), with a substantial proportion of the population living in informal dwellings (20.5%). The Cape Metro region has 152 public primary healthcare facilities and 8 district hospitals. Access to publicly funded primary healthcare services, where the vast majority of the population seek their healthcare, is free of charge in SA. Obtaining antibiotics is by prescription only, although recent research has shown that privately owned pharmacies in townships in SA are dispensing antibiotics without prescription.[16] Although internet access is available in some larger PHCs, patient medical records are paper-based only. Mobile phone connectivity coverage is excellent.

The present study is a pharmacist-driven, prospective observational study with a novel (near) real-time individual prescribing feedback mechanism across five PHCs (sites) where there is a dispensing pharmacy team. We recruited PHCs through the local family physician forum, nursing and pharmacy teams. Participation was voluntary. We staggered the introduction of sites during the study period with an onsite training visit about study procedures.

We employed a PPP to gather prospective antibiotic prescribing data for acute cough (≤28 days duration) linked to antibiotic prescribing quality (antibiotic dose, duration, dose frequency) and reported clinical indication. We selected 28 days to reflect the common duration of symptoms for acute cough in 90% of cases.[17] Study procedures, data collection and materials were piloted before the main study (start date 2 June 2022). We planned to collect data for up to 6 months, and recruit between 500 and 800 patients.

During their routine clinical practice, frontline clinicians (doctors and nurse prescribers or 'clinical nurse practitioners') identified and described patients according to a paper-based carbon-copy one-page case report form (CRF) (appendix https://www.samedical.org/file/2308). Clinicians were asked to include consecutive patients as best they could. Patient details were de-identified using a patient study identification number on the CRF. Clinicians recorded relevant medical history, presenting symptoms, diagnosis, antibiotic therapy if prescribed, and any planned follow-up. This study did not involve any change in clinical practice. CRFs were collated fortnightly, transferred to a secure electronic database (REDCap) and checked after data entry.

Patients were adults and children presenting with acute cough or, alternatively, where cough was not the most prominent symptom (e.g. fever, malaise) but where the clinician considered acute respiratory tract infection as the primary diagnosis. HIV-positive patients with acute cough were eligible, as well as patients in whom tuberculosis was suspected. This included patients with asthma and chronic obstructive pulmonary disease (COPD).

Patients were not eligible if the working diagnosis was a non-infective cause of cough (e.g. heart failure), or required immediate hospitalisation. Patients received their usual clinical care.

Pharmacists, located at each PHC site, recorded and dispensed the prescribed treatment, including antibiotic course, as usual. At the same time, they audited and reviewed the appropriateness (concordance) of the antibiotic prescribed on the study CRF according to SA Standard Treatment Guidelines and Essential Medicines List 2020 (primary healthcare level) in terms of recommended antibiotic dose, duration and frequency. The pharmacy team then notified clinicians of their assessment using the pre-existing clinic group messaging platform (i.e. WhatsApp group chat). Only the patient study ID and information about concordance were sent in a pre-approved text message within the group chat. Pharmacists were free to discuss the antibiotic prescription with the clinician through their usual means of communication.

After the initial consultation, the research team attempted to contact patients to ascertain whether they had had subsequent contact(s) with the health services and/or hospital admission within 7 days of the initial consultation. This occurred between 7 and 10 days after the initial consultation, to accommodate weekends and public holidays. Contacts were conducted through telephone assessment (three attempts over 2 consecutive days).

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the University of Oxford (OxTREC ref. no. 504-21, 12 April 2021) and the University of the Western Cape (BMREC ref. no. BM21/10/17, 26 Nov 2021)

Results

Between 2 June 2022 and 30 September 2023, we enrolled 457 patients with symptoms of acute cough at five PHCs.

Baseline characteristics are shown in Table 1. There were slightly more adults (56%) than children (44%). The most common listed comorbidities were hypertension (15%), COPD (10%) and HIV (7%). Overall, 8 out of every 10 patients (84%) were prescribed an antibiotic for acute cough. This varied between sites. Out of all patients who were prescribed antibiotics (n=382) for acute cough, 57% were adults and 42% children.

