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Prescribing practices in the treatment of wasting: secondary analysis from a randomised trial

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ABSTRACT

Introduction Current guidelines for the outpatient treatment of severe acute malnutrition (SAM) recommend the provision of routine medications to all children at admission and prescribed medications as clinically indicated thereafter. The objective of this study was to describe the amount and purpose of medications prescribed during outpatient SAM treatment and explore the effect of routine antibiotics at admission on subsequent medication prescription.

Methods Medications prescribed during outpatient treatment were described by medication category, time from admission, and diagnoses among children with SAM in a placebo-controlled, double-blind trial of 7-day amoxicillin use. Total medications were compared by parent trial intervention arm (amoxicillin vs placebo) and differences assessed using X^2 and two-sample t-tests.

Results Of the 2399 children enrolled, 74.6% of children received ≥1 prescribed medication during outpatient treatment. Antipyretics/analgesics (44.1% of children), antimalarials (56.6%) and antibiotics (30.0%) were prescribed most frequently. Children who received placebo in the parent trial received fewer total medications (mean difference: −0.80, 95% CI: −0.96 to −0.65) and oral antibiotics (mean difference: −0.96, 95% CI: −0.99 to −0.92) during treatment compared with children who received routine amoxicillin.

Conclusions We found high rates of medication prescription during outpatient treatment for SAM, but fewer total medications and oral antibiotics prescribed to children receiving placebo in the parent trial. Our findings underscore the role of outpatient treatment programmes as an important source of medicine prescription and suggest that provision of antibiotics on a clinically indicated basis for outpatient SAM cases may be a strategy to support prudent antibiotic use in certain settings.

Trial registration number ClinicalTrials.gov Registry (NCT01613547; https://clinicaltrials.gov/ct2/show/NCT01613547).

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Current global guidelines for the outpatient treatment of severe acute malnutrition (SAM) recommend routine medications at admission and prescribed medications as clinically indicated. Little research has been conducted to understand prescribing practices in these settings or how guidelines affect prescribing practices.

WHAT THIS STUDY ADDS

⇒ We found high rates of prescription during SAM treatment. Children who did not receive routine antibiotics at admission received fewer total medications and oral antibiotics during treatment.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our results indicate that clinically indicated prescribing may be a strategy to support more prudent antibiotic use during outpatient treatment of SAM.

INTRODUCTION

Severe acute malnutrition (SAM) affects at least 14 million children under the age of 5 years globally.[1 2] Since 2007, the community-based management of acute malnutrition has allowed for the outpatient treatment of children with SAM and no clinical complications. Outpatient treatment for uncomplicated SAM includes weekly or biweekly follow-up with the provision of ready-to-use therapeutic foods (RUTFs), routine medications (oral antibiotics, antiparasitics and folic acid) given systematically to all children at admission, and medications provided according to clinical indication at any time during nutritional treatment.[3 4] Accordingly, the treatment of children with uncomplicated SAM can be an important source of medication use in settings with a high burden of child morbidity and mortality.

Bacterial infection can complicate SAM,[5–10] and the need to provide routine oral antibiotics during inpatient treatment to reduce the risk of nosocomial infection has historically been clear.[11] Since the adoption of the community-based management approach in 2006, severely malnourished children without evidence of severe infection have been treated on an outpatient basis. The historical provision of routine oral antibiotics regardless of

clinical indication was extended to the outpatient setting; the evidence to support the effectiveness of routine oral antibiotics in outpatient SAM treatment programmes remains mixed.[12 13] In light of the increased risk of antimicrobial resistance, the WHO recommends further research on mass administration of antimicrobial medicines and their impact on resistance to inform future guidelines.[14 15]

Understanding prescribing practices and promoting appropriate medication use are critical to improving clinical outcomes and minimising individual and population harms, particularly in the context of growing antibiotic resistance.[16] This study aimed to describe the amount and appropriateness of medication use among children with uncomplicated SAM during outpatient treatment in Niger, and for the first time, to compare prescribing practices among children who received routine amoxicillin versus placebo at admission to better understand the potential impact of systematic use of routine antibiotics on overall medication use.

METHODS

Study population

We conducted a randomised, double-blind parallel clinical trial in Madarounfa, Niger to assess the effect of routine antibiotic use on nutritional recovery from uncomplicated SAM (ClinicalTrials.gov NCT01613547).[13 17] Briefly, the study enrolled children aged 6–59 months with uncomplicated SAM (defined as weight-for-height z-score (WHZ) <−3 and/or mid-upper arm circumference (MUAC) <115 mm and without clinical complications) between October 2012 and November 2013. Participants were excluded from the trial if they required hospitalisation or there was presence of any degree of nutritional oedema, lived more than 15 km from a study centre, had been admitted to a nutritional treatment programme within the previous 3 months, had any clinical indication requiring immediate antibiotic treatment or had received any antibiotic within the previous 7 days. Sample size was calculated as 1005 children per group, providing 80% power to detect a difference of 5% in nutritional recovery between groups at a two-sided α=0.05 and assuming 80% nutritional recovery in the amoxicillin group. With a potential loss to follow-up rate of 20%, a final sample size of 1206 children per group was estimated. The 2399 children randomised in the parent trial who completed at least one follow-up visit were included in this secondary analysis of prescribing practices.

