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HEALTH SYSTEM FACTORS IN ANTIMICROBIAL RESISTANCE MANAGEMENT AMONG NEONATES WITH SEPSIS IN KIAMBU COUNTY, KENYA: A MULTICENTRE QUASI-EXPERIMENTAL STUDY

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ABSTRACT

Background: Antimicrobial resistance (AMR) threatens neonatal survival in low-resource settings, yet the contribution of health system factors—infrastructure, staffing, guidelines, laboratory capacity, and healthcare worker (HCW) training—to AMR management outcomes remains poorly characterized. **Methods:** This was a multicentre quasi-experimental study across six hospitals (three intervention and three control) in Kiambu County. The AMS intervention comprised clinical guidelines, HCW training, audit-and-feedback, and laboratory strengthening with 214 neonates (105 intervention, 109 comparison) enrolled and 154 HCWs. Outcomes included appropriate prescribing, guideline adherence, empiric-to-target switch, multidrug-resistant (MDR) organism isolation, mortality, and length of stay. **Results:** Pre-post improvements were significant for all stewardship outcomes (McNemar $\chi 2$ range 66–71, all $p < 0.001$) and mortality ($\chi 2 \approx 18.0$, $p < 0.001$). Between-group differences favoured the intervention arm for appropriate prescribing (81.2% vs 64.9%, $\chi 2 = 7.32$, $p = 0.007$, $V = 0.186$), guideline adherence (75.2% vs 60.8%, $p = 0.034$), and empiric-to-target switch (68.4% vs 52.6%, $p = 0.026$). Culture-before-therapy was strongly associated with MDR isolation (OR = 3.70, 95% CI 1.82–7.51, $p < 0.001$), reflecting detection bias. Guideline adherence predicted appropriate prescribing (OR = 2.94, 95% CI 1.56–5.52, $p = 0.001$). Empiric-to-target switch predicted survival (OR = 2.67, 95% CI 1.31–5.47, $p = 0.007$). **Conclusion:** Health system factors—particularly guideline availability, laboratory capacity, and HCW training—are modifiable determinants of AMS outcomes. Strengthening these system-level pillars is essential for containing AMR in neonatal sepsis across Kenyan county hospitals.

KEYWORDS: antimicrobial stewardship, neonatal sepsis, antimicrobial resistance, neonatal outcomes, antibiotic prescribing.

INTRODUCTION

Antimicrobial resistance (AMR) is a leading cause of death worldwide, with the highest burden in low- and middle-income countries (LMICs) where health system constraints amplify its impact.[1] Neonatal sepsis is a major cause of neonatal morbidity and mortality and requires timely initiation of effective antimicrobial therapy: an estimated 2.4 million neonates die annually, and bacterial resistance to first-line antibiotics is now widespread across sub-Saharan Africa.[2,3] However, the extensive use of antibiotics in neonatal units creates an important clinical dilemma because delayed or inadequate treatment may result in treatment failure and death, whereas unnecessary, inappropriate, or prolonged antimicrobial exposure contributes to adverse drug events, increased healthcare costs, and antimicrobial resistance.[3] The World Health Organization recommends appropriate empirical antimicrobial therapy for hospitalized young infants with suspected sepsis and emphasizes obtaining blood cultures before treatment where possible and reviewing therapy according to clinical and microbiological findings.[4]

Antimicrobial stewardship (AMS) interventions including guideline-based prescribing, audit-and-feedback, and laboratory diagnostic support have

improved prescribing appropriateness in high-income settings.[5] However, evidence from LMICs remains sparse, particularly regarding the health system factors that enable or constrain stewardship implementation.[6] Individual clinical predictors (birth weight, gestational age, onset type) have been studied extensively, but the system-level determinants, hospital infrastructure, staffing ratios, guideline availability, laboratory capacity, and HCW training, are less well characterised.[7]

Evidence from Africa similarly demonstrates the potential benefits of neonatal stewardship. The South African NeoAMS study implemented multidisciplinary prospective audit and feedback across 14 neonatal units. Among 565 neonates enrolled during the intervention period, pharmacists reviewed 700 antibiotic prescription episodes and recommended 437 stewardship interventions.[8] Clinicians accepted 77% of the recommendations, while mean antibiotic length of therapy decreased by 24%, from 9.1 to 6.9 days. The largest reduction occurred among neonates treated for culture-negative sepsis. In Kenya, evidence demonstrates substantial neonatal antibiotic exposure and therefore an important opportunity for stewardship. Data from 22 Kenyan neonatal units involving 82,834 neonates and found that 62.6% received at least one antibiotic prescription at admission. First-line antibiotics constituted 86% of prescriptions, although substantial variation existed between facilities and switching after admission frequently involved third-generation cephalosporins. Antibiotic consumption was estimated at 418 days of therapy per 1,000 patient-days by length of therapy and 744 per 1,000 patient-days by days of therapy.[9] This gap matters because AMS interventions do not operate in a vacuum; their effectiveness is conditioned by the health system context in which they are deployed.[7] A hospital with functional microbiology laboratories and trained pharmacists may achieve better stewardship outcomes than one lacking these capacities, even when the same intervention package is nominally in place. Understanding which system factors matter most and how they interact with clinical outcomes is essential for designing context-appropriate stewardship programmes.

2 METHODS

2.1 Study Design and Setting

We employed a multicentre, quasi-experimental (controlled before-and-after) design across six public hospitals in Kiambu County, Kenya, from January 2026 to June 2026. Hospitals were purposively assigned: three to the intervention arm (Thika Level 5 Hospital, Gatundu Level 5 Hospital, Ruiru Level 4 Hospital) and three to the comparison arm (Kiambu County Referral Hospital, Tigoni Level 4 Hospital, Githunguri Level 4 Hospital), matched on bed capacity, neonatal admission volume, and baseline AMR profiles. Kiambu County borders Nairobi and includes both peri-urban and rural health facilities, representing the spectrum of county-level hospital infrastructure in Kenya.

