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Antimicrobial Stewardship in Low-Resource Hospitals: Barriers and Practical Interventions

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ABSTRACT

Antibiotics are used heavily in hospitals everywhere, but the conditions that make stewardship hardest, thin laboratory services, limited specialist staff, uncertain drug supply and weak surveillance, are the same conditions in which resistant infection does the most damage. This narrative review asks what is known about the barriers to antimicrobial stewardship in low-resource hospitals and which practical interventions the published literature supports. It draws on work on the burden and drivers of resistance, on the design and components of stewardship programmes, on prescribing behaviour, on diagnostic capacity and on the few programme reports from middle-income hospitals, and it reports no new data and no local findings. Barriers cluster around diagnostics, workforce, medicine supply and governance rather than around knowledge alone. Low-cost measures such as written local guidelines, documentation of indication and duration, review of therapy after the first days, selective restriction and prospective audit with feedback appear workable, while expensive tools depend on infrastructure that many hospitals lack. The evidence base is mostly uncontrolled before-and-after reporting from a small number of settings, with outcomes that are seldom comparable, and the risk of withholding needed treatment is rarely measured. The review concludes that stewardship is feasible in modest settings if it is built around local resources, and it lists what future reports should record.

Keywords: Antimicrobial stewardship; Antibiotic resistance; Low-resource hospitals; Prescribing behaviour; Diagnostic capacity; Narrative review

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Article Class: Review Article

1. Introduction

Antibiotics are among the most widely prescribed drugs in any hospital, and a good share of that prescribing is judged

unnecessary or inappropriate when it is audited (1). The consequences are not abstract. Resistant infections are associated with longer stays, higher costs and, in



many studies, worse outcomes, although separating the effect of resistance from the severity of the underlying illness is difficult (2). Professional bodies have described the spread of resistant organisms as an epidemic that outpaces the development of new drugs (3, 4).

Most of the guidance on how to respond was written for well-staffed hospitals with a microbiology laboratory on site, an infectious-disease physician down the corridor and a pharmacy that stocks what the guideline names (5). Many hospitals in low- and middle-income countries have none of these, yet they carry a heavy burden of hospital-acquired infection (6) and a high proportion of newborn sepsis (7). A programme that quietly assumes resources the hospital does not have is not a programme it can run.

This review therefore asks two linked questions. What stands in the way of antimicrobial stewardship in hospitals with limited resources, and which practical interventions does the published literature support there? The title refers to hospitals in general terms, and no local data from any single hospital are reported; the article is an account of the published literature and nothing more. We describe what is known, point out where evidence is thin and say what a convincing report would need to contain. The aim is a fair account of what has been shown, what is plausible and what is merely repeated.

2. Literature Review

2.1 Resistance and Its Burden in Low-Resource Settings

Resistance is an old biological phenomenon that human antibiotic use has greatly accelerated. Resistance determinants predate clinical antibiotics and circulate widely among bacteria (8), and selection pressure from use in people and animals favours their spread (9).

Reviews of developing-country experience describe rising resistance among common community and hospital pathogens, uneven surveillance, and a shortage of the data needed to guide policy (10). Cross-national comparisons of outpatient consumption have also linked higher antibiotic use with higher resistance, though such ecological associations cannot prove causation (11).

Poverty shapes the problem in ways that are easy to overlook. Crowded wards, limited water and sanitation, interrupted treatment courses and weak access to quality-assured drugs all play a part (12). Hospital-acquired infection appears to be considerably more frequent in developing countries than in high-income ones (6), and every such infection is a potential reason to start an antibiotic. In intensive care, resistant Gram-negative bacteria, including *Pseudomonas* and *Acinetobacter*, are a recurring concern wherever the units operate (13, 14).

Resistance also moves. A mechanism first described in patients with links to India, Pakistan and the United Kingdom (15) was later detected in water and seepage samples in an Indian city (16), a reminder that hospital resistance is entangled with sanitation and the wider environment. The acronym ESKAPE was coined to draw attention to a group of nosocomial pathogens for which treatment options are narrowing (17). None of this is a reason for despair, but it explains why hospitals in poorer settings cannot wait for new drugs to rescue them.

