

# Antibiotic Prescription Rationality And Associated In-Patient Treatment Outcomes In Children Under-Five With Severe Pneumonia At Bwizibwera Health Center IV, Mbarara District, South-Western Uganda

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## Research Article

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# Abstract

**Background:** Pneumonia is a major cause of morbidity and mortality in children under five. Antibiotic treatment must be started immediately in children with pneumonia. The irrational use of antibiotics may increase morbidity and mortality in children with pneumonia. Pneumonia accounted for approximately 16 % of the 5.6 million under-five deaths world wide in 2016. In Uganda, it kills approximately 2,400 children per year. Early diagnosis and appropriate case management with rational use of antibiotics remain the most effective intervention to reduce pneumonia-related mortality. This study aimed at determining antibiotic prescription rationality and associated in-patient treatment outcomes in children aged 2-59 months with severe community-acquired pneumonia at Bwizibwera Health Centre IV from 1<sup>st</sup> May 2018 to 30<sup>th</sup> April 2019.

**Methods:** We conducted a retrospective cohort design; data were collected from in-patient records of all children aged 2-59 months with severe community-acquired pneumonia who met the eligibility criteria for a period of one year. Data abstraction template was used for data collection. Health care records of children aged 2-59 months who had other co-morbidities and were on medication that could influence or impact on in-patient treatment outcomes from 1st May 2018 to 30th April 2019 were excluded. Data was entered and analyzed using Epi-info v 7.2 and STATA v 13.0 respectively, Descriptive statistics were reported and Chi-square test was used to compare the proportions.

**Results:** Of the total records of children retrieved and screened (N = 847), 229 prescription records of children fulfilled inclusion criteria, 57 (24.9 %) had rational prescriptions with good outcomes and 172 (75.1 %) had irrational prescriptions with 10 (4.4 %) having unfavorable outcomes. The majority (73.7 %) of those who received rational prescription were on treatment with a combination of benzyl penicillin plus gentamycin while (26.3 %) were on ampicillin plus gentamycin. The majority (32.4 %) of patients with good treatment outcomes were aged 6 – 11 months. This age category also doubled as the group that experienced the highest percentage (40.0 %) of unfavorable outcomes.

**Conclusion:** The majority of children 172 (75.1%) had received irrational antibiotic prescriptions. There were no statistically significant associations between patient characteristics and treatment outcomes.

## Background

Pneumonia is a form of acute respiratory infection that affects the lungs. When an individual has pneumonia, the alveoli are filled with pus and/or fluid, which make breathing painful and limits oxygen intake [1]. In 2016, pneumonia accounted for approximately 16 % of the 5.6 million under-five deaths, killing around 880,000 children. Most of these children were less than 2 years [2]. In 2015, pneumonia killed 920,136 children under the age of five, accounting for 16% of all deaths in this age group and is most prevalent in South Asia and sub-Saharan Africa [3]. In Uganda, it kills approximately 2,400 children per year [4].

Early diagnosis and appropriate case management with rational use of antibiotics remain the most effective intervention to reduce pneumonia-related mortality. Unfortunately, critical inequities in the access to antibiotics and health services exist in most developing countries, often leading to irrational medicines use. Irrational antibiotic use involves their use for incorrect indications, at incorrect doses, or for inappropriate durations [5]. Irrational use of antibiotics can take different forms; inappropriate prescriptions, over and under-prescribing, polypharmacy, unreasonable use of expensive medicines and inappropriate use [6]. Antibiotics are among the most prescribed medicines in in-patient, with almost half the prescriptions being irrational [3]. The irrational use of antibiotics may increase morbidity and mortality in children with pneumonia [4]. Rational use of antibiotics is important element in attaining quality of health and medical care [5]. Inappropriate antibiotics use has resulted in increase in development of drug resistance pathogens with high implication in terms of morbidity and mortality [6]. Much as the number of prescriptions for antibiotics for children decreased, the use of broad-spectrum antibiotics increased at the same time [7, 8]. Antibiotics are the most commonly prescribed medicines in hospitals, However, excessive and inappropriate use of antibiotics leads to increased drug resistance [9]. Limited data on the rationality of antibiotic prescriptions and its associated in-patient treatment outcomes, Therefore, this study was aimed at assessing antibiotic prescriptions rationality and its association with in-patient treatment outcomes for children aged 2–59 Months with severe community-acquired pneumonia at Bwizibwera Health Center IV, Mbarara District, in South-Western Uganda.

