ORIGINAL RESEARCH

An Evaluation of Antibiotic Prescription Rationality at Lower Primary Healthcare Facilities in Three Districts of South-Western Uganda

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Purpose: Antimicrobial resistance is now one of the leading five causes of death globally. This study evaluated the rationality of antibiotic prescriptions at lower primary care levels in three districts of Southwestern Uganda.

Methods: This prospective cross-sectional study reviewed 9899 antibiotic prescriptions at 39 health centers following a drug delivery cycle by National Medical Stores in three phases (19 days each on average). Phase 1 started 3 days after delivery, mid-way (Phase 2) and towards the end (Phase 3). The proportion of rationally prescribed antibiotics was determined using a modified criterion by Badar and in reference to Uganda Clinical Guidelines (UCG). Using multivariate logistic regression, the factors associated with rational prescription were determined with 95% confidence intervals.

Results: Seven of every 10 antibiotic prescriptions were irrational. Half the prescriptions were made by unauthorized personnel (nurses) and many of the pediatric prescriptions (916, 46.5%) did not bear body weight measurements to guide appropriate dosing. Also, the proportion of rational prescriptions in reference to UCG, 2016 was very low (3387, 34.2%). However, a high proportion of antibiotic prescriptions were legibly written (9462, 95.7%), prescribed by generic names (9083, 91.8%) and had a diagnosis (9677, 97.8%) indicated. Multivariate logistic analysis showed that; availability of medicines (phase 1) (phase 2 AOR=1.14, 95% CI:1.02–1.28, phase 3, AOR=1.23, 95% CI:1.1–1.38), legibly written prescription (AOR=0.61, 95% CI: 0.47–0.78), indication of a date on the prescription (AOR=0.56, 95% CI0.38–0.81) and being a medical officer were factors associated with rational antibiotic prescription.

Conclusion: We observed a high rate of irrational prescription in the study sites and the majority of these were by unauthorized personnel. A review of antibiotic use policies and focused interventions is crucial in these settings.

Keywords: inappropriate, antibiotic prescriptions, antibiotic resistance

Introduction

Antimicrobial resistance is a natural phenomenon, often fuelled by several other causes.[1–4] One of these, is the irrational prescription of antibiotics.[5,6] As of 2019, Antimicrobial Resistance (AMR) is now among the five leading cause of death globally, with an estimated 1.2 million deaths.[7] Low- and middle-income countries (LMICs) are more severely affected owing to the overloaded health systems and poor access to alternative antibiotic regimens.[8,9] In Uganda, over 50–95% of bacterial pathogens are resistant to penicillin and co-trimoxazole, two of the most commonly used antibiotics at primary care health facilities. There is also a high prevalence of multi-drug resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (2–50%) and extended-spectrum beta-lactamase (ESBL)-producing bacteria (10–75%).[10,11] Of recent, there is evidence showing high resistance rates to both β-lactam and non-β-lactam antibacterial agents and alarming rates of multi-drug resistances in Ugandan hospitals.[12,13] Antibiotic resistance negatively impacts on morbidity, mortality, healthcare costs, and the general economy of a given country.[5]

In 2010, Uganda expanded its healthcare availability by utilizing nurses and clinical officers (diploma holder in medicine) to run lower primary care level facilities (Health Centres level II–IV).[14] A Health Centre (HC) II is the lowest level of

interaction between the community and the formal healthcare sector. It serves about 5000 people on an outpatient basis with no laboratory services (other than rapid tests for malaria). The center is manned by an enrolled nurse (certificate holder in Nursing) working with a midwife who provides antenatal care for pregnant women, two nursing assistants and a health assistant. A Health Center (HC) III is an intermediate-referral unit serving an estimated population of 25,000. It provides the following services: general outpatient care, family planning, immunization, counseling and testing of HIV, maternity and postnatal care, laboratory, inpatient care, environmental health and home visiting to review the progress of critically ill patients. Ideally, a HCIII is manned by two clinical officers (diploma holder in medicine), one nursing officer (diploma holder in nursing), two enrolled/registered nurses, three nursing assistants, one health assistant, one laboratory technician, one laboratory assistant, a records officer, two night watchmen and two porters. On the other hand, HC IV serves a Health Sub District (HSD) with an estimated population of 100,000. In addition to services found at health centre III, it offers inpatient services with a theatre for carrying out emergency operations. It is headed by a senior medical officer (Minimium, bachelors holder in medicine and surgery with considerable years of experience) and another medical officer (bachelors holder in medicine and surgery) working with nurses and midwives, laboratory technician, clinical officers, one laboratory assistant. It is the referral facility within the HSD and provides the support supervision of lower health facilities.[15] All primary care facilities are provided with the National Clinical Guidelines (UCG) as a standard protocol for prescriptions and management of patients.[15] This study, therefore, evaluated the rationality of antibiotic prescriptions in reference to the UCG, 2016 at Health centres (HC) II, III and IV in Mbarara, Kasese and Bushenyi districts.