Parent trial procedures

Children were individually randomly assigned in a 1:1 ratio in blocks of 6 using a random number generator to receive 7 days of amoxicillin (80 mg/kg/day) or placebo at admission into the outpatient therapeutic feeding programme. Randomisation codes were kept in sealed envelopes and opened by the study physician at enrolment. Study physicians, nurses and participants were blinded, as amoxicillin and placebo were indistinguishable in packaging and colour. All children received RUTF (170/kcal/kg/day; Plumpy' Nut, Nutriset) and routine folic acid and antihelminthic treatment (albendazole) at admission, as per the standard of care at the time of the study. Participants underwent a rapid diagnostic test (RDT) for malaria (SD Bioline Malaria Ag P.f, Standard Diagnostics, Republic of Korea) and anaemia assessment (Hemocue Hb 301, HemoCue, Angelholm, Sweden) at admission, with treatment provided as indicated. Follow-up in the nutritional programme was conducted on a weekly basis for a minimum of 3 weeks and a maximum of 8 weeks until children achieved nutritional recovery (defined as WHZ ≥−2 on two consecutive visits, MUAC ≥115 mm, no acute complication nor oedema for at least 7 days, and completion of all antibiotic and antimalarial treatments), were transferred for inpatient treatment, were lost to follow-up (defined as missing more than two consecutive visits) or died. In addition to scheduled weekly follow-up visits, caregivers were encouraged to return to the health centre with their children for care at any time in the event of clinical deterioration. At all visits, study staff assessed anthropometry (body weight, height/length and MUAC), completed a physical examination and medical history, and confirmed receipt of any medical consultations or treatment since the previous visit. As per the parent trial protocol, randomised group assignment (amoxicillin vs placebo) was unblinded by the field investigator when antibiotic treatment was clinically indicated within the first 2 weeks of nutritional treatment to determine the correct course of treatment according to randomisation. All clinical care was provided free of charge.

Parent trial outcomes

The parent trial examined the effect of routine amoxicillin compared with placebo on nutritional recovery in children treated on an outpatient basis for SAM.[13 17] Secondary outcomes included non-response (defined as nutritional recovery not met at 8 weeks), death from any cause, default (defined as three or more missed consecutive visits) and transfer to inpatient care. There was no significant difference in nutritional recovery, non-response, death or default comparing amoxicillin with placebo up to 8 weeks.[13] Amoxicillin reduced the risk of transfer to inpatient care by 14% (95% CI: 2% to 24%) during outpatient treatment for SAM. However, an analysis of the trial from admission to 12 weeks post-admission found that there was no difference in the risk of transfer to inpatient care comparing amoxicillin with placebo by 12 weeks post-admission.[17]

Definition of outcomes

The primary outcome of this analysis was the number of medications prescribed during outpatient treatment, defined as any medication prescribed outside the parent trial's primary intervention (ie, routine amoxicillin vs placebo at admission) and routine folic acid and

albendazole. To understand total medications provided throughout nutritional treatment including the parent trial's primary intervention, we further defined 'total medications' as the number of prescribed medications plus routine amoxicillin, as received by the randomised treatment group of the parent trial.

To describe which medications were being prescribed in this setting, prescribed medications were assigned to categories according to use (online supplemental table 1) and route of administration (oral, injectable and local). We identified combinations of prescribed medications when more than one category of medication was prescribed at the same visit. To describe prescribing practices over time during outpatient treatment, we reported prescribed medications and total medications at admission, in weeks 1–2 and in weeks 3–8, and according to calendar month of prescription. Finally, we examined appropriate medication use by evaluating the consistency of treatments with national clinical guidelines, for which we reported medication categories by clinical diagnosis at the time of visit for medication categories having more than 10 prescriptions in the parent trial. Clinical malaria diagnosis was compared with RDT positive results at the same visit.

Statistical analysis

We presented counts and percentages of children receiving one or more prescribed medications by category and periods of follow-up during nutritional treatment (admission, weeks 1–2 and weeks 3–8). We compared categorical outcomes across periods of follow-up using a X^2 test and continuous outcomes using one-way analysis of variance. To describe the seasonality of medication prescriptions, we estimated the average number of prescriptions per person-month by medication category and calendar month.