## Methods

### Study setting

The study was conducted at Bwizibwera Health Centre IV, Mbarara District in South-western Uganda. Bwizibwera H/C IV is a primary care facility owned by the government of Uganda. It is located about 25 kilometres from Mbarara town on Ibanda road. Bwizibwera H/C IV has two medical officers, two clinical officers, a team of midwives and nurses who offer diagnostic and treatment services for common illnesses. The same team of health workers and support staff also provide antenatal care, acute medical, emergency obstetric care and surgical services. The Health Centre provides medical services for free of charge to patients. The medicines in this Health facility are supplied by the National Medical Stores under the supervision of MOH. Antibiotics are among the most frequently prescribed medicine in this Health facility.

### Design of the study

A retrospective cohort for a period of one year (from 1st May 2018 to 30th April 2019), this design was chosen because it minimizes the rate of change in behavior for prescribers that is likely to happen in a prospective cohort.

The prescription rationality was evaluated in reference to the Uganda Clinical Guidelines and a modified criteria set by Badar; *et al* [10].

A prescription was **rational** if the antibiotic prescribed is appropriate for the indication, in the right dose, frequency, duration and route of administration as guided by the UCG.

A prescription was **irrational**, if it was not appropriate for any one of the following; the indication, dose, frequency, duration and route of administration as guided by the UCG.

The prescription was **questionable** when insufficient clinical or laboratory data exists to clearly categorize as rational or irrational prescriptions.

## **Study population**

These were health care records of children aged 2–59 months with severe community acquired pneumonia who were admitted from 1st May 2018 to 30th April 2019.

## **Data collection procedure**

The data extraction form was developed in reference to the UCG on the management of severe pneumonia and the criteria for evaluating the prescriptions was used to record all information about each child from the selected records. The data extraction tool had information on the child's social demographic, clinical presentation on admission, date of admission, and subsequent days of follow-up, duration of hospitalization, complications, referrals out of the facility/date of discharged, prescribed treatment regimens on the daily basis that was evaluated for; rationality, de-escalation, change from intravenous to oral regimens, and finally deaths. Data was retrieved by the principal investigator and trained research assistants.

## **Data analysis**

Data was entered and analyzed using Epi-info v 7.2 and STATA v 13.0 respectively. Descriptive statistics were reported and Chi-square test was used to compare the proportion.

## **Ethical considerations**

Ethical clearance was obtained from Faculty of Medicine Research Committee (FRC) and MUST-Research Ethics Committee (REC). Permission was sought from the District Health Officer and the in-charge Bwizibwera H/C IV to access health care records of children aged 2–59 months prior to data collection. Confidentiality was ensured by coding the data abstraction templates instead of using names. The data collected were kept under key and lock and accessed by the research team only. Soft data was kept in a computer with a password known only by the research team.

## **Results**

A total of 847 records of children were retrieved and screened, 229 records were included for data collection and analysis. A total of 618 records of children were excluded as follows; 431 records had no

diagnosis of severe pneumonia, 183 records had a diagnosis of severe pneumonia with other comorbidities and 4 records had no diagnosis indicated.

## 4.2 Socio-Demographic Characteristics

**Table 1: Socio-demographic characteristics of the study population**

Characteristic	N=229	Frequency, n (%)
<b>Mean age in months (SD)</b>		15.6 (11.9)
<b>Age categories in months</b>		
2-5		35 (15.3)
6-11		75 (32.8)
12-23		58 (25.3)
24-59		61 (26.6)
<b>Gender</b>		
Female		119 (52.0)
Male		110 (48.0)
<b>Sex of next of kin</b>		
Female		212 (92.6)
Male		17 (7.4)
<b>Referred from lower health facility</b>		
No		223 (97.4)
Yes		6 (2.6)

From Table 1 above; the mean age of children was 15.6 months, with the largest group 75 (32.8 %) between the age of 6–11 months. The majority of children 119 (52.0%) were female. Female care takers dominated being next of kin 212 (92.6%), and only 6 (2.6%) were referred from lower health facilities.

### 4.3 Proportion of children 2–59 months that received rational antibiotic prescriptions

In this analysis, a child was considered to have rational antibiotic prescription if he or she received right regimen for right: indication, route of administration, dose, dose frequency, duration of treatment.

Note: the following parameters were not analyzed for the proportion:

1. Right indication; because our study narrowed to all children 2–59 months with severe pneumonia. This means we already had the clear indication for our study. All the 229 children had severe pneumonia as reflected in inclusion criteria.
2. The right dose; according to UCG dose is based on weight. Therefore, it could not be ascertained, whether it was appropriate dose for the child age because the in-patient register did not have the weight of these children indicated, therefore, according to the dose all the 229 children had questionable prescriptions because some clinical information was lacking to categorize as rational or irrational prescriptions.
3. Route of administration; all the regimens were injectable, both rational and irrational prescriptions had the right route of administration.