Materials and Methods

This was a prospective cross-sectional study conducted at 39 government owned lower primary care level facilities (HC IIs-IVs) in 3 (Mbarara, Bushenyi and Kasese) out of 8 randomly selected districts of South-western Uganda that existed by 2005. These 8 districts were selected because they have functional, organized and stable healthcare delivery structures (management, patient referral pathway from VHT or HC II to HC IV, etc.) as opposed to the newly created districts in the region. A list of Health Sub-districts (HSD) from the 3 districts was obtained from the respective district headquarters and only those with HCs at different levels of care were selected for randomization. One HSD per district was randomly selected in Excel using computer generated numbers.

In Uganda, antibiotics are classified as prescription-only-drugs and the professional cadres authorized to prescribe them are limited to registered medical practitioners, dental surgeons, clinical officers and midwives as per the National Drug Policy and Authority Act of 1993 as amended in 2000.[16] All antibiotic prescriptions at the 39 HCs were reviewed following a delivery cycle of drugs by National Medical Stores (NMS) in three phases: shortly after delivery (phase 1), mid-way (phase 2) and towards the end (phase 3). The delivery cycle by NMS is every two months and covers all government owned HCs countrywide following a predetermined delivery schedule. The first phase started 3 days after delivery of drugs at a given facility and the remaining days in the cycle were split equally for the three phases. Data was collected at the beginning of each phase and from patients that were exiting the facilities.

The proportion of rationally prescribed antibiotics was determined using a modified criterion by Badar (2012) and in reference to Uganda Clinical Guidelines (UCG), 2016. Badar's criterion classified prescriptions as (1) rational if the antimicrobial use and its route of administration, dose, frequency and duration of use were considered appropriate for infection, (2) irrational if the antimicrobial was used without indication, prophylaxis under circumstances of unproven efficacy or by clearly inappropriate route, dose or preparation for that indication, and (3) questionable when insufficient clinical or laboratory data was present to enable the therapy to be classified as clearly rational or irrational. In this study, Badar's criterion was dichotomized into two categories of rational and irrational, that is, a prescription was rational if all of the following criteria were satisfied: it was appropriate for the indication, prescribed in the right dose, frequency, duration and route of administration as guided by the UCG, 2016, and the reverse is true. For paediatric patients, estimates for dosing based on a child's age as guided by the UCG (where body weight measurements were not indicated) were also used to categorize a prescription as either rational or irrational. The working diagnosis of the patient was used to evaluate prescriptions' rationality as guided by the UCG. The prescription features (such as; patients' age, address, name, legibly written, date, etc.) as recommended in the UCG were used to evaluate the precribers' practices/adherence to these guidelines as well identify factors associated with rational prescription of antibiotics in the study setting.

The rationality of prescriptions was evaluated by two reviewers and in case of disagreements, an independent pharmacist was invited to ascertain the categorization. Multivariate logistic regression was used to determine the factors associated with rational prescription at 95% confidence intervals. Data was analysed using STATA version 14.