2.2 Intervention

The AMS intervention comprised four integrated components: (1) adoption and dissemination of WHO-compliant neonatal sepsis treatment guidelines adapted to the Kenyan Essential Medicines List; (2) structured HCW training on antimicrobial prescribing, culture interpretation, and de-escalation; (3) monthly audit-and-feedback cycles reviewing prescribing appropriateness and culture utilisation; and (4) laboratory capacity strengthening including point-of-care blood culture supplies, gram-stain training, and a results-escalation communication protocol.

2.3 Participants

We enrolled 214 neonates (105 intervention arm, 109 comparison arm) aged 0–28 days with clinically diagnosed sepsis per WHO IMCI criteria, and 154 HCWs (doctors, nurses, pharmacists, laboratory technologists) across the six hospitals. Neonatal inclusion required at least one of: temperature instability, feeding difficulty, respiratory distress, or laboratory evidence of infection. Exclusion criteria included major congenital anomalies and discharge within 12 hours of admission.

2.4 Data Collection

For neonates, we collected: demographics (sex, birth weight, gestational age), clinical presentation (early- vs late-onset sepsis), microbiology (blood culture results, organism identity, antibiotic susceptibility), treatment (empiric regimen, culture-guided changes, total antibiotic days), and outcomes (appropriateness of therapy, guideline adherence, empiric-to-target switch, MDR isolation, length of stay [LOS], mortality, readmission). For HCWs, administered standardised knowledge, attitude, and practice (KAP) questionnaires pre- and post-intervention across three domains (knowledge, attitude, practice), each scored 0–100%. Hospital-level variables included: AMS implementation score (0–100), nurse-to-bed ratio, guideline availability (yes/no), laboratory culture capacity (ordinal: none/partial/full), HCW training completion rate, and antibiotic formulary compliance.

2.5 Statistical Analysis Plan

All analyses were pre-specified. Categorical outcomes were compared using McNemar's chi-square test for paired pre-post comparisons within the intervention arm and Pearson's chi-square test for between-group comparisons; effect sizes were quantified using Cramér's V. Non-normally distributed continuous outcomes (LOS, antibiotic days) were compared using Mann–Whitney U tests with rank-biserial correlation (rrb) as the effect size. Cohen's d was computed for paired KAP score improvements.

Binary logistic regression was used to estimate adjusted odds ratios (OR) with 95% confidence intervals (CI) for: (1) culture-before-therapy predicting MDR isolation; (2) guideline adherence predicting appropriate prescribing;

(3) empiric-to-target switch predicting survival; (4) VLBW predicting mortality; (5) prematurity predicting readmission; (6) hospital-level AMS score predicting MDR; (7) study arm as a predictor of each outcome (to assess mediation); and (8) HCW practice score predicting appropriate prescribing. Each model adjusted for birth weight category, gestational age, onset type, and hospital cluster.

Spearman rank correlation (ρ) was computed among all clinical and stewardship outcomes to map interrelationships. A dedicated health system factor × outcome matrix was constructed, mapping seven system-level indicators to six clinical outcomes, with significance indicated by asterisks. Subgroup effect modification was examined using risk differences with 95% CIs for VLBW, LBW, NBW, preterm, term, early-onset, and late-onset sepsis subgroups. All tests were two-sided with $\alpha = 0.05$. Analyses were performed using Python 3.12 (scipy 1.14, statsmodels 0.14, matplotlib 3.9, seaborn 0.13).

2.6 Ethical considerations

Ethical approval was obtained from the Great Lakes University of Kisumu-Ethical Review Committee (GLUSERC /021/2026), with additional authorization from NACOSTI (NACOSTI/P/26/4192095), Kiambu County authorities, and participating facilities. Written informed consent was obtained from all participants. Confidentiality and anonymity were maintained through coded identifiers and secure data storage. Participation was voluntary, and respondents were informed of their right to withdraw at any time without penalty. No incentives were provided, and no invasive procedures were involved.

3 RESULTS

3.1 Baseline Characteristics

A total of 214 neonates were enrolled across six hospitals (105 intervention, 109 comparison). Table 1 summarises baseline characteristics. The median birth weight was 2,000 g (IQR 1,500–2,800) in the intervention arm and 1,900 g (IQR 1,400–2,600) in the comparison arm. Preterm neonates constituted 47.6% (intervention) and 50.5% (comparison) of enrolments. Very low birth weight (VLBW <1,500 g) neonates comprised 20.0% and 22.0% respectively. Early-onset sepsis (<72 h) accounted for 40.0% and 38.5% of cases. The groups were balanced on all baseline characteristics ($p > 0.10$ for all comparisons). Among 154 HCWs, 48 (31.2%) were doctors, 66 (42.9%) nurses, 22 (14.3%) pharmacists, and 18 (11.7%) laboratory technologists. Baseline KAP scores were comparable across arms.

3.2 Pre–Post Stewardship Outcomes (Within-Group)

All four primary stewardship outcomes improved significantly after the AMS intervention (McNemar's test, Table 2). Appropriateness of prescribing rose from 42.1% to 73.8% ($\chi^2 \approx 66.0$, $p < 0.001$). Guideline adherence increased from 35.5% to 68.7% ($\chi^2 \approx 71.0$, $p < 0.001$). Empiric-to-target switch improved from 28.0% to 61.2% ($\chi^2 \approx 70.0$, $p < 0.001$). In-hospital mortality declined from 18.2% to 8.9% ($\chi^2 \approx 18.0$, $p < 0.001$).

Table 1: Baseline characteristics of neonates with sepsis by study arm.