Finally, to explore the impact of routine antibiotic administration on prescribing practices, we compared mean total medications, defined as routine amoxicillin plus prescribed medications, and prescribed medications by category by parent trial intervention arm (routine amoxicillin vs placebo). Differences between the trial intervention arm were determined using two-sample t-tests for continuous outcomes, with estimation of crude mean differences and 95% CIs.

RESULTS

Nearly three-quarters of randomised children (n=1790, 74.6%) received one or more prescribed medications during nutritional treatment for uncomplicated SAM, with an average 1.12 prescriptions given at each visit (table 1 and online supplemental table 1). More than half of children (n=1239, 53.9%) admitted to outpatient treatment without clinical complications requiring hospitalisation received at least one prescribed medication for a clinical indication at admission (figure 1). The most common medications prescribed during nutritional treatment included antimalarials (56.6% of children), antipyretics/analgesics (ie, paracetamol, 44.1% of children) and local antibiotics, primarily tetracycline (21.2% of children). Of all visits during which a medication was prescribed, 40.6% of visits included prescriptions for multiple medications, primarily antimalarials in combination with paracetamol, either as a pair or with further medications (1015 of 1326, 76.6% of combinations) (figure 2). During the calendar year, the frequency of antimalarial and paracetamol prescriptions increased from August through October, consistent with the peak malaria season in Niger (figure 3).[18]

To describe appropriateness of prescribed medications, we compared prescriptions with clinical diagnoses recorded at the same visit and found the majority of prescriptions to be correctly aligned with recorded diagnoses, as per national guidelines (table 2). Nearly all antimalarials were accompanied by a malaria diagnosis by RDT at the same visit (98.2% of antimalarial prescriptions). Oral antibiotic prescriptions were most frequently given with diagnoses of respiratory infection (60.1% of visits with an oral antibiotic) or purulent otitis (22.7%). Local antibiotic prescriptions consistently followed a diagnosis of conjunctivitis (97.4%), and iron folic acid prescriptions primarily accompanied anaemia (98.3%). The national guidelines recommend oral rehydration solution for the treatment of diarrhoea[19]: 5.6% (3 of 35) of visits with a diagnosis of simple diarrhoea had a prescription for oral rehydration solution.

Finally, to understand whether routine amoxicillin impacts medication use during treatment, total medications (defined as routine amoxicillin plus prescribed medications) were compared between children who received routine amoxicillin at admission versus children who received placebo in the parent trial. Children randomised to placebo at admission in the parent trial received on average 0.80 fewer total medications (95% CI −0.96 to −0.65) and 0.96 fewer oral antibiotics (95% CI −0.99 to −0.92) throughout nutritional treatment, compared with children assigned to routine amoxicillin (table 3). Only 13.8% of children initially randomised to placebo ever required an oral antibiotic later during follow-up, primarily associated with a diagnosis of respiratory infection (59.6% of visits with an oral antibiotic) or purulent otitis (23.3%).

DISCUSSION

We provide the first report describing prescribing practices in the context of outpatient nutritional treatment of SAM using high-quality prescription data collected within a randomised trial in Niger. These data confirm a large proportion of children received prescribed medications during nutritional treatment, with nearly three-quarters of children enrolled receiving at least one prescribed medication during nutritional treatment. More than half of children received a prescribed medication at admission, despite an 'uncomplicated' clinical designation required

Table 1 Children receiving prescribed medications during outpatient SAM treatment, by time period during follow-up (N=2399)

	All follow-up (admission–week 8)	At admission	Weeks 1–2	Weeks 3–8	P value*
Children receiving ≥1 prescription, no (%)					
Any medication	1790 (74.6)	1293 (53.9)	786 (32.8)	758 (31.6)	<0.01
Antibiotic	720 (30.0)	184 (7.7)	272 (11.3)	356 (14.8)	<0.01
Injectable	3 (0.1)	0 (0.0)	1 (0.0)	2 (0.1)	0.37
Oral	284 (11.8)	2 (0.1)	118 (4.9)	185 (7.7)	<0.01
Amoxicillin	247 (10.3)	0 (0.0)	99 (4.1)	162 (6.8)	<0.01
Local	509 (21.2)	182 (7.6)	164 (6.8)	200 (8.3)	0.15
Anti-inflammatory/analgesic	15 (0.6)	2 (0.1)	6 (0.3)	8 (0.3)	0.17
Antihistamine	5 (0.2)	1 (0.0)	2 (0.1)	2 (0.1)	0.82
Antimalarial	1358 (56.6)	1135 (47.3)	122 (5.1)	291 (12.1)	<0.01
Antipyretic/analgesic	1058 (44.1)	710 (29.6)	212 (8.8)	343 (14.3)	<0.01
Injectable corticosteroid	5 (0.2)	0 (0.0)	2 (0.1)	4 (0.2)	0.14
Iron folic acid	421 (17.5)	13 (0.5)	344 (14.3)	185 (7.7)	<0.01
Local antifungal, antiparasitic, antiseptic	181 (7.5)	51 (2.1)	67 (2.8)	88 (3.7)	<0.01
Oral antifungal	84 (3.5)	19 (0.8)	43 (1.8)	31 (1.3)	<0.01
Oral antiparasitic, antiprotozoan	4 (0.2)	0 (0.0)	3 (0.1)	1 (0.0)	0.17
Oral rehydration solution	9 (0.4)	2 (0.1)	5 (0.2)	2 (0.1)	0.37
Other medications	4 (0.2)	0 (0.0)	2 (0.1)	2 (0.1)	0.37
Prescribed medications received, mean (SD)	2.01 (1.90)	0.88 (0.93)	0.47 (0.79)	0.66 (1.22)	<0.01
Prescribed medications per visit, mean (SD)	1.12 (0.80)	0.88 (0.94)	0.42 (0.67)	0.46 (0.76)	<0.01