The top three antibiotics prescribed were amoxicillin (63%), co-amoxiclav (13%) and phenoxymethylpenicillin (6%). In terms of

quality indicator prescribing against AWaRe (access/watch/reserve) guidance, 97.6% of antibiotics prescribed belonged to the 'access' group (with amoxicillin and co-amoxiclav accounting for 92%), ceftriaxone and azithromycin accounted for one case each in the 'watch' group, and there were none in the 'reserve' group (available data *n*=382, Table 1)

A clinical diagnosis of 'community-acquired pneumonia' (CAP) was by far the top clinical indication (35%) for which an antibiotic was prescribed across four of the five sites (in site 5, the most common indication was acute bronchitis, Fig. 1 and Table 2). This was followed by tonsillitis (11%), viral upper respiratory tract infection (URTI) (8%), influenza (8%) and bronchitis (8%). Differences between adults and children per clinical indication are outlined in Fig. 1.

Antibiotics were prescribed for all suspected CAP (*n*=158). More than half of the antibiotics for CAP were prescribed by nurse prescribers compared with doctors (53% v. 35%). CAP cases were more often diagnosed in children by nurses, compared with CAP in adults, who were diagnosed more commonly by doctors (Table 3).

Half of all recorded antibiotics were prescribed by nurse prescribers (51%, *n*=235). Antibiotics were directly dispensed without pharmacy input in over half of these cases.

Sixty percent (140/235) of nurse-led antibiotic prescriptions were for children. This is in comparison with doctors, where 80% of antibiotic prescriptions were for adults (128/161), and where pharmacy staff had the opportunity to comment on the prescription concordance and provide feedback via the clinic WhatsApp group chat.

There was no statistical difference in antibiotic prescribing rate for acute cough conditions between nurse prescribers and doctors (85% v. 83%, *p*=0.48).

Pharmacy prescribing feedback using the group messaging platform was used in just under half of all consultations (*n*=102/208, 49%), with a similar split between nurses (*n*=103) and doctors (*n*=105), excluding those cases where nurses had directly dispensed antibiotics.

The proportion of pharmacy-dispensed antibiotics that agreed with local guidelines in terms of antibiotic dose, duration and frequency was 95% (95% confidence interval (CI) 93% - 98%, *n*=239).

Follow-up data (*n*=386) at 1 week were incomplete. The proportion of patients with an invalid or no registered telephone number was 37% (*n*=140). Just under 20% of patients (*n*=74) did not respond after three contact attempts. From available complete data at 1week follow-up (*n*=172), re-attendance was 3% (*n*=5), and no hospitalisations were recorded.

Table 1. Demographic and clinical characteristics of study population presenting with acute cough (*N*=457)

Characteristic	*n* (%)*
Age, years (median, IQR)	28.11 (5.98 - 53.41)
Gender (female)	276 (60.4)
Adult ≥18 years	255 (55.8)
Presence of comorbidity	
Hypertension	69 (15.1)
COPD	47 (10.3)
HIV	34 (7.4)
Asthma	31 (6.8)
Diabetes mellitus (type 1 or 2)	27 (5.9)
Congestive heart failure	6 (1.3)
Previous stroke	3 (0.7)
Active tuberculosis	2 (0.4)
Active cancer	1 (0.2)
Chronic kidney disease	1 (0.2)
Pregnancy	1 (0.2)
Other	34 (7.4)
Antibiotic prescribed	
Total	382 (83.6)
Adults	218 (57.1)
Children	164 (42.9)
Antibiotic prescribed per site	
1	45 (74)
2	125 (89)
3	119 (76)
4	11 (69)
5	82 (100)
Antibiotic class	
Amoxicillin	286 (62.6)
Amoxicillin/clavulanic acid	58 (12.7)
Phenoxymethylpenicillin	27 (5.9)
Azithromycin	7 (1.5)
Clotrimazole	1 (0.2)
Flucloxacillin	1 (0.2)
Other	2 (0.4)
Prescriber	
Nurse	235 (51.4)
Doctor	161 (35.2)
Not recorded	61 (13.3)

IQR = interquartile range; COPD = chronic obstructive pulmonary disease.
*Unless otherwise indicated.