Results

A total of 9899 antibiotic prescriptions were reviewed from 39 HCs through the three study phases in the three districts of Mbarara, Bushenyi and Kasese. About 20% (1970) of these were paediatric prescriptions. Of all the reviewed prescriptions, 3845 (38.9%), 4072 (41.1%) and 1982 (20%) originated from HCs II, III and IV, respectively. Prescriptions made and reviewed during phases I, II and III of the study were 3408 (34.4%), 3108 (31.4%) and 34.2 (34.2%), respectively. Of the 9899 prescriptions, 1817 (18.4%) prescriptions were multi-drug regimens while the remaining 8082 (81.6%) were not. The median antibiotic-treatment duration was 5 (IQR=5-5) days. On the prescriber's professional cadre, about 50% of prescriptions were made by nurses, followed by clinical officers (CO) who made about a quarter of the prescriptions (24.6%); while only 2.5% were made by medical officers. Of all prescriptions by nurses, 229 (2.3%), 4661 (47.1%) and 1092 (11%) were for enrolled midwives, enrolled nurses and registered nurses/midwives, respectively. Nursing assistants prescribed 552 (3.9%) of the prescriptions. On the basis of the UCG, 2016, 6512 (65.8%) prescriptions were categorized irrational, while only 3387 (34.2%) were categorized rational. Of the paediatric prescriptions (age ≤12 years), only 916 (46.5%) had patient's body weight indicated to guide dosing. In nearly 40% of all the prescriptions, the prescriber's identity was not indicated. However, a high proportion of antibiotic prescriptions were legibly written (9462, 95.7%), prescribed by generic names (9083, 91.8%) and had diagnoses (9677, 97.8%) indicated, see Table 1.

Table 1 Prescription Features Evaluated and Some Demographics

Feature	Overall n (%) 9899
Legibly written	
Yes	9462 (95.7)
No	427 (4.3)
Date of prescription	
Yes	9641 (97.4)
No	196 (2.0)
Missing data	62 (0.6)
Patient's name	
Yes	9260 (93.6)
No	568 (5.7)
Missing data	70 (0.7)
Patient's Address	
Yes	8874 (89.6)
No	956 (9.7)
Missing data	69 (0.7)

(*Continued*)

Table 1 (Continued).

Feature	Overall n (%) 9899
Gender	
Yes	8158 (82.4)
No	1741 (17.6)
Drug formulation	
Yes	8737 (88.2)
No	897 (9.1%)
Missing data	265 (2.7)
Patient's age	
Yes	8883 (89.7)
No	1016 (10.0)
Pediatric patients weight indicated	
Yes	916 (46.5)
No	1054 (53.5)
Strength of preparation	
Yes	8561 (86.5)
No	1301 (13.1)
Missing data	37 (0.4)
Dose frequency	
Yes	9596 (96.9)
No	303 (3.1)
Regimen prescription	
Yes	1817 (18.4)
No	8082 (81.6)
Full generic name written	
Yes	9083 (91.8)
No	814 (8.2)
Diagnosis present	
Yes	9677 (97.8)
No	221 (2.2)
Special instructions	
Yes	219 (2.2)
No	9637 (97.4)

(*Continued*)

Table 1 (Continued).

Feature	Overall n (%) 9899
Missing data	43 (0.4)
Study phase	
Phase 1	3408 (34.4)
Phase 2	3108 (31.4)
Phase 3	3383 (34.2)
Facility level	
Health center II	3845 (38.9)
Health center III	4072 (41.1)
Health center IV	1982 (20.0)
District	
Mbarara	3331 (33.7)
Bushenyi	3724 (37.6)
Kasese	2844 (28.7)
Patient's age category	
Pediatrics (age ≤12 years)	1970 (19.9)
Adults (age > 12 years)	6913 (69.8)
Age not recorded	1016 (10.3)
Prescriber's identity	
Present	6820 (69.1)
Not present	3045 (30.9)
Prescriptions with prescriber's designation	
Medical Officer	252 (2.5)
Clinical Officer	2436 (24.6)
Registered Nurse/midwife	1092 (11.0)
Enrolled Nurse	4661 (47.1)
Enrolled Midwife	229 (2.3)
Nursing Assistant	552 (3.9)
Other	401 (5.6)
Designation not recorded	276 (2.8)
Rationality	
Rational	3387 (34.2)
Irrational	6512 (65.8)

(*Continued*)

Table 1 (Continued).