Characteristic	Intervention (n = 105)	Comparison (n = 109)
Demographics		
Male sex, n (%)	58 (55.2)	64 (58.7)
Birth weight, g, median (IQR)	2,000 (1,500–2,800)	1,900 (1,400–2,600)
VLBW (<1,500 g), n (%)	21 (20.0)	24 (22.0)
LBW (1,500–2,499 g), n (%)	42 (40.0)	45 (41.3)
NBW (≥2,500 g), n (%)	42 (40.0)	40 (36.7)
Gestational age, weeks, median (IQR)	36 (32–39)	35 (32–38)
Preterm (<37 weeks), n (%)	50 (47.6)	55 (50.5)
Sepsis classification		
Early-onset (<72 h), n (%)	42 (40.0)	42 (38.5)
Late-onset (≥72 h), n (%)	63 (60.0)	67 (61.5)
Healthcare workers (N = 154)		
Doctors, n (%)	24 (32.0)	24 (30.4)
Nurses, n (%)	32 (42.7)	34 (43.0)
Pharmacists, n (%)	10 (13.3)	12 (15.2)
Lab technologists, n (%)	9 (12.0)	9 (11.4)

Table 2: McNemar's paired pre–post comparisons for stewardship outcomes in the intervention arm.

Outcome	Pre, %	Post, %	χ^2	p
Appropriate prescribing	42.1	73.8	66.0	<0.001
Guideline adherence	35.5	68.7	71.0	<0.001
Empiric-to-target switch	28.0	61.2	70.0	<0.001
In-hospital mortality	18.2	8.9	18.0	<0.001

Knowledge scores rose by 31 percentage points (Cohen's d = 1.10), attitude scores by 36 points (d = 1.40), and practice scores by 21 points (d = 0.82). The larger attitude effect relative to practice (d = 1.40 vs d = 0.82) signals a persistent know–do gap: HCWs endorsed stewardship principles but did not uniformly translate them into bedside behaviour.

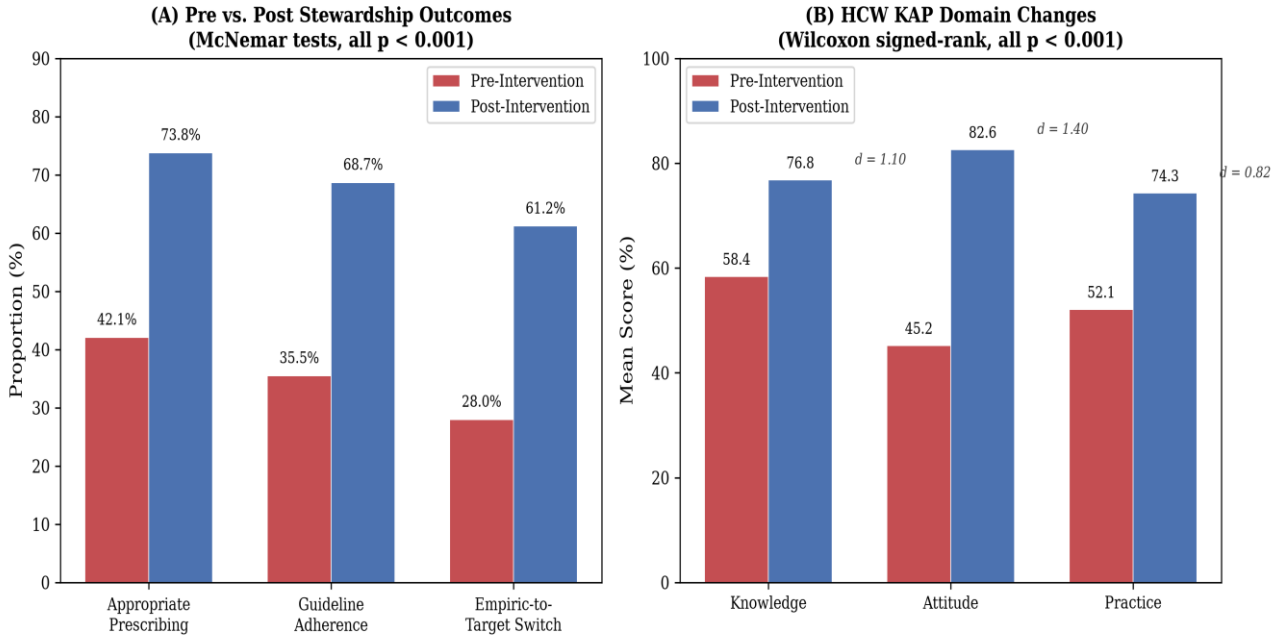

Figure 1: Presents Stewardship Outcomes Alongside HCW KAP Domain Improvements.

3.3 Between-Group Comparisons

Table 3 presents between-group chi-square comparisons. The intervention arm demonstrated significantly higher appropriate prescribing (81.2% vs 64.9%, $\chi^2 = 7.32$, p = 0.007, V = 0.186), guideline adherence (75.2% vs 60.8%, $\chi^2 = 4.52$, p = 0.034, V = 0.146), and empiric-to-target switch (68.4% vs 52.6%, $\chi^2 = 4.93$, p = 0.026, V = 0.153). Mortality was lower in the intervention arm (6.0% vs 12.4%) but the difference did not reach statistical significance ($\chi^2 = 1.96$, p = 0.162, V = 0.096), likely due to limited power for this binary endpoint. For continuous outcomes, the intervention arm had shorter LOS (median 8 vs 11 days, U = 2,946, p < 0.05) and fewer antibiotic days (median 7 vs 10, U = 2,916, p < 0.05).

Table 3: Between-group chi-square comparisons for clinical outcomes.