Table 2  
Antibiotic prescription rationality

<b>Rational prescription</b>	<b>Frequency n (%)</b>
No	172 (75.1)
Yes	57 (24.9)
<b>Total</b>	<b>229 (100)</b>

Out of the 229 children whose records were retrieved and analyzed, 57 (24.9%) had rational prescription and were treated with the recommended first line antibiotic combinations for treatment of severe pneumonia i.e. ampicillin plus gentamicin or benzyl penicillin plus gentamicin.

Of the 57 rational prescriptions, 42 (73.7%) were of benzyl penicillin plus gentamycin while the other 15 (26.3%) were of ampicillin plus gentamycin.

Table 3: Description of different components of rational antibiotic prescription

<b>Variable</b>	<b>Frequency n (%)</b>
<b>Right regimen</b>	
No	172 (75.1)
Yes	57 (24.9)
<b>Duration (continued for at least 5 days)</b>	
No	40 (70.2)
Yes	17 (29.8)
<b>Frequency of administration</b>	
No	3 (5.3)
Yes	54 (94.7)

The majority 172 (75.1%) did not have a rational prescription for regimen. while 57 (24.9 %) had it. Of those with rational prescription, only 17 (29.8 %) had a rational duration prescribed as per records. Further still, most 54 (94.7 %) had a rational prescribed frequency of administration.

### **Stratification of rational antibiotic prescription by age and gender**

Table 4: Stratification of rationality of antibiotic prescription by age and gender

<b>Variable</b>	<b>Irrational prescription, n (%)</b>	<b>Rational prescription, n (%)</b>	<b>P-value</b>
<b>Age categories (months)</b>			0.347
2-5	31 (18.0)	4 (7.0)	
6-11	44 (25.6)	31 (54.4)	
12-23	47 (27.3)	11 (19.3)	
24-59	50 (29.1)	11 (19.3)	
<b>Gender</b>			0.671
Female	92 (53.5)	27 (47.4)	
Male	80 (46.5)	30 (52.6)	

Rational antibiotic prescription was stratified by age. Analysis revealed that of the 57 with rational prescriptions, the majority (54.4%) were between the ages of 6–11 months. Of those with irrational prescriptions, the majority (29.1%) were aged between 24–59 months.

### 4.3 In-Patient treatment outcomes

In this analysis, a child was considered to have an unfavorable outcome if he or she had any of the following outcomes: developed complication, referred to hospital, died, or were discharge on request. A child was considered to have a good outcome if he or she had improved and discharged home. (See Table 5)

Table 5  
In-patient treatment outcomes

<b>Condition at discharge</b>	<b>Irrational n (%)</b>	<b>Rational n (%)</b>
Good outcomes	162 (94.2)	57 (100)
Unfavorable outcomes	10 (5.8)	0 (0)

Of the 229 analyzed records of children on rationality of antibiotic prescription and treatment outcomes, 10 (5.8%) had unfavorable treatment outcomes with irrational prescriptions. The commonest unfavorable outcomes were referral to hospital and discharge on request. (See Fig. 5)

Duration of hospitalization; out of 229 records, 132 observations were made; 87 were questionable because of insufficient clinical data. The duration of hospitalization ranged from 1–13 days, the mean duration was 3days, the interquartile range of 2 days.

#### 4.4 Associations between irrational antibiotic prescriptions with in-patient treatment outcomes

Based on chi-square test, all the 10 children with unfavorable treatment outcomes had irrational prescriptions and therefore could not allow further analysis for establishing the strength of association in both bivariate and multivariate analysis (Table 6).

Table 6  
Association between irrational antibiotic prescription and in-patient treatment outcomes

<b>Irrational prescription</b>	<b>Good n (%)</b>	<b>Unfavorable n (%)</b>	<b>P value</b>
No	57 (26.0)	0 (0)	1.000*
Yes	162 (74.0)	10 (100)	
*p value based on Fishers exact chi-square			

In further analysis, we described the socio-demographic characteristics of the children and the in-patient treatment outcomes (Table 7).

Table.7.Description of socio-demographic characteristics and treatment outcomes

Demographic Characteristics	Good outcome n (%)	Unfavorable outcome n (%)	P value
<b>Age categories (months)</b>			0.227
2-5	32 (14.6)	3 (30.0)	
6-11	71 (32.4)	4 (40.0)	
12-23	58 (26.5)	0 (0.0)	
24-59	58 (26.5)	3 (30.0)	
<b>Gender</b>			0.899
Female	114 (52.0)	5 (50.0)	
Male	105 (48.0)	5 (50.0)	
<b>Sex of next of kin</b>			0.360
Female	202 (92.2)	10 (100)	
Male	17 (7.8)	0 (0.0)	
<b>Referred from lower health facility</b>			0.135
No	214 (97.7)	9 (90.0)	
Yes	5 (2.3)	1 (10.0)	

In relation to age, majority of children aged 6–11 months 71(32.4%) had good outcomes. Similarly, they had highest number of those with unfavorable outcome. Females had slightly better outcomes 114 (52.0%), compared to males. The majority (97.7%) of children with good outcomes were none referred from lower health facilities.