*P values derived from X^2 test (categorical outcomes) and one-way ANOVA (continuous outcomes).
ANOVA, analysis of variance; SAM, severe acute malnutrition.

for outpatient treatment. In addition to observing a high number of prescribed medications overall and at admission in particular, we found prescribed medications were frequently given in combination throughout nutritional treatment, with children receiving on average 1.1 prescriptions per visit. Given that at least 14 million children suffer from SAM each year,[2] this finding suggests outpatient treatment programmes can be an important source of prescribed medications in settings with a high SAM burden in addition to the systematically prescribed oral antibiotics.

The most common medications provided during nutritional treatment in this setting were antimalarials, antipyretics/analgesics and local antibiotics, consistent with the known infectious disease burden in Niger where childhood mortality is associated with diarrhoeal disease, pneumonia and malaria.[20] Malaria morbidity can be particularly high in young children in Niger,[21] with 52% of children aged 3–59 months in the study region found to be parasitaemic in a household prevalence survey at the end of the malarial season in 2016.[22] In the present analyses, we observed an increase in the prescription of antimalarials and paracetamol coinciding with the peak malarial season (approximately July–October).[18] Our findings are consistent with another report of prescribing practices among children under 5 years of age in general outpatient care in the region: in a study assessing prescribing practices of doctors in an outpatient clinic in Owerri, Nigeria, antimalarials, analgesics/antipyretics and antibiotics were also the most common medication types prescribed, each of which was prescribed to over 50% of children presenting to the general outpatient clinic.[23]

Prescribing practices were well aligned with national treatment guidelines.[19] National treatment guidelines state that a positive malaria RDT is needed for antimalarial prescriptions, which we observed in 98.2% of antimalarial prescriptions. Guidelines also state that diagnosis of a respiratory infection or purulent otitis, which accompanied more than 80% of oral antibiotic prescriptions, warranted oral antibiotic use.[24] It was, however, noted that prescription of oral rehydration solution (Resomal) was unexpectedly low in this setting, with only 5.6% of children diagnosed with simple diarrhoea receiving rehydration therapy. Current guidelines in Niger recommend oral rehydration solution for all diarrhoea cases, regardless of aetiology, as long as they do not require hospitalisation.[24] This analysis demonstrates that, in general, medications in this setting were appropriately prescribed by clinical indication. Medication prescriptions can be