2.2 What Stewardship Is and What It Asks

Concern about hospital antibiotic use is not new: an early paper set out the problem of unnecessary prescribing and suggested tentative remedies (18). Hospital guidelines in the late 1990s called for programmes to monitor and guide



antimicrobial use as part of preventing resistance (19), and the idea was developed into the modern concept of stewardship (20, 21). The aim is to secure the best clinical outcome for the individual patient while limiting the harm of selection pressure on everyone else (22).

The core strategies are well described. Prospective audit with feedback and prior authorisation or restriction of selected agents are the two main active approaches; education, local guidelines and formulary management support them; and de-escalation, dose optimisation and a switch from intravenous to oral therapy are common clinical elements (5, 23). Reviews written for hospital physicians emphasise a handful of simple principles: obtain cultures before treatment when they can be obtained, choose the narrowest agent that will do the job, and review the choice when results return (24, 25). In a hospital with few staff, the most useful of these are the ones that cost attention rather than money. None of these steps is technically difficult, but each is easy to skip when the ward is busy.

2.3 Prescribing Behaviour and Access to Drugs

Prescribing is a human habit before it is a pharmacological decision. Studies of low-income settings describe prescribers who respond to patient expectation, fear of treatment failure, limited diagnostic support and the commercial environment around medicines (26). A systematic review found that antibiotics are obtainable without prescription in many countries, so patients often arrive having already taken them (27). A stewardship team inside the hospital walls is working against pressures that begin outside them.

Behaviour-change research offers some guidance. A systematic review of strategies to influence prescribing in acute care concluded that interventions work

through a mixture of persuasion, restructuring of the environment and enablement, and that effects differ with the setting (28). A Cochrane review of hospital inpatient interventions likewise found that approaches that change the prescribing environment can improve practice, while it noted the limits of the designs available (29). Another line of argument holds that antibiotic prescribing should be handled like a care bundle, with a fixed set of expected actions, instead of a series of unrelated individual choices (30).

2.4 Diagnostics and Laboratory Capacity

Laboratory services are the quiet foundation of stewardship, and in many African and Asian hospitals they are the weakest part of the structure. Accounts of laboratory medicine in Africa describe shortages of trained staff, reagents, equipment and maintenance (31), and a broader review of clinical microbiology in developing countries describes the same pattern together with a lack of quality assurance (32). Susceptibility testing itself depends on standardised methods and careful interpretation (33).

Biomarkers have been proposed as a shortcut. Procalcitonin-guided treatment reduced antibiotic use in lower respiratory tract infection in a randomised trial in Switzerland (34) and reduced exposure to antibiotics in intensive care units in France (35). Both were conducted in well-resourced hospitals, and the assay is costly, so the finding says little about whether the approach is affordable or feasible elsewhere. Slow results are a related problem. When a culture takes several days to return, the clinician has usually committed to a regimen by then, and stewardship must work with the clinical picture instead. Each delay seems tolerable on its own; across a hospital and a year the cost accumulates.



2.5 The Risk of Doing Too Little

Any account of stewardship that speaks only of restraint is incomplete. In septic shock, the interval before effective antimicrobial therapy is begun has been identified as a critical determinant of survival (36), and international sepsis guidelines recommend giving effective antimicrobials early (37). A programme that pushes prescribers to hold back, or that makes approval slow, risks harm exactly where hesitation is most dangerous. This is the main honest complication in the literature: stewardship is justified by the long-run value of effective drugs, but its costs fall on today's patient, and few reports look for them.

3. Materials and Methods

3.1 Scope

This is a narrative review of published literature up to and including the year of the issue. It addresses barriers to stewardship and practical interventions in hospitals with limited laboratory, workforce and financial resources. It does not attempt a quantitative synthesis, and it reports no data collected by the authors and no findings from any particular hospital.

3.2 Literature Assembly

The sources were assembled by the authors through a purposive reading of the literature and of the reference lists of key papers, not through a formal systematic search, and no protocol was registered. Guidelines, systematic reviews, trials and programme reports were included where they bore directly on the barriers or interventions discussed. Because the selection was not exhaustive and was shaped by what the authors knew or could find, relevant reports, especially those published in local-language journals or outside indexed databases, may have been missed.