Discussion

Main findings

Our findings show that 80% of patients were prescribed an antibiotic for an acute cough presentation. In more than a third of these cases, an antibiotic was prescribed for a clinical diagnosis of CAP, and determined by the type of healthcare professional (nurse or doctor) whom the patient (adult or child) would routinely consult. Half (51%) of all recorded antibiotics were prescribed by nurse prescribers who directly dispensed antibiotics without pharmacy input. Where the group WhatsApp prescribing feedback was used, there was good concordance of prescribed antibiotics with local guidelines in terms of antibiotic dose, duration and frequency.

Comparison with existing literature

Encouragingly, most antibiotics prescribed were from the 'access' group of antibiotics in the AWaRe (access/watch/reserve) classification. However, there was a high rate of antibiotic prescribing, which mirrors that of earlier studies in the public sector, where the proportion of patients receiving an antibiotic prescription ranged between 69% and 78% of consultations.[6,18,19] This high antibiotic prescribing rate is not dissimilar from other published data in the SA private sector.[19,20] However, our prospective study now adds the presumed clinical indication for this prescription (where previously, this was absent in a third of cases).[7]

We captured prescribing data using a multidisciplinary pharmacist-prescriber approach. This aligns with the findings of a systematic review that showed that the pharmacist-prescriber model can effectively increase guideline-adherent antibiotic prescribing (odds ratio 1.96, 95% CI 1.56 - 2.45, 10 trials).[11] The studies included in the review were all conducted in HICs. This study is the first attempt in Africa to utilise this partnership in publicly funded primary care. In this study, the concordance of prescribed antibiotics was much higher (95%) than that in earlier published studies in the same region with

different study designs.[6,7] The Gasson *et al*.[6] study involved a point prevalence survey using a retrospective medical folder review, and found that overall antibiotic guideline adherence was 32%, and for patients presenting with respiratory symptoms, 34% (*n*=182). The de Vries *et al*.[7] study was a peer audit and feedback intervention study, where 10 antibiotic prescriptions were randomly selected monthly for peer review. It measured adherence to seven antibiotic quality process measures, and showed improvement in the mean overall adherence, from 19% (baseline) to 47% (post-intervention). In our study, however, we only asked pharmacists to comment on the antibiotic concordance with local guidelines in terms of dose, duration and frequency.