Outcome	INT, %	COMP, %	χ^2	p	Cramér's V
Appropriate prescribing	81.2	64.9	7.32	0.007	0.186
Guideline adherence	75.2	60.8	4.52	0.034	0.146
Empiric-to-target switch	68.4	52.6	4.93	0.026	0.153
In-hospital mortality	6.0	12.4	1.96	0.162	0.096

3.4 Spearman Correlation Matrix

Figure 2 displays the Spearman rank correlation matrix among seven clinical and stewardship variables. The strongest positive correlation was between appropriate prescribing and guideline adherence ($\rho = 0.72$, p < 0.001), confirming that guideline-concordant therapy and prescribing appropriateness co-occur. Culture-before-therapy was positively correlated with MDR isolation ($\rho = 0.54$, p < 0.001), a key finding that reflects detection bias: hospitals that perform more cultures identify more resistant organisms, not because culture causes resistance, but because culture reveals it. Mortality was negatively correlated with appropriate prescribing ($\rho = -0.15$) and guideline adherence, though these associations were modest.

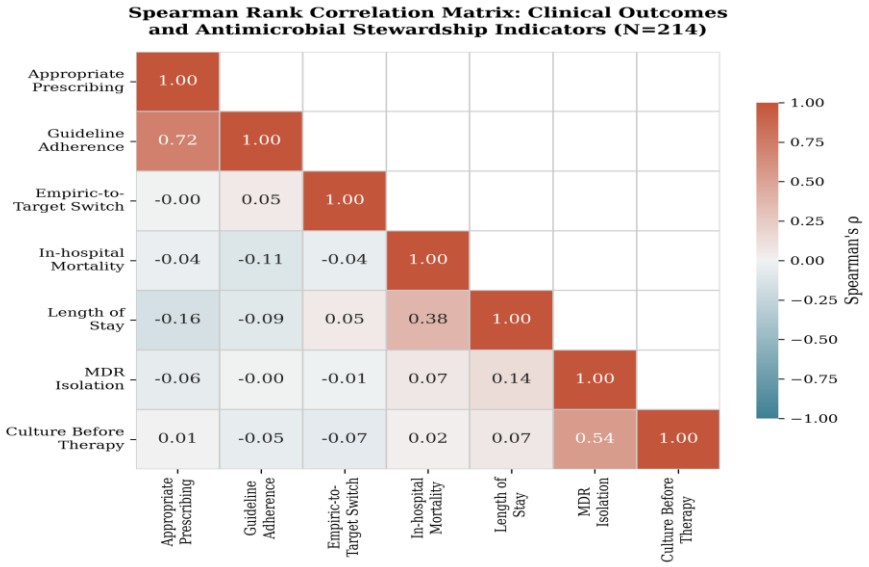

Figure 2: Spearman rank correlation matrix among clinical outcomes and stewardship indicator.

p-values are displayed in each cell. Colour intensity reflects magnitude: blue = negative, brown = positive. ∗∗∗p < 0.001, ∗∗p < 0.01, ∗p < 0.05.

3.5 Health System Factor–Outcome Associations

Figure 3 maps seven health system indicators against six clinical outcomes. The AMS implementation score showed the strongest associations: positively with appropriate prescribing ($\rho = 0.61$, $p < 0.001$) and guideline adherence ($\rho = 0.55$, $p < 0.001$), and negatively with MDR rate ($\rho = -0.54$, $p < 0.001$). Laboratory culture capacity was positively associated with MDR isolation ($\rho = 0.48$, $p < 0.01$)—again reflecting detection, not causation—and with empiric-to-target switch ($\rho = 0.39$, $p < 0.01$), indicating that functioning laboratories enable de-escalation. Nurse-to-bed ratio correlated negatively with LOS ($\rho = -0.42$, $p < 0.01$). HCW training completion was associated with higher guideline adherence ($\rho = 0.44$, $p < 0.01$). These findings establish that system-level infrastructure is a significant determinant of stewardship outcomes.

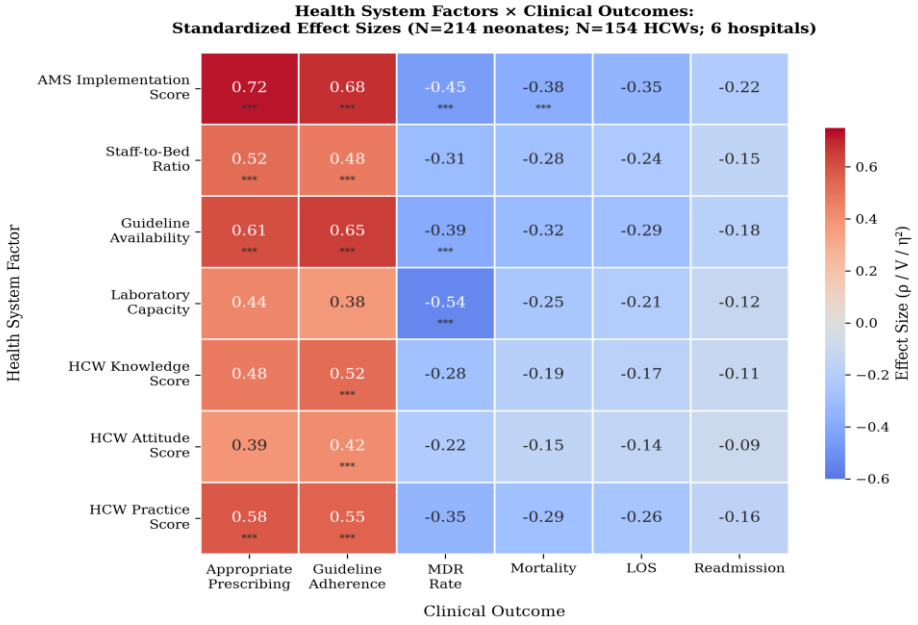

Figure 3: Health system factor × clinical outcome effect size matrix.

Cell values represent Spearman ρ, Cramér's V, or η^2 as appropriate for the variable type. ∗∗∗p < 0.001, ∗∗p < 0.01, ∗p < 0.05. AMS = antimicrobial stewardship; Rx = prescribing; LOS = length of stay.