3.3 Appraisal Framework

Each source was read with a small set of questions in mind: whether the setting resembled a resource-limited hospital, whether the design allowed a comparison, whether outcomes were defined and measured in a comparable way, whether harms were considered, and whether costs were counted completely. The questions are summarised in Table 3. They are a reading aid for narrative purposes, not a validated quality score, and no source was excluded solely because it scored poorly. Reviews of this kind are more useful when they say where the evidence stops than when they smooth it over.

Table 3. Questions to ask of a stewardship report from a resource-limited hospital.

Question	What to look for	Common gap
Was there a comparison?	A control ward or time series (29)	Single before-and-after snapshot
Was the case mix stable?	Description of wards and patients	Not reported
Was use measured fairly?	Stated denominator and unit	Units not comparable
Were harms sought?	Mortality, readmission, delayed treatment (36)	Rarely looked for
Were costs complete?	Staff time and tests included	Drug purchases only
Did it last?	Follow-up beyond the launch	Short follow-up

Note: Compiled from the methodological literature cited in the text; not a validated instrument.

4. Results

4.1 Barriers Identified in the Literature

The barriers reported across the sources fall into six groups, summarised in Table 1. Diagnostics and laboratory capacity head the list (31, 32). Without cultures and susceptibility results, therapy remains empirical, and de-escalation, the commonest stewardship manoeuvre, has



little to work on. Workforce comes next. The guideline model assumes a team with a physician and a pharmacist trained in infectious disease (5), but in many hospitals no single person has this role, and a programme with no owner tends to fade. Medicine supply is a third barrier. When the recommended drug is out of stock, the prescriber uses what is on the shelf, and a guideline that cannot be followed loses credibility (26). Access outside the hospital is a fourth (27). The remaining two are weak surveillance, which leaves guidelines resting on figures from other countries (38), and the infection-control conditions that increase the demand for antibiotics in the first place (6, 39). Prevention is part of stewardship in this sense: every infection avoided is a prescription avoided. Figure 1 sketches how these barriers line up against the interventions described in the next section.

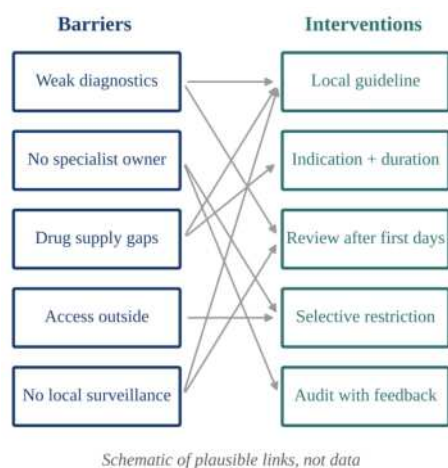


Figure 1. From barriers to interventions in a low-resource hospital (schematic, not data).

4.2 Interventions That Appear Workable

Table 2 lists the interventions most often described and what each asks of a hospital, and Figure 2 sets them against the resources they draw on. A local written guideline is the cheapest starting point, and it can be built from national or international guidance adapted to the drugs

the hospital actually stocks (5, 19). A guideline alone seldom changes behaviour, but it gives audit and feedback something to be measured against. Documenting the indication and the planned duration in the notes is almost free, and fits the care-bundle idea (30). It is a habit worth keeping even when the answer seems obvious.

Table 1. Barriers to stewardship in low-resource hospitals.

Domain	Typical barrier	Why it matters
Diagnostics	Few cultures, slow or absent susceptibility results (31, 32)	Therapy stays empirical and broad
Workforce	No infectious-disease or microbiology specialist (5)	No one owns the programme
Medicines	Gaps in supply, substitution of what is available (26)	Guidelines cannot always be followed
Access	Antibiotics sold without prescription (27)	Pressure on use arrives before admission
Surveillance	No local resistance data (38)	Guidelines rest on foreign figures
Infection control	Crowding, limited hand hygiene (6, 39)	Spread raises the need for antibiotics

Note: Qualitative grouping drawn from the cited literature; the barriers overlap and their relative weight differs between hospitals.