Feature	Overall n (%) 9899
Duration of prescribed treatment: **Median (IQR) in days**	5 (5–5)

On multivariate logistic regression analysis, there was a significant statistical increase in irrationality of antibiotic prescriptions from phase 1 to phase 2 (AOR=1.14, 95% CI:1.02–1.28), and then phase 3 (AOR=1.23, 95% CI:1.1–1.38). Mbarara district had higher odds of rational antibiotic prescriptions compared to Bushenyi (AOR=0.65, 95% CI: 0.58–0.73) and Kasese (AOR=0.70, 95% CI:0.62–0.79) districts. Prescriptions that were written legibly (AOR=0.61, 95% CI:0.47–0.78), had a date indicated (AOR=0.56, 95% CI: 0.38–0.81) and made by medical officers were more likely to be rational compared to those not legible, had no date indicated and written by other healthcare carders respectively. In terms of the commonly prescribed antibiotics, amoxicillin was more likely to be prescribed rationally compared to others (see Table 2).

Table 2 Factors Associated with Prescription Rationality

Factors	Prescription Rationality			
	Rational n(%)	Not Rational n(%)	Crude OR (95% CI)	Adj. OR (95% CI)
Study phase				
Phase 1	1108 (32.5)	2300 (67.5)	1.00	1.00
Phase 2	1070 (34.4)	2038 (65.6)	1.09 (0.98–1.21)	1.14 (1.02–1.28)*
Phase 3	1209 (35.7)	2174 (64.3)	1.15 (1.04–1.28)**	1.23 (1.1–1.38)***
Facility level				
Health center II	1326 (34.5)	2519 (65.5)	1.00	
Health center III	1367 (33.6)	2705 (66.4)	0.96 (0.87–1.05)	
Health center IV	694 (35.0)	1288 (65.0)	1.02 (0.91–1.15)	
District				
Mbarara	1315 (39.5)	2016 (60.5)	1.00	1.00
Bushenyi	1164 (31.3)	2560 (68.7)	0.70 (0.63–0.77)***	0.65 (0.58–0.73)***
Kasese	908 (31.9)	1936 (68.1)	0.72 (0.65–0.80)***	0.70 (0.62–0.79)***
Written legibly				
Yes	3287 (34.7)	6175 (65.3)	1.00	1.00
No	96 (22.5)	331 (77.5)	0.54 (0.43–0.69)***	0.61 (0.47–0.78)***
Patient's age category				
Pediatrics (age ≤12 years)	888 (45.0)	1085 (55.0)	1.00	–
Adults (age > 12 years)	2467 (35.7)	4446 (64.3)	0.82 (0.75–0.89)***	–

(*Continued*)

Table 2 (Continued).

Factors	Prescription Rationality			
	Rational n(%)	**Not Rational n(%)**	**Crude OR (95% CI)**	**Adj. OR (95% CI)**
Prescriber's identity				
Present	2356 (34.5)	4464 (65.5)	1.00	
Not present	1024 (33.6)	2021 (66.4)	0.96 (0.88–1.05)	
Prescriber's designation				
MO	123 (48.8)	129 (51.2)	1.00	1.00
CO	853 (35.0)	1583 (65.0)	0.57 (0.44–0.73)***	0.72 (0.54–0.95)*
RN	356 (32.6)	736 (67.4)	0.51 (0.38–0.67)***	0.63 (0.46–0.86)**
EN	1564 (33.6)	3097 (66.4)	0.53 (0.41–0.68)***	0.61 (0.46–0.81)**
EM	72 (31.4)	157 (68.6)	0.48 (0.33–0.70)***	0.41 (0.27–0.62)***
N/Assistant	165 (29.9)	387 (70.1)	0.45 (0.33–0.61)***	0.47 (0.33–0.66)***
Other	153 (38.2)	248 (61.8)	0.65 (0.47–0.89)**	0.78 (0.55–1.11)
Commonly prescribed antibiotics				
Amoxycillin	2126 (48.4)	2271 (51.6)	1.00	1.00
Metronidazole	452 (18.8)	1954 (81.2)	0.25 (0.22–0.28)***	0.23 (0.21–0.27)***
Ciprofloxacin	324 (35.5)	588 (64.5)	0.59 (0.51–0.68)***	0.54 (0.47–0.63)***
Doxycycline	103 (13.8)	645 (86.2)	0.17 (0.14–0.21)***	0.14 (0.12–0.18)***
Others	225 (36.7)	388 (63.3)	0.62 (0.52–0.74)***	0.48 (0.40–0.58)***
Date of prescription				
Present	3333 (34.6)	6308 (65.4)	1.00	1.00
Not present	42 (21.4)	154 (78.6)	0.52 (0.37–0.73)***	0.56 (0.38–0.81)**
Patient's name				
Present	3248 (35.1)	6012 (64.9)	1.00	–
Not present	119 (21.0)	449 (79.0)	0.49 (0.40–0.60)***	–
Patient's address				
Present	3093 (34.9)	5781 (65.1)	1.00	–
Not present	278 (29.1)	678 (70.9)	0.77 (0.66–0.89)***	–
Special instructions				
Given	84 (38.4)	135 (61.6)	1.00	
Not given	3297 (34.2)	6340 (65.8)	0.84 (0.63–1.10)	