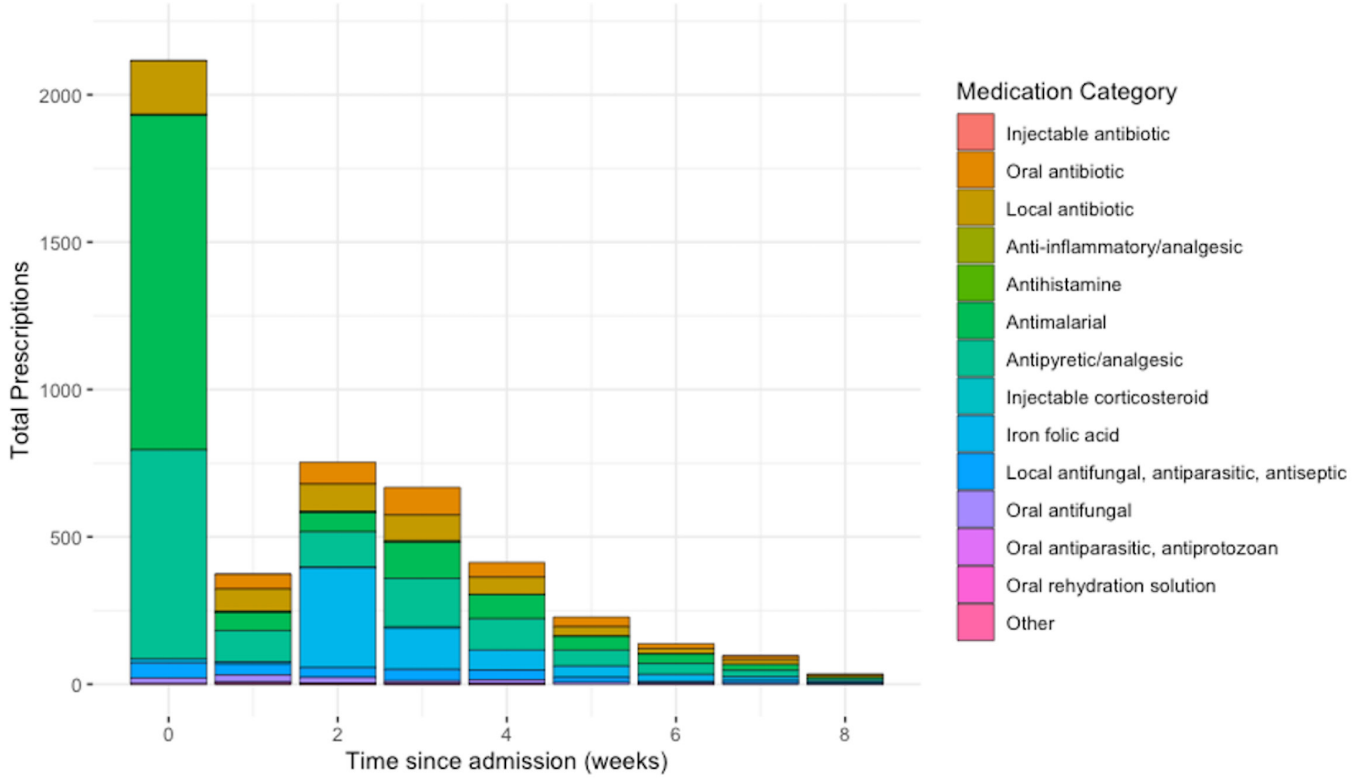

Figure 1 Number of prescribed medications by medication category over time since admission to outpatient nutritional treatment programme.

carefully monitored to avoid potential toxicities and ensure effective allocation of medications and medical supplies, particularly in resource-poor contexts.

Monitoring of antibiotic prescriptions is of particular importance due to the growing concerns of global antibiotic resistance.[14] Guidelines for outpatient SAM