## Discussion

This study aimed at determining the rationality of antibiotic prescriptions and associated in-patient treatment outcomes in children aged 2–59 months with severe pneumonia at Bwizibwera Health Center IV, Mbarara District in south-western Uganda from 1st May 2018 to 30th April 2019.

The 75.1% of irrational antibiotic prescriptions, this could be as a result of the indicators that were used to measure irrational antibiotic prescriptions in this study. This finding is higher than the 35.1% reported by a retrospective study conducted at Mekelle General Hospital, Ethiopia on irrational use of antibiotics in children [6]. The difference in the reported proportions of irrational antibiotic prescriptions might be due to the use of dissimilar indicators for classification of irrational prescriptions, and different study sites. The

study by Sebsibie and Gultie [6] utilized antibiotic use indicators like percentage of antibiotics prescribed, frequency, route of administration, antibiotics prescribed from Standard treatment guideline, proportion of antibiotics, cost of antibiotics per antibiotics days, incidence and antibiotics utilization ratio while in the current study we looked at indication, regimen, dose, dose frequency route of administration and duration of treatment, in relation to the Uganda clinical guidelines [11].

In the previous studies slightly smaller percentages of irrational prescribing were reported in Mongolia (56.6%) and Turkey (56.5%) [7, 8]. These differences may have been due to studying only children below 5 years of age. The study by Remesh, Salim [9] showed that most of the prescribed antibiotics are inappropriately prescribed.

While this current study revealed a higher percentage (75.1 %) of irrational antibiotic prescription than the one reported in Kenya, probably because we focused on right regimen, duration of treatment and frequency of administration. A one year retrospective chart review in Kenya evaluated 394 cases and revealed inappropriate prescriptions with 33.4% treatment antibiotics and mean duration of antibiotic administration of 6 days [3]. This could be because their inappropriate antibiotic use focused on the choice, duration and indication of the antibiotics prescribed.

The findings from this study revealed that 24.9% of antibiotic prescriptions were rational. This was based on the right regimen, right duration and frequency of drug administration. The percentage of rational antibiotic prescriptions in the current study is lower than that reported by an earlier study in Tanzania. The study conducted in health care facilities in Tanzania showed that rational antibiotic prescribing was 44 % [12]. The difference in the reported percentage of rational prescriptions by the study in Tanzania and our study could have risen due to the fact that the Tanzanian study was a multi-center study and involved patients with several disease conditions other than just pneumonia.

Another study revealed that during patients' hospital stay, up to 60% of the children received at least one antibiotic with a high appropriate use of antibiotics in children [13]. The high appropriate use of antibiotics reported by Herigon, Hersh [13] was not surprising since the study was conducted in a developed country with good health systems and adequate enforcement of health policies regarding appropriate antibiotic use.

A study conducted by Trap, Ladwar [14] in public health care facilities in Uganda reported that rational prescribing was 12.4%. This percentage of rational prescription is lower than the 24.9% revealed by the current study. The earlier study recorded, low use of generic names, over-use of antibiotics and low adherence to standard treatment guidelines [14]. The variation in percentage could be because this study looks at antibiotic prescription in one condition and in only one health facility, while Trap, Ladwar [14] looked at all levels of health care facilities in Uganda and the general performances in the country.

The study conducted in Kampala International University Teaching Hospital, Western Uganda on assessment of rational prescribing reported 61.88% of antibiotic prescriptions, and 78.96 % of all prescriptions were in line with the UCG 2016 and rational drug prescribing index of 4.85 [5]. Akunne, Lam

[5] conducted their study in the general Outpatient department unlike in our study which was conducted among paediatric in-patients.

In Turkey, the rate of appropriate antibiotic use was reported to be 11.3 % [15]. Compared to the current study which reports 24.9 % rational antibiotic prescriptions, Tunger and colleagues evaluated the rational antibiotic use and the impact of the implementation of a new restriction policy on the hospital wide use of antibiotics.

Our study used the Uganda clinical guide line and included children aged 2–59 months with pneumonia only. The difference in study settings could also explain the observed differences. In addition, we used a retrospective study design while they combined both retrospective and prospective study design [15].