Review of therapy after the first days is the next step. A named person looks at each patient on antibiotics, asks whether the diagnosis still stands, whether a culture has returned and whether a narrower or oral drug will serve, as sketched in Figure 3. The step depends on information, so it works best where at least some microbiology exists, and it works in a weaker form when it is based on the clinical course alone (23, 24). Restriction of a few broad-spectrum agents can be run with a single approver on call, though reviews warn of delays and workarounds



(20, 29). Prospective audit with feedback is more demanding of time but is persuasive rather than coercive (28).

Education on its own is the least convincing option. Behavioural reviews suggest that it is helpful as part of a package but weak and short-lived when used alone (28, 29). The practical implication is to treat teaching as a way of launching other measures and not as the intervention itself.

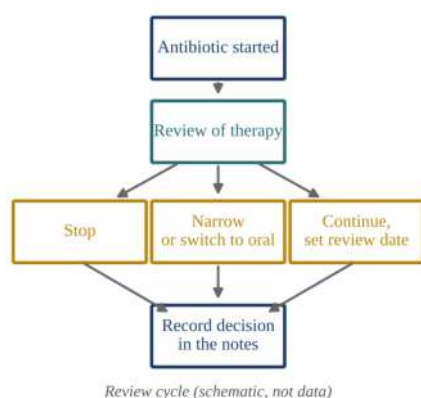


Figure 3. Cycle of a prescription review after the first days of therapy (schematic, not data).

4.3 Reports From Hospitals With Limited Resources

Reports from middle-income hospitals show that programmes can be run outside the best-resourced centres, though the reports are few and their designs modest. A hospital-wide programme in Argentina reported effects on prescribing practice, antibiotic consumption, cost savings and bacterial resistance (40). A Thai tertiary hospital reported that an education and antibiotic-control programme was associated with improved antibiotic use (41). A multidisciplinary programme in a United States hospital, run over seven years, described favourable changes in use and in the susceptibility of some organisms (42). The last was not a low-resource setting, but it is often cited as showing what sustained effort can do. A hospital manager reading a programme report

wants an answer to a plain question: would this work here?

Table 2. Practical stewardship interventions and what they ask of a hospital.

Intervention	Resource needed	Main caveat
Local written guideline	Committee time, local data where available (5, 19)	Ignored unless owned by clinicians
Indication and duration in notes	A line on the chart (30)	Compliance fades without feedback
Review after the first days	A named reviewer, daily	Needs diagnostic or clinical data to act on
Restriction of selected agents	An approver on call (20, 29)	Delays, workarounds, resentment
Audit with feedback	Pharmacist or physician time (40, 41)	Effect may wane when stopped
Education	Teaching sessions (28)	Weak alone and short-lived

Note: Resource needs are the authors' qualitative reading of the cited reports and reviews, not measured costs.

	Staff time	Laboratory	Specialist	Money
Local guideline	some	low	some	low
Indication + duration	low	low	low	low
Review after first days	higher	some	some	low
Selective restriction	some	some	higher	low
Audit with feedback	higher	some	some	low
Education sessions	some	low	some	some

Qualitative reading of demand, schematic, not data

Figure 2. Qualitative matrix of interventions against the resources they draw on (schematic, not data).

These reports share limitations. Most compare a period before with a period after, which cannot separate the intervention from other changes such as new staff, a changed case mix or a general fall in prescribing. Outcomes are chosen differently from one report to the next, and the denominators used for antibiotic



consumption are not always comparable. Harms such as delayed treatment, readmission or death are rarely examined, which matters given the evidence in Section 2.5. This is why the same kind of intervention can look excellent in one report and unremarkable in the next.

4.4 Sustaining a Programme

Launching a programme is easier than sustaining it. Several reviews note that effects fade when audit or feedback stops, and that programmes with a named lead and support from hospital management last longer than those that depend on enthusiasm (20, 25). Because most reports follow hospitals for short periods, little can be said with confidence about what happens after the first year or two. A ward that has had time to absorb a new routine behaves differently from one in its first month.

5. Discussion

5.1 Interpretation

The literature suggests that the main obstacles to stewardship in low-resource hospitals are structural, not matters of knowledge. Prescribers in these settings often know the principles; what they lack is a laboratory result, a stocked drug, a colleague with time to review the chart, or a manager who treats the programme as part of the hospital's work (26, 31). That points towards interventions that fit around such gaps. Guidelines adapted to local stock, documentation of indication and duration, review after the first days and selective restriction ask mostly for organisation and attention (5, 30).