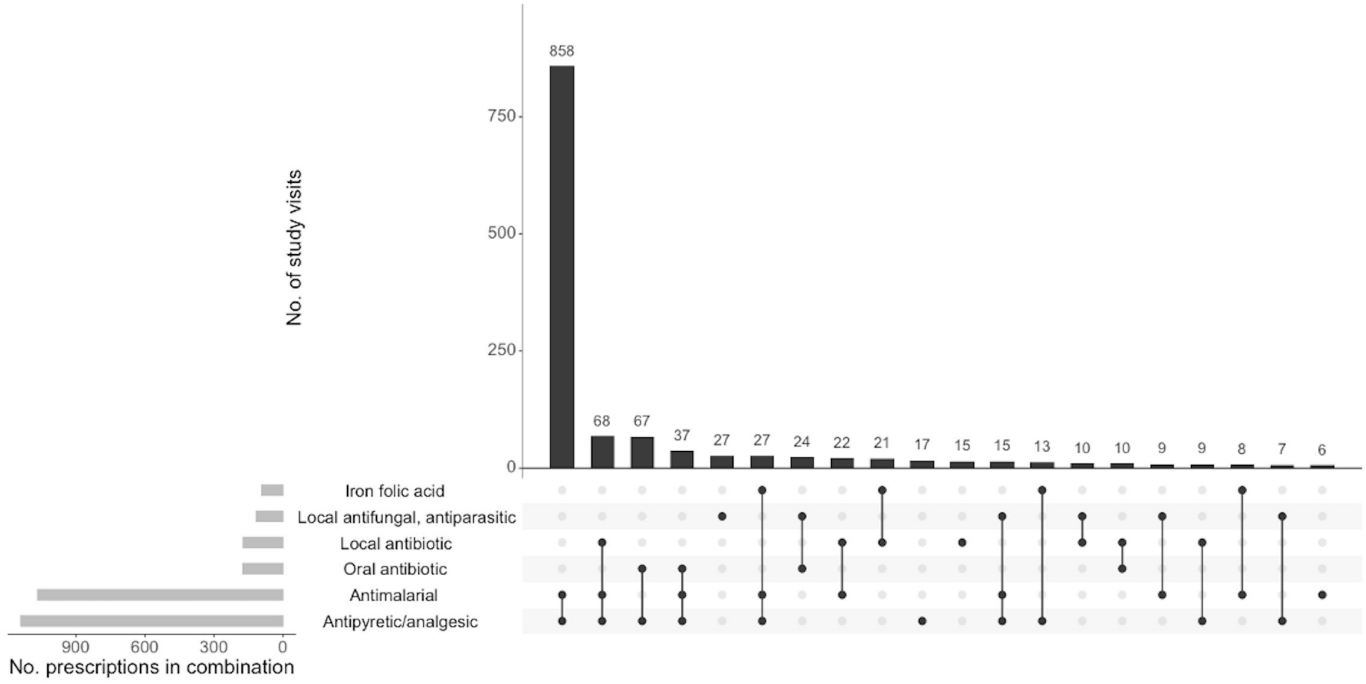

Figure 2 Number of study visits at which a given combination of medications was prescribed at the same visit during outpatient treatment. Plot includes only combinations that have at least one of the top six medication categories found in combination. Single dots indicate combinations with a medication category not included.

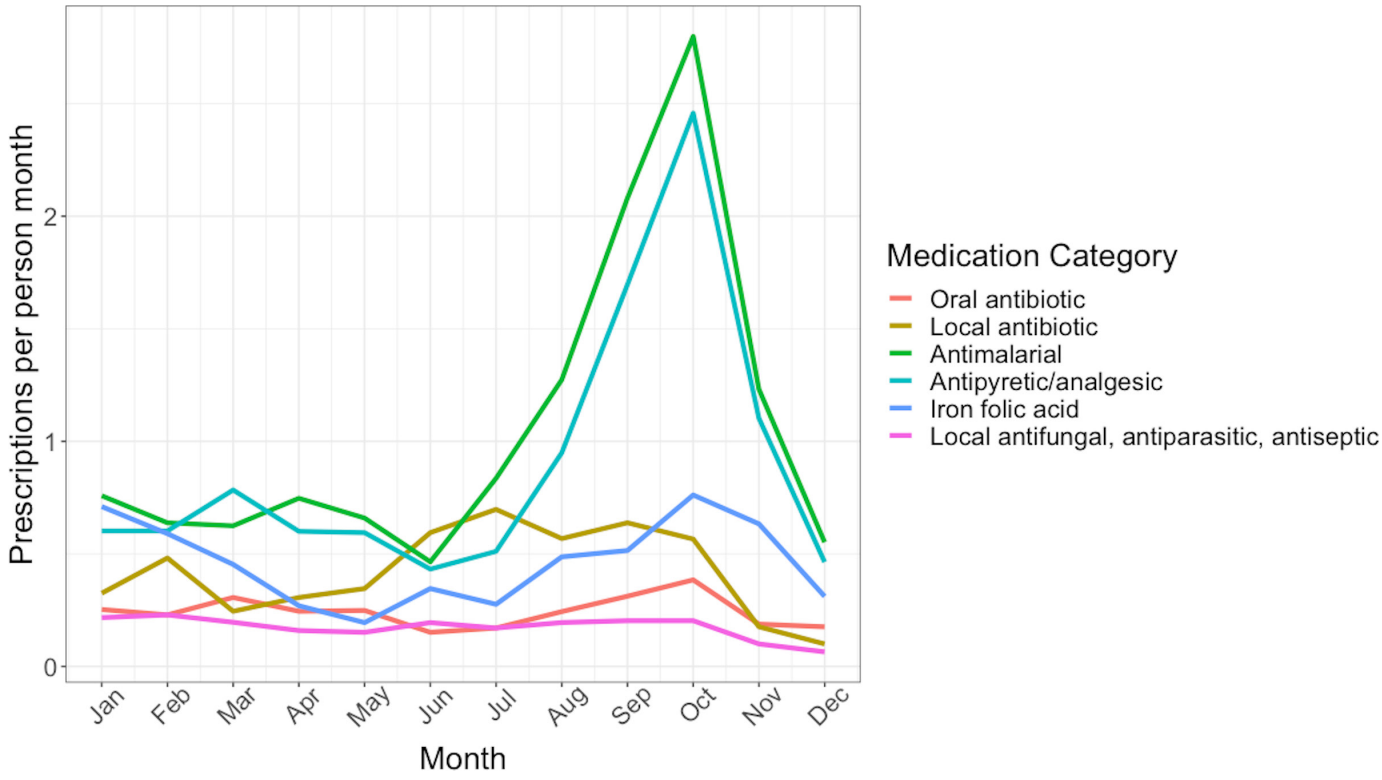

Figure 3 Prescribed medications given per person-month of follow-up, by medication category and calendar month.

treatment currently recommend the provision of routine antibiotics; outpatient SAM treatment is therefore a potentially important source of these medications.[25] To better understand the impact of routine amoxicillin on medication prescription in Niger, we looked at differences in the number of total medications received by children randomised to routine amoxicillin versus placebo in the parent trial. We found that children who received placebo received on average fewer total medications and fewer oral antibiotics than children who received routine amoxicillin. Only 13.8% of children randomised to placebo required an oral antibiotic later during nutritional treatment, suggesting that providing antibiotics on clinical indication (eg, not routinely at admission) could reduce the number of total medications and oral antibiotics prescribed in SAM treatment programmes.