The majority (73.7%) of those who received rational prescription were on treatment with a combination of benzyl penicillin plus gentamycin while the other 26.3% were on a combination of ampicillin plus gentamycin. These findings are consistent with the recommendations for treatment of severe pneumonia in children under 5 years [16].

All patients in this study received empirical antibiotics treatment but the empirical antibiotics therapy was not always given according to the recommended guideline, such as with the use of Ampicillin plus cloxacillin and Cotrimoxazole. Earlier studies found that despite the availability of treatment guidelines, Uganda's health care system is still challenged with high rates of irrational antibiotic use [17–20]. The outcomes of antibiotic treatment were categorized into good and unfavorable in the current study. A child was considered to have a good outcome if he or she improved and was discharged home. Development of complications, referral to the hospital, death, and discharge on request were considered unfavorable outcomes.

The majority (95.6%) of children in the current study exhibited good outcomes following treatment irrespective of the rationality of a prescription. For those (4.4%) with unfavorable outcomes 2 died, 1 developed complication, 4 referred to hospital and 3 were discharged on request.

All the 57 (24.9%) patients who received rational antibiotic prescriptions had good outcomes, meaning they improved following treatment with the right regimen, administered at the right frequency and for the right duration and were discharged home. However, also the 162 patients who had irrational antibiotic prescription also had good outcomes.

In this study, the duration of hospitalization ranged from 1–13 days, the mean duration was 3 days, the interquartile range of 2 days. However, Keng, Thallner [21] in their study reported a range of 1–33 days of hospitalization. Another study reported that improved use of antibiotics among hospitalized children can improve outcome by shortening length of stay [22]. In another study, the mean value of hospitalization length in children with prescribed antibiotic therapy was 5 days. The longest hospitalization length was 14 days, and the shortest hospitalization length was 3 days [23].

This study reported 2 deaths (20%), which is near to the study done in pediatric ward at Dr. Sardjito Hospital, Yogyakarta, Indonesia on the prevalence of irrational prescription and clinical outcomes in children with pneumonia which revealed that out of 46 children who met eligibility criteria, 13 (28.3%) used antibiotics irrationally and 7 (15.2%) died [4]. The Sardjito study reported that the majority of children were less than 1 year (54.3%) and 1-<5 years (39.1%), 50% were referred from other hospitals and 60.95 stayed in hospital for more than 7 days. The female to male ratio was 1:1 [4]. Looking at the current study children with unfavorable outcomes aged less than 1 year (70%) and 1-<5 years (30%); the female to male ratio was 1:1, which is similar to the findings by Yusuf, Murni [4]. This could be attributed to study design, they did a cross sectional study for 2 year versus one year retrospective in this study, although both studies obtained data from medical records.

In relation to age, majority of children aged 6–11 months 71(32.4%) had good outcomes. Similarly, they had high number of those with unfavorable outcome. Females had slightly better outcomes 114 (52.0%), compared to males. The majority (97.7%) of children with good outcomes were non referrals from lower health facilities.

## **Conclusion**

In conclusion, majority of the children 172 (75.1%) had received irrational antibiotic prescriptions. There were no statistically significant associations between patient characteristics and treatment outcomes.

## **Abbreviations**

ARI: Acute Respiratory infection; CAP:Community-Acquired Pneumonia; DHO:District Health Officer; EIN:Emerging Infections Network; H/C:Health Center; MMS:Medicine Management Supervisors; MOH:Ministry of Health; SPARS:Supervision, Performance Assessment, and Recognition Strategy; UCG:Uganda Clinical Guidelines; UNICEF:United Nations International Children’s Emergency Fund; WHO:World Health Organization; FRC:Faculty Research Committee; REC:Research Ethics Committee.

## **Declarations**

### **Acknowledgments**

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### **Authors’ contributions**

CJA, VN and CO designed and made substantial contributions to the concept and design. CJA, VN and JPB participated in data analysis and report writing. CJA, JPB and CO critically revised the manuscript; all authors read and approved the final manuscript prior to submission.

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## **Availability of data and materials**

All data generated and analyzed during this study are included in this article.

## **Ethics approval and consent to participate**

Ethical clearance was obtained from Faculty of Medicine Research Committee (DMS 6) and MUST- Research Ethics Committee (MUREC 1/7). Permission was sought from the District Health Officer and the in-charge Bwizibwera H/C IV to access health care records of children aged 2-59 months prior to data collection.

## **Consent for publication**

Not applicable

## **Competing interests**

The authors declare that there were no competing interests.