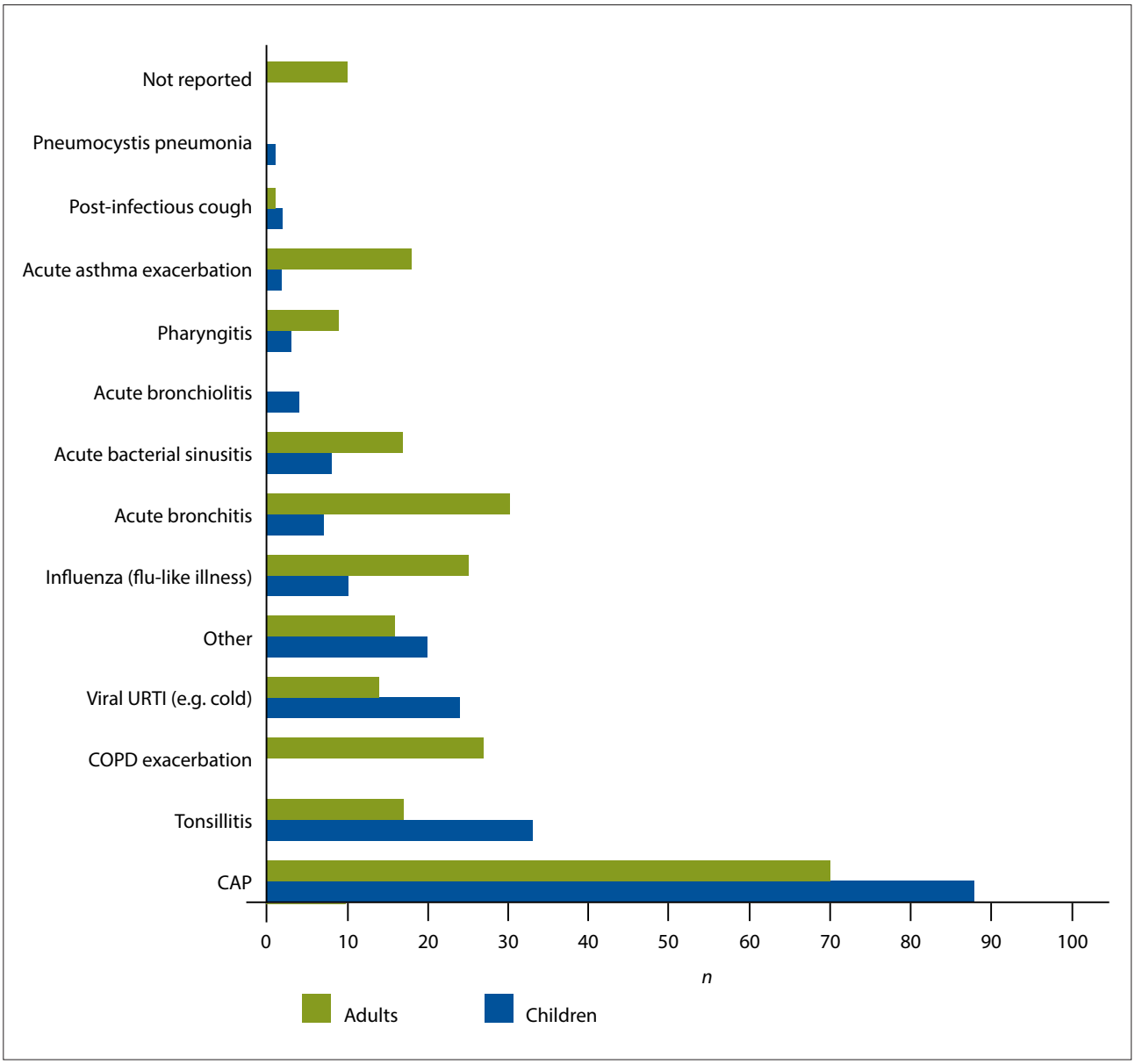

*Fig. 1. Reported clinical indication for 'acute cough' antibiotic prescription (*N=*457). (URTI = upper respiratory tract infection; COPD = chronic obstructive pulmonary disease; CAP = community-acquired pneumonia.)*

Table 2. Top three reported clinical indications for an antibiotic prescription per site

Site, *n*		Clinical indication, *n*	
Site 1, 54	CAP (22)	Tonsillitis (12)	Viral URTI (7)
Site 2, 140	CAP (53)	Sinusitis (21)	COPD exacerbation (12)
Site 3, 157	CAP (75)	Viral URTI (24)	Tonsillitis (16)
Site 4, 16	CAP (4)	Tonsillitis (3)	Acute bronchitis (2)
Site 5, 80	Acute bronchitis (26)	COPD exacerbation (13)	Tonsillitis (10)

CAP = community-acquired pneumonia; URTI = upper respiratory tract infection; COPD = chronic obstructive pulmonary disease.

Study strengths and limitations

Antibiotic prescribing data are not routinely available in publicly funded primary care. Where prescribing data are available, these data are often from the private sector[21,22] and/or inpatient settings,[9,23] retrospective[24] and not linked to clinical indication.[6,20] To our knowledge, this is the first study to capture prospective prescribing data for acute cough linked to clinical indication in publicly funded primary care in the region. This study builds on previous research into where and how a cross-disciplinary team could work in these specific settings to optimise antibiotic prescribing.[12-14] Collecting this baseline information is critical to set a benchmark for antimicrobial stewardship initiatives, provide consistency and improve the quality of antibiotic prescribing for common infection syndromes.

We have included both nurse and doctor prescribers to reflect the breadth of antibiotic prescribing practice in the region, recognising that nurses see most patients.[25] Our team-based approach to collecting these data ensured that we used limited resources advantageously, and empowered prescriber-pharmacist teams to co-design and participate in the study.

We harnessed the high mobile data connectivity across SA to provide efficient and low-cost (near) real-time individual prescribing feedback, mindful of the confines of data privacy and regulations. This feedback mechanism, therefore, has the potential to be refined and scaled up across the region.

There are several limitations, which have prompted further research questions. First, we were not able to incorporate our prescribing feedback mechanism to nurses dispensing antibiotics from their own consulting rooms. However, this has shed light on the significant proportion of antibiotics prescribed and dispensed by nurses, and provides impetus for future targeted antimicrobial stewardship initiatives.