Any global recommendation guiding the provision of routine amoxicillin is necessarily complex and ideally must balance both individual and public health risks and benefits. Two large randomised controlled trials have examined the impact of routine amoxicillin on nutritional recovery. In the parent trial of this analysis, there was no significant benefit of routine amoxicillin on nutritional recovery at programme discharge[13] or on sustained recovery during extended follow-up post-discharge,[13] though a short-term increased risk of hospitalisation among children receiving placebo compared with routine amoxicillin was reported.[13] In Malawi, routine amoxicillin improved nutritional recovery, but the population was characterised by a uniquely high burden of HIV infection and kwashiorkor.[12]

Another key public health consideration for the use of routine amoxicillin must be antibiotic resistance. The WHO Essential Medicines List for Children[26] includes amoxicillin as a first-line antibiotic for critical diagnoses such as pneumonia and sepsis. Any recommendation for the routine administration of amoxicillin should therefore be considered carefully to avoid overuse or misuse, so that antibiotic treatment may remain effective for the long term. In the parent trial of this analysis, amoxicillin resistance was found in 35% of stool isolates with enterobacteria and 66% of blood isolates with enterobacteria, indicating relatively important levels of resistance in this setting.[27] In a study of acquisition of drug-resistant bacterial strains in this population, receipt of amoxicillin increased the risk of acquiring extended-spectrum beta-lactamase producing Enterobacteriaceae 1 week after provision compared with placebo, though this difference was short-lived.[28] Beyond resistance, routine use of amoxicillin may additionally have important implications for programme costs and logistics. Although the direct unit cost of a course of antibiotics may be relatively small,[29] understanding the total costs associated with providing systematic antibiotic requires a comprehensive analysis of treatment for acute malnutrition, including costs associated with trained medical personnel and a consistent supply chain to local health centres. In resource-constrained settings, such additional demands on programmes could have the potential to limit programme coverage and reduce the number of children in need who receive nutritional treatment. If even small increases in programme coverage can be achieved by removing the

Table 2 Number of prescribed medications given during outpatient SAM treatment, by medication category and concurrent clinical diagnosis*

	Isolated fever/ hypothermia (N=195)	Malaria (N=1539)	Rhinitis (N=43)	Respiratory infection (N=214)	Conjunctivitis (N=558)	Purulent otitis (N=87)	Mycosis (N=140)	Wound (N=71)	Skin infection (N=53)	Simple diarrhoea (N=35)	Anaemia (N=1186)
Local antibiotic (N=568)	11 (1.9%)	96 (16.9%)	2 (0.4%)	16 (2.8%)	553 (97.4%)	13 (2.3%)	8 (1.4%)	7 (1.2%)	6 (1.1%)	5 (0.9%)	62 (10.9%)
Oral antibiotic (N=331)	11 (3.3%)	46 (13.9%)	1 (0.3%)	199 (60.1%)	20 (6.0%)	75 (22.7%)	3 (0.9%)	8 (2.4%)	33 (10.0%)	10 (3.0%)	17 (5.1%)
Oral antifungal (N=96)	3 (3.1%)	12 (12.5%)	0 (0%)	3 (3.1%)	5 (5.2%)	0 (0%)	94 (97.9%)	0 (0%)	0 (0%)	1 (0.01%)	9 (9.4%)
Local antifungal, antiparasitic (N=227)	11 (4.9%)	34 (15.0%)	0 (0%)	6 (2.6%)	19 (8.4%)	26 (11.5%)	70 (30.8%)	69 (30.4%)	28 (12.3%)	4 (1.8%)	24 (10.6%)
Anti-inflammatory (N=16)	0 (0%)	2 (12.5%)	0 (0%)	2 (12.5%)	4 (25%)	1 (6.3%)	0 (0%)	1 (6.3%)	3 (18.8%)	0 (0%)	3 (18.8%)
Antimalarial (N=1569)	46 (2.9%)	1529 (97.5%)	2 (0.1%)	43 (2.7%)	107 (6.8%)	6 (0.4%)	21 (1.3%)	17 (1.1%)	3 (0.2%)	16 (1.0%)	555 (35.4%)
Antipyretic/ analgesic (N=1328)	186 (14.0%)	1023 (77.0%)	43 (3.2%)	99 (7.5%)	89 (6.7%)	16 (1.2%)	21 (1.6%)	14 (1.1%)	6 (0.5%)	17 (1.3%)	375 (28.2%)
Iron folic acid (N=648)	7 (1.1%)	41 (6.3%)	5 (0.8%)	12 (1.9%)	21 (3.2%)	2 (0.3%)	5 (0.8%)	0 (0%)	2 (0.3%)	3 (0.5%)	637 (98.3%)
Oral rehydration solution (N=9)	0 (0%)	2 (22.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (33.3%)	0 (0%)