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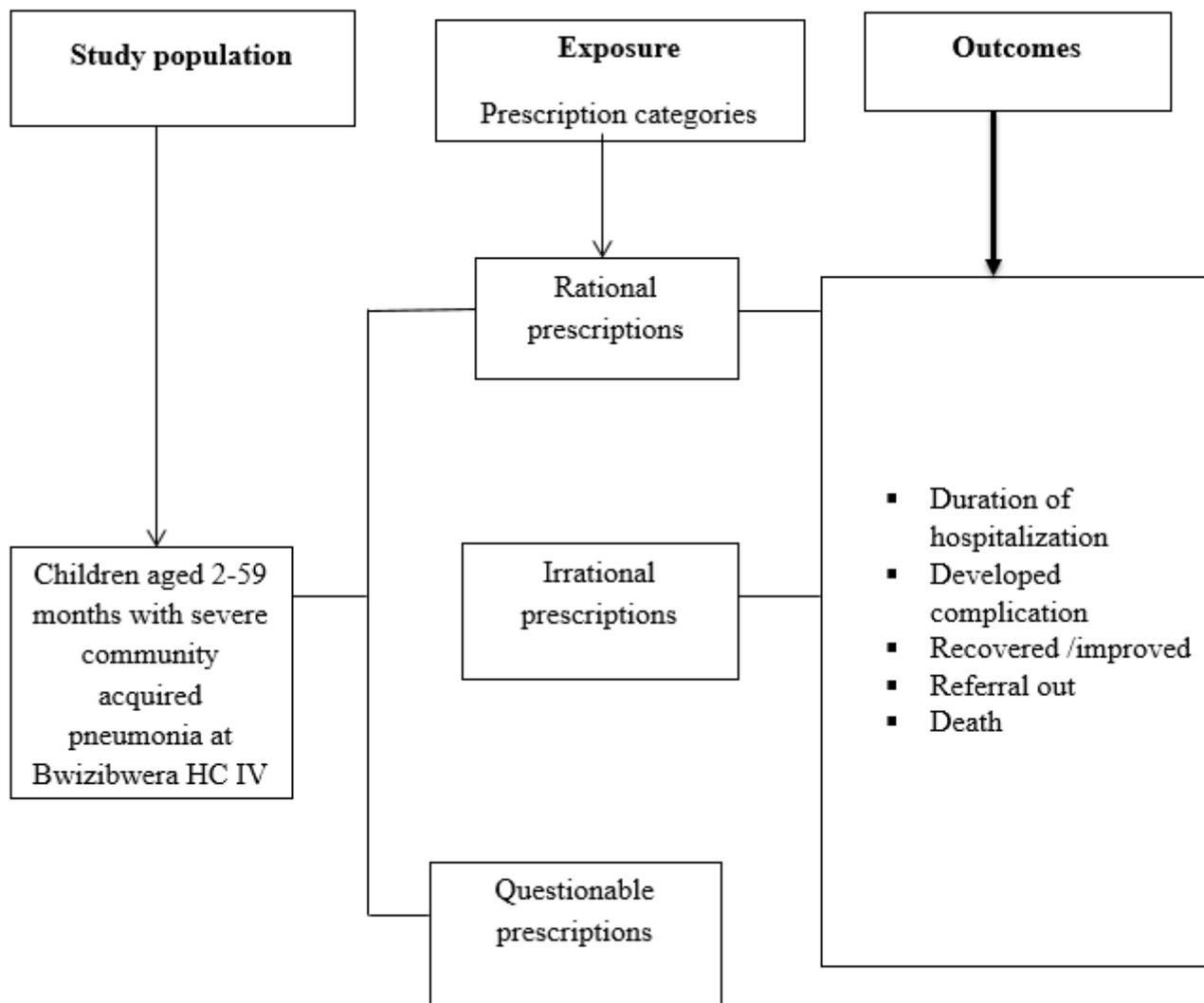
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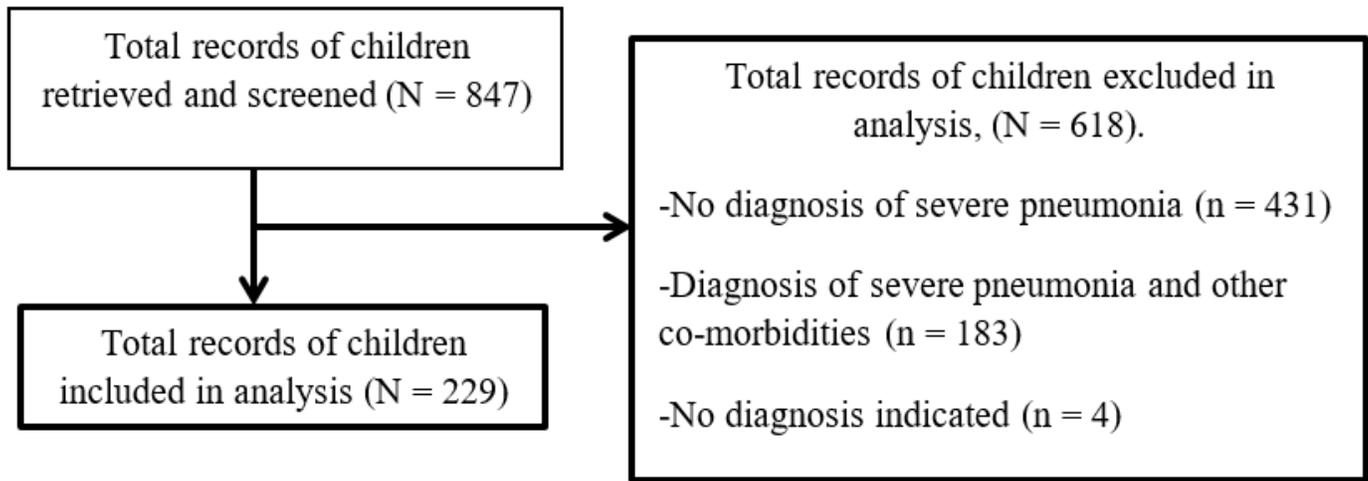
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## Figures