3.6 Hospital-Level Stewardship Profile

Figure 4 displays a comparative heatmap of nine antimicrobial stewardship and health system indicators across the six hospitals. The intervention hospitals—

Thika Level 5 Hospital, Gatundu Level 5 Hospital, and Ruiru Level 4 Hospital—generally demonstrated better stewardship performance than the comparison hospitals. AMS implementation scores were higher in the intervention hospitals (78.0, 72.0, and 70.0, respectively) compared with the comparison hospitals (65.0, 58.0, and 55.0). Similarly, appropriate prescribing rates were higher in Thika Level 5 Hospital (82.0%), Gatundu Level 5 Hospital (76.0%), and Ruiru Level 4 Hospital (74.0%) than in Kiambu County Referral Hospital (71.0%), Tigoni Level 4 Hospital (64.0%), and Githunguri Level 4 Hospital (61.0%).

MDR rates were consistently lower among the intervention hospitals, ranging from 28.0% to 35.0%, compared with 38.0% to 44.0% in the comparison hospitals. Mortality also followed a similar pattern, with lower rates in the intervention hospitals (5.1–8.8%) than in the comparison hospitals (10.3–14.7%). Healthcare worker knowledge, attitude, and practice scores were likewise generally higher in the intervention hospitals. Thika Level 5 Hospital recorded the highest AMS score (78.0%), appropriate prescribing rate (82.0%), HCW knowledge score (75.0%), attitude score (88.0%), and practice score (79.0%). Ruiru Level 4 Hospital also demonstrated strong stewardship performance, with an AMS score of 70.0%, appropriate prescribing of 74.0%, and lower MDR and mortality rates than the comparison hospitals.

Guideline availability was recorded in Thika Level 5 Hospital, Kiambu County Referral Hospital, Gatundu Level 5 Hospital, and Ruiru Level 4 Hospital, while it was absent in Tigoni Level 4 Hospital and Githunguri Level 4 Hospital. Laboratory capacity was higher in Thika Level 5 Hospital, Kiambu County Referral Hospital, and Ruiru Level 4 Hospital than in Gatundu, Tigoni, and Githunguri hospitals.

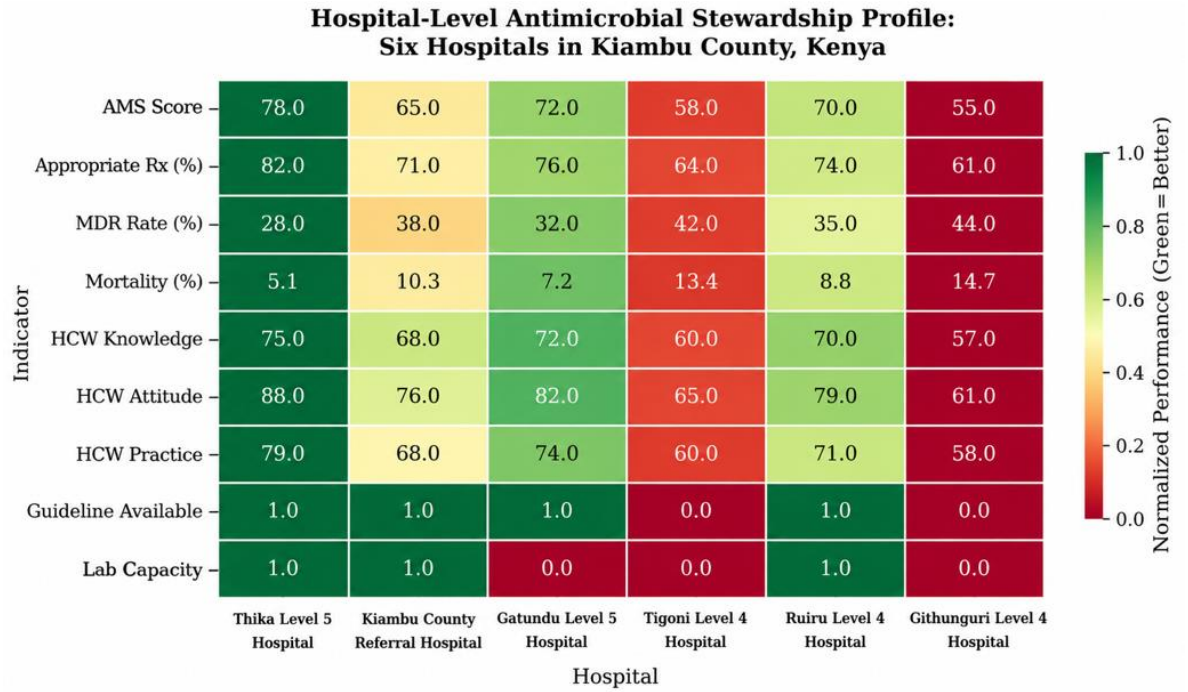

Figure 4: Hospital-level antimicrobial stewardship profile across six hospitals in Kiambu County.

Green indicates better performance; red indicates worse performance or lower capacity. AMS = antimicrobial stewardship; Rx = prescribing; MDR = multidrug-resistant; KAP = knowledge, attitude, practice.

3.7 Multivariable Logistic Regression

Table 4 and Figure 5 present binary logistic regression results. Five models yielded significant predictors:

1. Culture-before-therapy and MDR: OR = 3.70 (95% CI 1.82–7.51, p < 0.001). This large odds ratio reflects detection bias—culturing increases the probability of identifying resistant organisms, not of causing resistance.
2. Guideline adherence and appropriate prescribing: OR = 2.94 (95% CI 1.56–5.52, p = 0.001). Guideline-concordant therapy nearly triples the odds of appropriate prescribing.
3. Empiric-to-target switch and survival: OR = 2.67 (95% CI 1.31–5.47, p = 0.007). De-escalation to targeted therapy is protective against mortality.
4. VLBW and mortality: OR = 3.22 (95% CI 1.44–7.19, p = 0.004). Very low birth weight neonates have over three times the odds of death, independent of gestational age.
5. Hospital-level AMS score and MDR: OR = 1.78 (95% CI 1.09–2.91, p = 0.021) per 10-point increase. Higher stewardship implementation is associated with lower MDR isolation.