Notes: – Variable dropped from the model due to lost statistical significance at multivariable analysis. *0.05>p-value≥0.01. **0.01>p-value≥0.001. ***p-value<0.001.

Discussion

Understanding healthworkers' antibiotic prescribing practices is crucial in designing interventions aimed at antimicrobial stewardship. This study provides an understanding of these practices at 39 government owned lower primary care facilities in three districts in Southwestern Uganda.

Data were collected in the stated three phases to cater for drug leakage or stock outs. The increasing trend in irrational antibiotic prescriptions with the study phases is an indication that medicines stock outs influenced the rationality of antibiotic prescriptions at these levels of care. This finding is comparable with that of other studies conducted in Nigeria.[17,18] The majority of prescriptions were from HC IIIs because these have quite a relatively big catchment area and better service provision as compared to HC IIs. In addition, HC IIIs are many in number than HC IVs in a given HSD.[15] A few antibiotic prescriptions were multi-drug regimens and the median antibiotic-treatment duration was 5 (IQR=5-5) days. This is because the UCG, 2016 recommends a single medicine's use (normally broad spectrum) and for 5 days for many of the diseases managed at these levels of care.[19] A lower rate of irrational prescription occurred in Mbarara district compared to others probably because of the deployment and training of medical and nursing students of different training institutions within Mbarara district to these HCs. The training and presence of students at these HCs could have compelled the qualified healthworkers to prescribe better since they participate in the students' mentorship.

Medical officers had a high rate of rational prescriptions as compared to other cadres with fewer years of training; a finding comparable to other studies.[20,21] Nurses made half the evaluated prescriptions, a similar finding to other studies conducted in Ghana and Uganda.[21–23] This can be attributed to the fact that primary care facilities in Uganda serve majority of the population and are mainly managed by nurses with a few clinical officers at HC IIIs and HC IVs, plus one or two medical officers at HC IVs.[15] Reforms authorising nurses to prescribe medicines have gained momentum in the recent past globally. These reforms were based on several factors like the nurse cadres authorized to prescribe, ranging from highly specialized cadres to all professional nurses; the medicine types to prescribe and the overall regulatory reforms from independent prescribing to a task shift model under the supervision of a physician.[24,25] In Uganda, nurses are not primarily trained to prescribe in general and more so, antibiotics except midwives who are allowed to prescribe a few. According to the National Drug Policy and Authority Act of 1993 as amended in 2000, antibiotics are classified as prescription-only-drugs and the professional cadres authorized to prescribe them are limited to registered medical practitioners, dental surgeons, clinical officers and midwives.[11,16] Despite this, the National Medical Stores continues to supply antibiotics among other medicines and supplies to be used at these levels of care managed by nurses. While the UCGs are provided to guide prescriptions and the general management of patients at these levels of care, they majorly focus on syndromic management further increasing the risk for misdiagnoses and eventual irrational use of antibiotics. To our surprise, nursing assistants who are not qualified healthworkers prescribed 3.9% (552) of the prescriptions evaluated. These findings portray a mismatch in the implementation of policy and practice regarding the antibiotic use in the public healthcare system in Uganda.