It also points towards accepting that a limited programme is still worth running. Whether such adaptations preserve the benefits seen in better-resourced hospitals has not been tested directly, and the claim that stewardship is feasible in modest settings is supported by a handful of

reports rather than by controlled trials. That is a modest claim, and it is the one the literature will currently carry.

5.2 Limitations

The review shares the limits of its sources. The literature is dominated by uncontrolled before-and-after reports, outcomes are not standardised, and publication bias probably favours programmes that appeared to work. The selection of sources was purposive and not systematic, so relevant reports may be missing, and the grouping of barriers and interventions reflects our reading. Several of the best-known trials of diagnostic and stewardship strategies come from well-resourced hospitals and may not transfer. The point is not that a report is poor, only that its result travels less far than its abstract suggests.

There are also gaps in what the reviewed reports measured. Few examined clinical harm, few counted staff time and fewer still followed hospitals for long enough to see whether benefits endured. In small studies the confidence intervals, where they are reported at all, are wide. Absence of a demonstrated effect in a small before-and-after study is not evidence that no effect exists.

5.3 Future Work

Three needs stand out. First, better designs: interrupted time series or controlled comparisons with defined outcomes, and a record of the case mix. Second, routine measurement of safety alongside consumption, so that restraint is not purchased at the cost of delayed treatment (36, 37). Third, cost accounting that counts staff time, tests and failed attempts and not only drug purchases, since a programme that looks cheap on paper may not be cheap to run. A saving that disappears once staff time is priced is not a saving that a hospital director would



see. These points apply with equal force to any new hospital programme, not only to stewardship.

6. Conclusion

Antimicrobial stewardship in low-resource hospitals is constrained less by ignorance than by the absence of laboratory support, specialist staff, reliable drug supply and surveillance. The published literature supports a pragmatic set of interventions, namely local guidelines, documentation of indication and duration, review of therapy after the first days, selective restriction and audit with feedback, and it cautions that education alone is not enough. The evidence for each in truly resource-limited settings is thin, and the risk of withholding needed treatment is seldom measured.

For the hospital team, the message is practical: begin with what costs attention rather than money, name an owner, record what is done and look for harm as well as savings. For the researcher, the opportunity is better-designed, fully costed studies from the settings where the problem is greatest.

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

K.R. conceived the review and wrote the sections on resistance and prescribing behaviour. V.C. wrote the sections on clinical management and the risks of under-treatment. C.V. wrote the sections on laboratory capacity and the appraisal of

programme reports. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No human participants or animals were involved and no ethical approval was required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

13. References

1. Hecker, M. T., Aron, D. C., Patel, N. P., Lehmann, M. K., & Donskey, C. J. (2003). Unnecessary use of antimicrobials in hospitalized patients: Current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. *Archives of Internal Medicine*, 163(8), 972–978. DOI: [10.1001/archinte.163.8.972](https://doi.org/10.1001/archinte.163.8.972)
2. Cosgrove, S. E. (2006). The relationship between antimicrobial resistance and patient outcomes: Mortality, length of hospital stay, and health care costs. *Clinical Infectious Diseases*, 42(Suppl 2), S82–S89. DOI: [10.1086/499406](https://doi.org/10.1086/499406)
3. Spellberg, B., Guidos, R., Gilbert, D., Bradley, J., Boucher, H. W., Scheld, W. M., ... Edwards, J. (2008). The epidemic of antibiotic-resistant infections: A call to action for the medical community from the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 46(2), 155–164. DOI: [10.1086/524891](https://doi.org/10.1086/524891)
4. Boucher, H. W., Talbot, G. H., Bradley, J. S., Edwards, J. E., Gilbert, D., Rice, L. B., ... Bartlett, J. (2009). Bad bugs, no drugs: No ESCAPE! An update from the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 48(1), 1–12. DOI: [10.1086/595011](https://doi.org/10.1086/595011)
5. Dellit, T. H., Owens, R. C., McGowan, J. E., Gerding, D. N., Weinstein, R. A., Burke, J. P., ... Hooton, T. M. (2007). Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clinical Infectious Diseases*, 44(2), 159–177. DOI: [10.1086/510393](https://doi.org/10.1086/510393)
6. Allegranzi, B., Nejad, S. B., Combescure, C., Graafmans, W., Attar, H., Donaldson, L., & Pittet, D. (2011). Burden of endemic health-care-associated infection in developing countries: Systematic review and meta-analysis. *The Lancet*, 377(9761), 228–241. DOI: [10.1016/S0140-6736\(10\)61458-4](https://doi.org/10.1016/S0140-6736(10)61458-4)