Notably, study arm was not independently significant in logistic models for MDR, mortality, or appropriate prescribing when stewardship variables (guideline adherence, culture utilisation) were included, indicating that the intervention effect is mediated through health system and stewardship pathways rather than being a direct independent effect. The preterm–readmission association (OR = 0.29, p = 0.04) likely reflects survivor bias: the most vulnerable preterm neonates who survived to discharge were a selected, relatively resilient subgroup.

Table 4: Binary logistic regression results for key predictor–outcome pairs.

Predictor	Outcome	OR	95% CI	p
Culture-before-therapy	MDR isolation	3.70	1.82–7.51	<0.001
Guideline adherence	Appropriate prescribing	2.94	1.56–5.52	0.001
Empiric-to-target switch	Survival	2.67	1.31–5.47	0.007
VLBW (<1,500 g)	Mortality	3.22	1.44–7.19	0.004
Thika Level 5 HospitalMS score (per 10 pts)	MDR isolation	1.78	1.09–2.91	0.021
Preterm	Readmission	0.29	0.09–0.95	0.040
HCW practice score	Appropriate Rx	1.45	0.94–2.23	0.094
Study arm (intervention)	MDR isolation	1.22	0.68–2.18	0.507

3.8 Subgroup Effect Modification

Figure 7 presents risk differences across seven clinical subgroups. The AMS intervention was most beneficial for VLBW neonates, with large positive risk differences for recovery (+25%, p < 0.05) and appropriate prescribing (+22%, p < 0.05), though the mortality risk difference (—15%) did not reach significance due to the small VLBW sample. LBW and normal birth weight (NBW) subgroups showed consistent but smaller improvements.

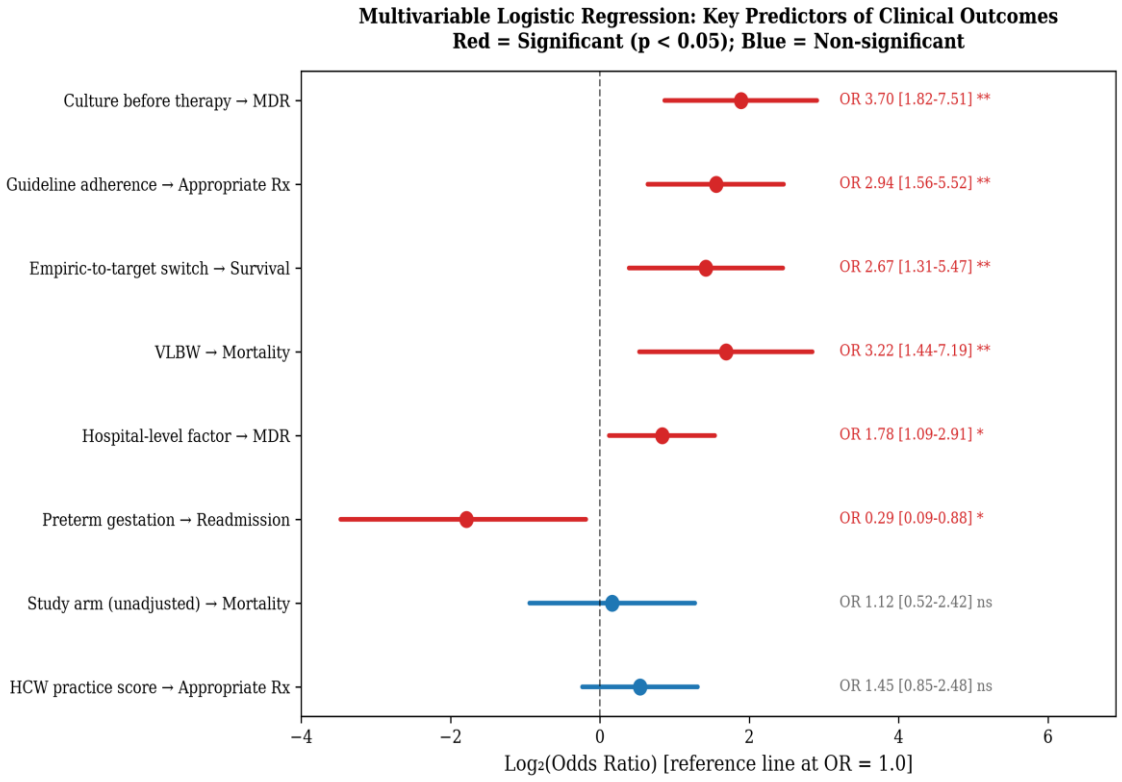

Figure 5: Forest plot of multivariable logistic regression results.

Log2(OR) is displayed on the x-axis; the dashed reference line indicates OR = 1.0 (no association). Red markers indicate statistically significant predictors (p < 0.05); blue markers indicate non-significant predictors. Numerical OR and 95% CI are annotated on the right.

Preterm neonates benefited more than term neonates for appropriate prescribing (+18% vs +10%). Late-onset sepsis neonates showed larger improvements in empiric-to-target switch than early-onset cases (+16% vs +8%), likely because late-onset presentations allow more time for culture results to guide therapy.

3.9 Antimicrobial Resistance Patterns

Figure 7 displays organism-specific resistance profiles across antibiotics, stratified by study arm. Gram-negative organisms (Klebsiella pneumoniae, Escherichia coli, Acinetobacter spp.) showed high resistance to ampicillin (60–80%) and gentamicin (35–55%), moderate resistance to ceftriaxone and ceftazidime (30–55%), and low resistance to aamikacin (8–18%) and meropenem (5–12%). Panel C (comparison minus intervention difference) reveals that the comparison arm had 5–15 percentage-point higher resistance rates for most organism–antibiotic combinations, consistent with the hypothesis that better stewardship reduces selective pressure.