**Figure 1**

Flow chart showing study design.



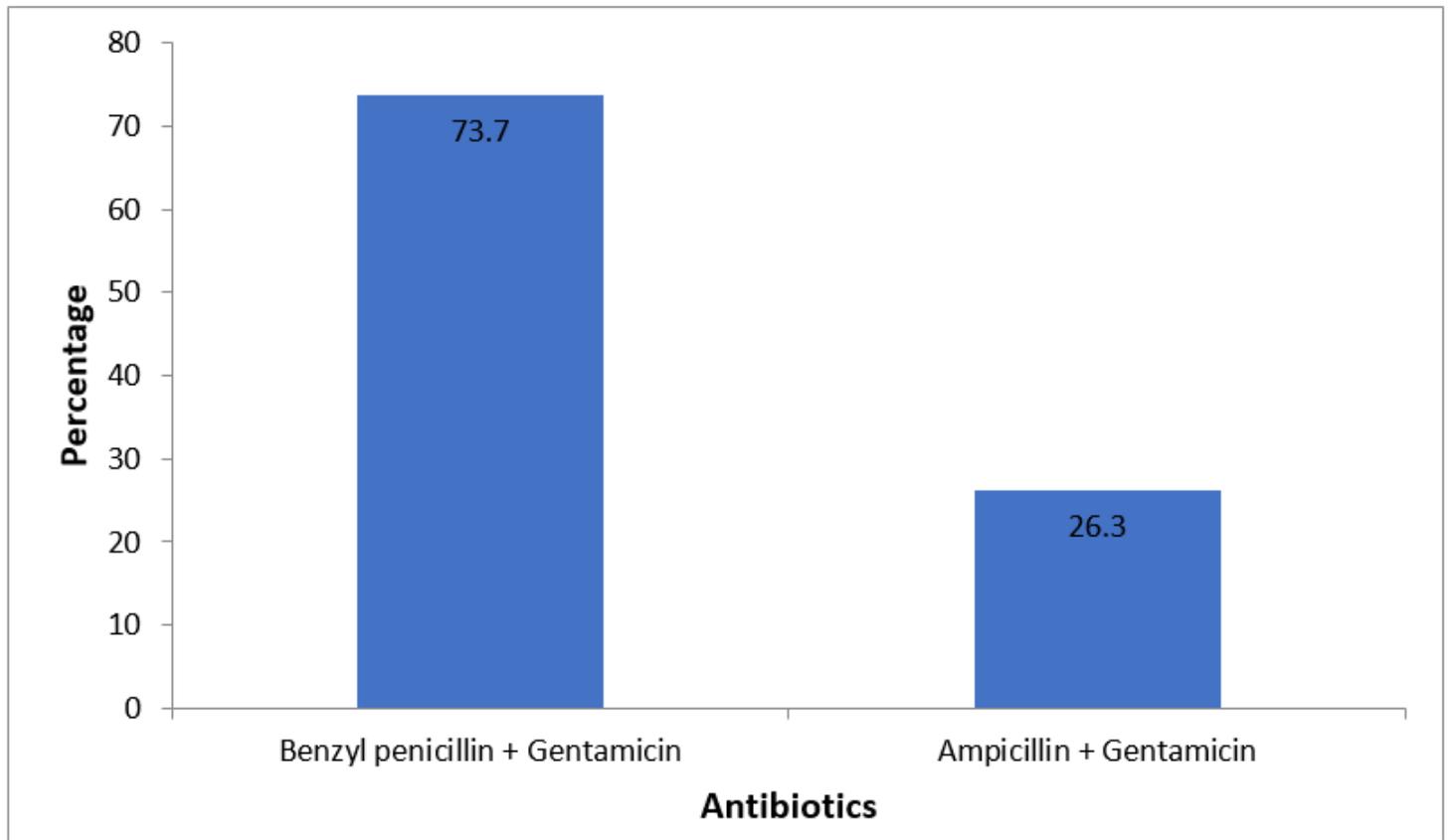
**Figure 2**

Study profile

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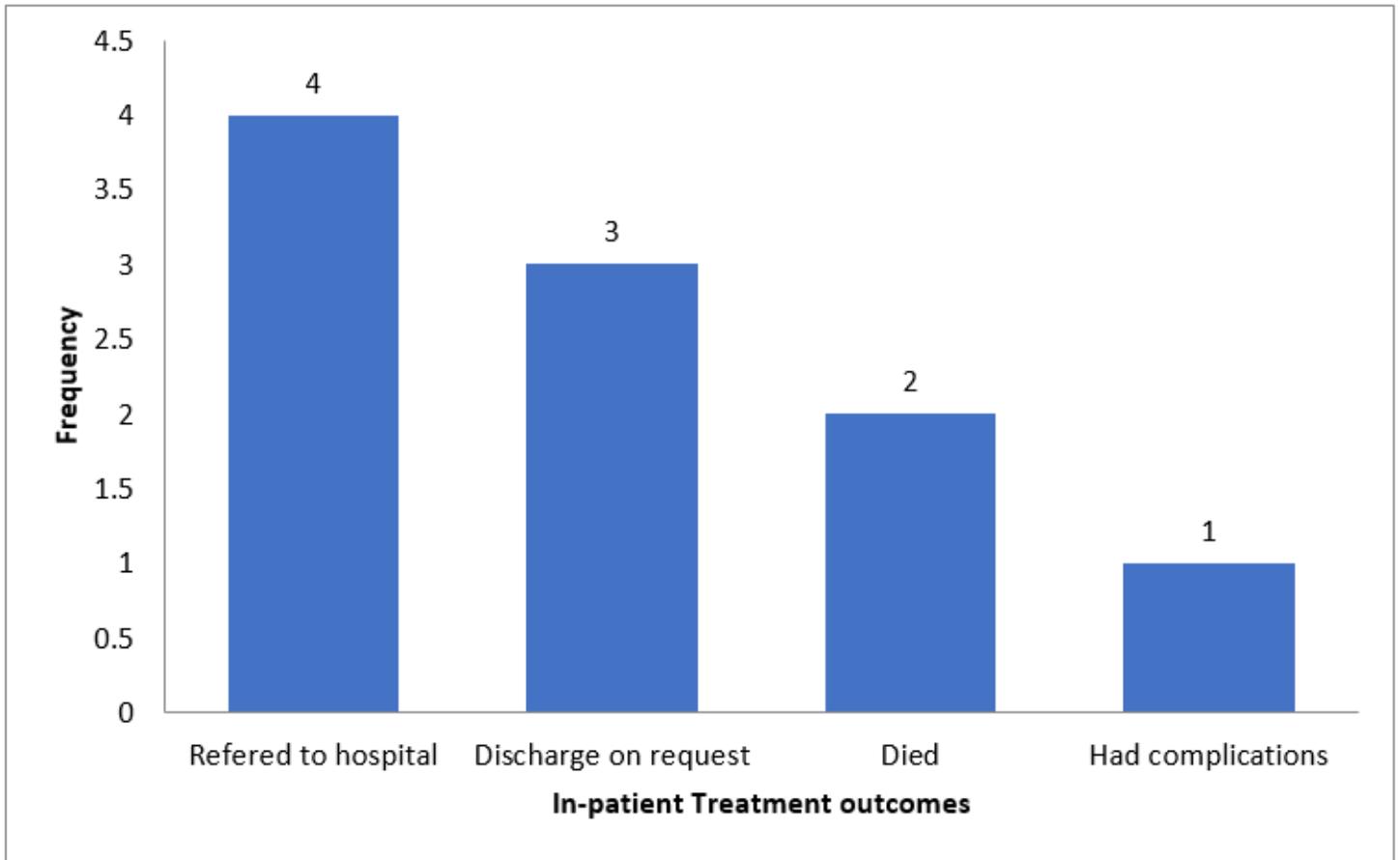
**Figure 3**

Figure 3



**Figure 4**

Graph showing the percentages of recommended first line combination regimens used for treatment of severe pneumonia.



**Figure 5**

Distribution of different in-patient treatment outcomes among children with unfavorable outcomes.