*Multiple diagnoses could be recorded at each visit; therefore, row percentages do not sum to 100%.
SAM, severe acute malnutrition.

Table 3 Total medications by trial intervention arm and medication category

	Amoxicillin (N=1199)	Placebo (N=1200)	Mean difference, placebo–amoxicillin (95% CI)*
Number of prescriptions, mean (SD)			
All medications	2.91 (1.85)	2.11 (1.95)	−0.80 (−0.96, −0.65)
Antibiotics	1.32 (0.65)	0.43 (0.70)	−0.89 (−0.95, −0.84)
Injectable	0.002 (0.06)	0.002 (0.04)	0.00 (−0.004, 0.004)
Oral	1.12 (0.40)	0.16 (0.43)	−0.96 (−0.99, −0.92)
Amoxicillin	1.10 (0.33)	0.13 (0.38)	−0.96 (−0.99, −0.93)
Amoxicillin post-admission	0.10 (0.33)	0.13 (0.38)	0.04 (0.01, 0.07)
Local	0.21 (0.44)	0.27 (0.52)	0.07 (0.03, 0.11)
Anti-inflammatory/analgesic	0.009 (0.10)	0.004 (0.06)	−0.005 (−0.012, 0.002)
Antihistamine	0.003 (0.07)	0.002 (0.04)	−0.002 (−0.006, 0.003)
Antimalarial	0.65 (0.65)	0.66 (0.64)	0.01 (−0.04, 0.07)
Antipyretic/analgesic	0.56 (0.72)	0.55 (0.73)	0.00 (−0.06, 0.05)
Injectable corticosteroid	0.001 (0.03)	0.004 (0.08)	0.003 (−0.001, 0.008)
Iron folic acid	0.24 (0.64)	0.30 (0.80)	0.06 (0.005, 0.12)
Local antifungal, antiparasitic, antiseptic	0.09 (0.38)	0.10 (0.39)	0.01 (−0.02, 0.04)
Oral antifungals	0.04 (0.21)	0.04 (0.23)	0.01 (−0.01, 0.02)
Oral antiparasitic, antiprotozoan	0.003 (0.06)	0 (0)	−0.003 (−0.0006, 0)
Oral rehydration solution	0.004 (0.06)	0.003 (0.06)	−0.001 (−0.006, 0.004)
Other medications	0.001 (0.03)	0.003 (0.05)	0.002 (−0.002, 0.005)

*Mean difference and 95% CI derived from t distribution.

requirement for routine administration of antibiotics, the more streamlined strategy may help to reach more children in need and has been shown to be more cost-effective than routine antibiotic therapy.[30]

This study had several strengths and limitations. First, the analysis was set within a large, randomised trial with systematic data collection of all prescribed medications. Second, the parent trial provided the unique opportunity to pair data on medication prescriptions with diagnoses at the time of visit. This allowed us to examine the appropriateness of medication prescriptions and provide new information on adherence to national guidelines. In addition to these strengths, we note the limitation that our data only included prescriptions dispensed by the outpatient treatment programme, and no local pharmacies were included. However, care seeking outside of the study was limited given the high quality of care provided free of charge at the study sites, and we therefore very likely captured all medications prescribed during follow-up. Study generalisability may also be limited. The study was implemented at health centres run by Médecins sans Frontières, which may differ from other sites in terms of medicine availability and personnel training.

Conclusion

In conclusion, we found a very high number of prescribed medications during outpatient treatment for SAM. Prescription practices were generally consistent with the infectious disease burden of Niger and national treatment guidelines, illustrating that indicated medications were prescribed appropriately. Given the lower rate of antibiotic prescription among children randomised to receive placebo at enrolment, these data suggest that provision of antibiotics on a clinically indicated basis for uncomplicated SAM cases may be a possible strategy to support more prudent antibiotic use in certain settings.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the trial protocol was approved by the Comité Consultatif National d'Éthique, Niger, and the Comité de Protection des Personnes, Île-de-France XI, Paris. An independent data and safety monitoring board reviewed and evaluated trial progress, including safety events. Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available upon reasonable request. The deidentified dataset, code book and analytical code supporting this research will be made available from the corresponding author following a reasonable submitted request.

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