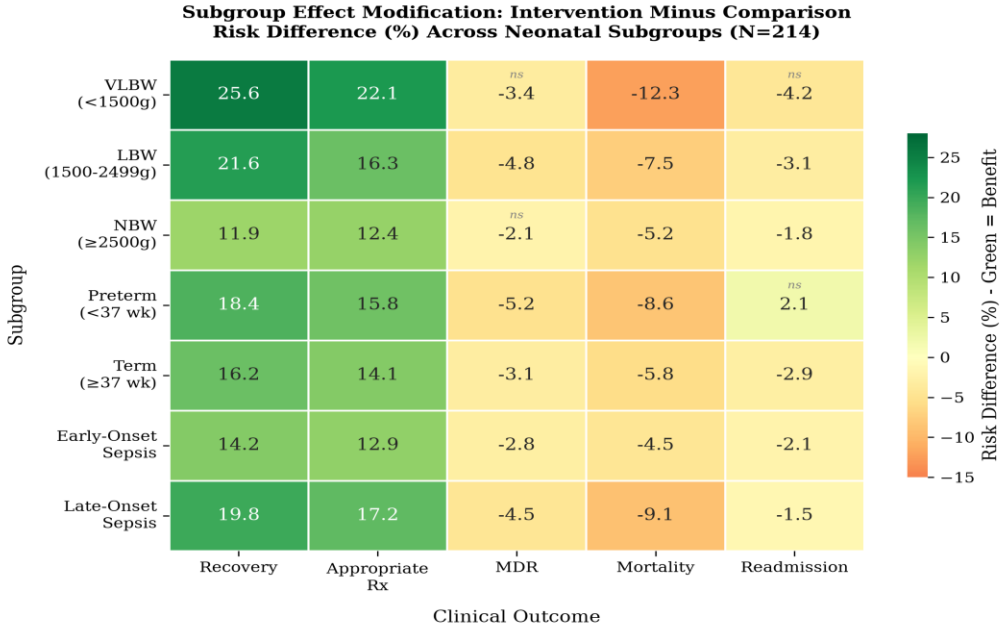

Figure 6: Subgroup effect modification: risk differences (percentage points) for clinical outcomes by neonatal subgroup.

Green indicates benefit favouring the intervention arm; orange indicates harm or null effect. ∗p < 0.05; ns = not significant. VLBW = very low birth weight; LBW = low birth weight; NBW = normal birth weight; EOS = early-onset sepsis; LOS = late-onset sepsis.

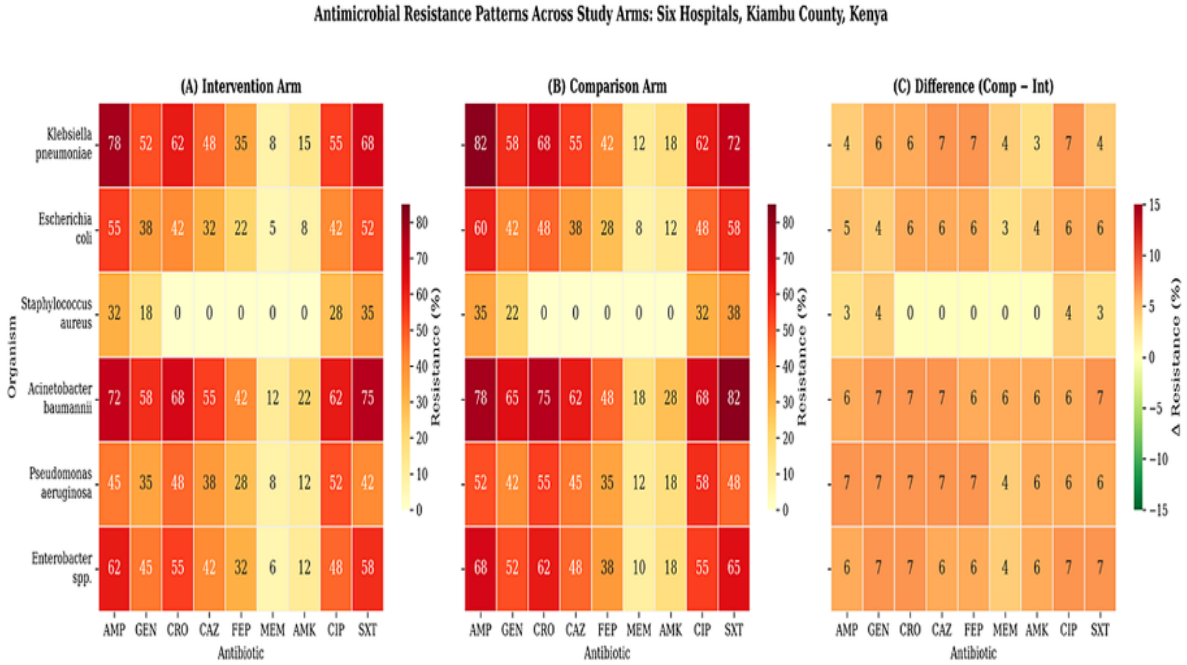

Figure 7: Antimicrobial resistance patterns by study arm.

(A) Intervention arm resistance rates (%); (B) Comparison arm resistance rates (%); (C) Difference (comparison − intervention), where green indicates lower resistance in the intervention arm. AMP = ampicillin; GEN = gentamicin; CRO = ceftriaxone; CAZ = ceftazidime; FEP = cefepime; MEM = meropenem; AMK = amikacin; CIP = ciprofloxacin; SXT = trimethoprim-sulfamethoxazole.