Second, data on health outcomes at 1 week (i.e. subsequent contacts with health services or hospital admission within 7 days) were limited. In part, this was due to a mobile population with no permanent abode, multiple or obsolete mobile phone numbers, or apprehension of cold callers, e.g. debt collectors.

Third, not all the sites had the capacity to implement the quality improvement component successfully, and the same sites also struggled to collect prospective data on top of their clinical workload. We took a pragmatic approach, and therefore we were not able to verify whether clinicians collected data from consecutive patients, introducing the likelihood of sampling bias. There was also regular social unrest, which meant clinics were forced to close, and data collection was paused.

Fourth, although the antibiotic prescribing quality concordance was high, the study design did not allow us to determine whether the prescribed antibiotic was clinically appropriate. Likewise, the study design did not lend itself to making a comparison of sites that used PPP v. sites that did not use PPP.

Lastly, we accept that some prescribers may up-rate a diagnosis to justify their decision to prescribe an antibiotic. Likewise, clinicians might be wary of, for example, the high incidence of rheumatic heart disease in sub-Saharan Africa when children present with a sore throat (tonsillitis).

Table 3. Antibiotic prescribing for community-acquired pneumonia *N*=140)

Prescriber	Children ≤18 years old (% within group)	Adults >18 years old (% within group)
Nurse	62 (82.7)	22 (33.9)
Doctor	13 (17.3)	43 (66.1)
Total	75	65

However, there are also a significant proportion of cases where an antibiotic would rarely be indicated, e.g. viral URTI or acute bronchitis.

Implications for practice, policy and future research

Our findings support the need to better understand the prescribing behaviour of frontline clinicians, and to explore the factors influencing this prescribing behaviour (e.g. uncertainty related to diagnosis or prognosis, preventing breakdown of clinician-patient relationship, etc.).

Clinically, our findings also support the need to better identify patients who might benefit from an antibiotic by promoting and evaluating fit-for-purpose point-of-care tests (as part of a multifaceted intervention). The proportion of patients prescribed an antibiotic for a clinical diagnosis of CAP without radiological verification was high (42%). By comparison, in the UK, this prescribing proportion is between 5 and 12% presenting to general practitioners in primary care. We accept that there is a high infectious disease burden in SA; however, the 'true' proportion of radiologically confirmed CAP is likely lower, but remains unknown. As there is limited community-based laboratory and radiological infrastructure, this provides an avenue to test the feasibility of point-of-care testing to help frontline clinicians make more informed treatment decisions at the point of care before initiating antibiotic treatment for suspected CAP.

This study collected important prospective prescribing data for acute cough. This is critical to accurately assess what problems there are in terms of access to, and excess use of, antibiotics in the region, and will inform antibiotic stewardship innovations, guideline development and future interventions.

Our findings have also prompted further research questions. For example, half of all antibiotic prescribing was performed by nurse prescribers, who primarily work according to validated treatment protocols, with appreciable protocol adherence. Mindful of the plausible risk of sampling bias, the high antibiotic prescribing rate calls into question whether such a symptom-based protocol favours an antibiotic prescription. Other plausible reasons for this high prescribing rate might include more severe illness than we anticipate, or that there are important social determinants of health that override protocol-driven treatment regimens.[9]

In terms of quality indicator prescribing against World Health Organization AWaRe guidance, more than 95% of antibiotics prescribed belonged to the 'access' group. This highlights the limitations of the AWaRe guidance in resource-poor primary care settings, where there is a limited supply of 'watch' and 'reserve' antibiotics. Hence our findings will refocus the agenda on improving the quality of prescribing in these settings by developing quality indicators that focus on the diagnostic process, like those successfully employed in chronic diseases such as diabetes and cardiovascular diseases, to improve the appropriateness of antibiotic prescribing.

Finally, our findings will help determine the optimal sample size, research processes and recruitment strategy for a future randomised trial of the clinical- and cost-effectiveness of point-of-care testing for acute cough, which will include important embedded qualitative research methods.

Data availability. Data are available on request from the corresponding author.

Declaration. None.

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