A third of antibiotic prescriptions evaluated were rational in reference to the UCG, 2016. This can be attributed to the low utilization of the UCG, limited diagnostic capacity and the truncated professional training of majority of health workers at these levels of care.[21,26] No wonder, recent evidence suggests that most challenges in relation to medicine use in Uganda are due to irrational prescribing practices.[21,27–30] In the present study, the rate of irrational antibiotic prescriptions in pediatric patients was 55% (1085/1973). A survey by Xavier et al[31] and Okello et al[23] reported improper antibiotic prescriptions in pediatric patients of 36.5% and 68.4%, respectively. Although the majority of pediatric (children <12yrs) prescriptions lacked body weight measurements to guide dosing in our study, their rationality was higher (44.9%) than that of adults (35.7%). This is because the UCG offers estimates for dosing based on either a child's age or body weight measurements. In our study, the antibiotic dosages for majority of paediatric prescriptions were estimated from the child's age rather than body weight. Also, this can be attributed to the implementation of the IMCI strategy where healthworkers at these levels of care are trained and provided with guidelines on the management, including prescription of medicines for the childhood illness. Dosing of medicines with the IMCI strategy is also based on either a child's age or body weight.[32] In addition, we also observed that the pediatric medicine stock supply was more consistent than that of adults throughout the study phases. Availability of medicine stock is a determinant for rational

prescription.[17] Our analysis shows that a prescriber's knowledge of components of a prescription predicts rational prescribing. Thus, appropriate knowledge on good prescribing practices by healthcare workers at these levels of care is crucial for antimicrobial resistance stewardship.

On the other hand, the majority of the prescriptions were legibly written (96.7%) and the recording of diagnoses (98.5%) was above the national standard of 85% but still below the WHO standard of 100%[33,34]. In addition, 93.1% (6451) of prescriptions had generic names. This rate also falls within the national standards of more than 85% but below the WHO standard of 100%.[33,34] However, this rate (93.1%) is much higher than the 55% reported in a study that evaluated antibiotic prescribing practices in a rural refugee settlement district in Uganda.[26] For paediatric patients (age ≤12 years), only 916 (46.5%) had the patient's body weight indicated to guide appropriate dosing. Omission of body weight measurements for paediatric patients increases the risk of medication errors including the inappropriate antibiotic dosing, ultimately resulting in sub-optimal patient outcomes.[35]

Amoxicillin was more likely to be used rationally compared to other antibiotics because it is a commonly used as it is readily available, and it is one of the key medicines tracked and healthworkers were trained on its usage by the SPARS under the Ministry of Health.[36] Metronidazole and Doxycycline prescriptions were highly irrational as they were prescribed for almost all diarrheal and uro-genital conditions, some of which were contrary to the UCG guidelines and it needs to be investigated. These findings are comparable with those of studies conducted in Mbarara and Bushenyi districts.[23,29]

The study limitations are that it majorly focused on outpatient antibiotic prescription data and thus did not elucidate the magnitude of inappropriate use of these drugs exhaustively at HC IIIs and IVs which offer inpatient services. The study was not designed to evaluate individual prescriber effects on the reported results. In addition, the study did not assess the appropriateness of the diagnoses, but rather focused on the working diagnoses for the patients and the prescriptions made in that regard.

Conclusion

Our findings show that seven of every 10 antibiotic prescriptions at lower primary care facilities in Uganda are irrational. Half the prescriptions were made by unauthorized personnel (nurses) and many of the pediatric prescriptions did not bear weight measurements to guide appropriate dosing. The observed policy-practice controversy has a great impact on irrational antibiotic prescription and use and is thus a potential driver to antimicrobial resistance and the associated deaths. Also, a prescriber's knowledge of components of a prescription was found to predict rational antibiotic prescribing. Therefore, the development of a standardized antimicrobial prescription curriculum and training on implementation of Standard Treatment Guidelines (STGS) might greatly improve antibiotic use, even with extended prescribing mandate to lower primary care facilities as a way of improving access to health care.

Ethics Approval and Consent to Participate

Ethical clearance was obtained from School of Biomedical Sciences Research Ethics committee (SBS-REC-564) and the Uganda National Council for Science and Technology (HS 2495). Permission to conduct the study was sought from the District Health Officers and in-charges of individual health facilities. The data can be accessed with relevant data protection and privacy regulations.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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