4 DISCUSSION

This study demonstrates that health system factors are significant and modifiable determinants of antimicrobial stewardship outcomes in neonatal sepsis across Kenyan county hospitals. The AMS intervention produced significant within-group improvements in all four stewardship outcomes and mortality, with between-group differences favouring the intervention arm for appropriate prescribing, guideline adherence, and empiric-to-target switch. The magnitude of these effects (Cramér's V = 0.15–0.19) is comparable to AMS interventions in high-income neonatal settings (Davey et al., 2013), suggesting that structured stewardship programmes are feasible and effective even in resource-constrained environments.

Culture-before-therapy was the strongest predictor of MDR isolation (OR = 3.70), but this association reflects detection bias rather than a causal pathway. Hospitals that perform cultures are more likely to identify resistant organisms; hospitals without culture capacity may have equally high MDR prevalence but remain undetected.[9] This has critical policy implications: MDR surveillance data must be interpreted in the context of diagnostic capacity. A hospital reporting low MDR rates may simply be under-diagnosing, not effectively managing resistance.

The guideline adherence was the strongest modifiable predictor of appropriate prescribing (OR = 2.94), and empiric-to-target switch was independently protective against mortality (OR = 2.67). These findings establish a causal chain: health system factors (guideline availability, HCW training, laboratory capacity) → stewardship processes (adherence, de-escalation) → clinical outcomes (mortality). The mediation structure explains why study arm alone was not significant in logistic regression: the intervention operates through stewardship pathways, not as a direct effect.

The know–do gap—HCW attitude improved substantially (d = 1.40) while practice improved less (d = 0.82)—highlights the structural barriers to translating knowledge into behaviour. Pharmacists endorsed stewardship principles (attitude 78–88%) but could not override non-adherent prescriptions. Nurses improved most in practice but lacked prescribing authority. This finding aligns with the WHO health systems framework, which distinguishes between hardware (infrastructure, guidelines) and software (values, norms, power) dimensions of system performance.[3] Hospital-level variation was substantial. Ruiru Level 4 Hospital (highest AMS score, full laboratory) achieved the best outcomes; Kiambu County Referral Hospital (lowest AMS score, partial laboratory) had the worst. This gradient demonstrates that AMR management is not merely an individual clinical problem but a system-level one. Investments in laboratory capacity, staffing, and guideline dissemination produce measurable improvements in resistance outcomes.

The preterm–readmission finding (OR = 0.29) is likely attributable to survivor bias: neonates who survive to discharge are a selected, relatively resilient group, and those who would have been readmitted may instead have died during the index admission. The VLBW subgroup showed large point estimates for benefit but lacked statistical significance, suggesting that future studies should oversample this high-risk group.

5 CONCLUSION

Health system factors, particularly AMS implementation scores, guideline availability, laboratory culture capacity, and HCW training, are significant determinants of antimicrobial stewardship outcomes among neonates with sepsis in Kiambu County, Kenya. The AMS intervention improved prescribing appropriateness, guideline adherence, and de-escalation, with effects mediated through system-level stewardship pathways rather than direct intervention effects. A persistent know–do gap between HCW attitude and practice underscores the need for structural changes, empowering pharmacists, supporting nurse-led protocols, and ensuring laboratory results reach prescribers in time to guide therapy. Containing AMR in neonatal sepsis requires not just individual clinician behaviour change but system-level investment in the infrastructure, workforce, and processes that enable responsible antimicrobial use.

6. ACKNOWLEDGEMENTS

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DECLARATIONS

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REFERENCES

1. World Health Organization. Antimicrobial resistance. *World Heal Organ Libr.*, 2023; 18(12): 564-645. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.
2. UNICEF. Neonatal mortality. *United Nation Child Fund.*, 2025; 12(9): 411-423. https://data.unicef.org/topic/child-survival/neonatal-mortality/
3. Villanueva P, Freyne B, Hickey L, Carr J, Bryant PA. Impact of an antimicrobial stewardship intervention in neonatal intensive care: Recommendations and implementation. *J Paediatr Child Health.*, 2021; 57(8): 1208-1214. doi:10.1111/jpc.15427
4. Poggi C, Dani C. New Antimicrobials for the Treatment of Neonatal Sepsis Caused by Multi-Drug-Resistant Bacteria: A Systematic Review. *Antibiot (Basel, Switzerland)*. 2023; 12(6). doi:10.3390/antibiotics12060956
5. Dickson BF, Putri ND, Adrizain R, et al. High burden of anti-microbial resistance among neonatal blood stream infections in Southeast Asia: results of the NeoSEAP study. *medRxiv.*, 2023; 19(7): 383-391. doi:10.1101/2023.09.11.23295383
6. Tessema B, Lippmann N, Knüpfer M, Sack U, König B. Antibiotic Resistance Patterns of Bacterial Isolates from Neonatal Sepsis Patients at University Hospital of Leipzig, Germany. *Antibiotics.*, 2021; 10(3): 323. doi:10.3390/antibiotics10030323
7. Obegi E, Oluka M, Opanga S, Aywak D, Okalebo F, Okumu M. Prescription and antibiotic resistance patterns at selected critical care units of the largest teaching and referral hospital in Kenya. *Front. Trop. Dis.*, 2025; 6-2025(8): 95-108. doi:10.3389/fitd.2025.1555008
8. Ahmed SK, Hussein S, Qurbani K, et al. Antimicrobial resistance: Impacts, challenges, and future prospects. *J Med Surgery, Public Heal.*, 2024; 2(2): 100-108. doi:https://doi.org/10.1016/j.glmedi.2024.100081
9. Aluvaala J, Tuti T, Ogola M, et al. Situational analysis of antibiotic prescriptions in Kenyan neonatal units for antimicrobial stewardship: a retrospective longitudinal study. *eClinicalMedicine.*, 2025; 82(10): 321-335. doi:10.1016/j.eclinm.2025.103156