7. Zaidi, A. K. M., Huskins, W. C., Thaver, D., Bhutta, Z. A., Abbas, Z., & Goldmann, D. A. (2005). Hospital-acquired neonatal infections in developing countries. *The Lancet*, 365(9465), 1175–1188. DOI: [10.1016/S0140-6736\(05\)71881-X](https://doi.org/10.1016/S0140-6736(05)71881-X)
8. Davies, J., & Davies, D. (2010). Origins and evolution of antibiotic resistance. *Microbiology and Molecular Biology Reviews*, 74(3), 417–433. DOI: [10.1128/MMBR.00016-10](https://doi.org/10.1128/MMBR.00016-10)
9. Levy, S. B., & Marshall, B. (2004). Antibacterial resistance worldwide: Causes, challenges and responses. *Nature Medicine*, 10(12 Suppl), S122–S129. DOI: [10.1038/nm1145](https://doi.org/10.1038/nm1145)
10. Okeke, I. N., Laxminarayan, R., Bhutta, Z. A., Duse, A. G., Jenkins, P., O'Brien, T. F., ... Klugman, K. P. (2005). Antimicrobial resistance in developing countries. Part I: Recent trends and current status. *The Lancet Infectious Diseases*, 5(8), 481–493. DOI: [10.1016/S1473-3099\(05\)70189-4](https://doi.org/10.1016/S1473-3099(05)70189-4)
11. Goossens, H., Ferech, M., Vander Stichele, R., & Elseviers, M. (2005). Outpatient antibiotic use in Europe and association with resistance: A cross-national database study. *The Lancet*, 365(9459), 579–587. DOI: [10.1016/S0140-6736\(05\)17907-0](https://doi.org/10.1016/S0140-6736(05)17907-0)
12. Planta, M. B. (2007). The role of poverty in antimicrobial resistance. *The Journal of the American Board of Family Medicine*, 20(6), 533–539. DOI: [10.3122/jabfm.2007.06.070019](https://doi.org/10.3122/jabfm.2007.06.070019)
13. Kollef, M. H., & Fraser, V. J. (2001). Antibiotic resistance in the intensive care unit. *Annals of Internal Medicine*, 134(4), 298–314. DOI: [10.7326/0003-4819-134-4-200102200-00014](https://doi.org/10.7326/0003-4819-134-4-200102200-00014)
14. Paterson, D. L. (2006). The epidemiological profile of infections with multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter* species. *Clinical Infectious Diseases*, 43(Suppl 2), S43–S48. DOI: [10.1086/504476](https://doi.org/10.1086/504476)
15. Kumarasamy, K. K., Toleman, M. A., Walsh, T. R., Bagaria, J., Butt, F., Balakrishnan, R., ... Woodford, N. (2010). Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: A molecular, biological, and epidemiological study. *The Lancet Infectious Diseases*, 10(9), 597–602. DOI: [10.1016/S1473-3099\(10\)70143-2](https://doi.org/10.1016/S1473-3099(10)70143-2)
16. Walsh, T. R., Weeks, J., Livermore, D. M., & Toleman, M. A. (2011). Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: An environmental point prevalence study. *The Lancet Infectious Diseases*, 11(5), 355–362. DOI: [10.1016/S1473-3099\(11\)70059-7](https://doi.org/10.1016/S1473-3099(11)70059-7)
17. Rice, L. B. (2008). Federal funding for the study of antimicrobial resistance in nosocomial pathogens: No ESKAPE. *The Journal of Infectious Diseases*, 197(8), 1079–1081. DOI: [10.1086/533452](https://doi.org/10.1086/533452)
18. Kunin, C. M., Tupasi, T., & Craig, W. A. (1973). Use of antibiotics: A brief exposition of the problem and some tentative solutions. *Annals of Internal Medicine*, 79(4), 555–560. DOI: [10.7326/0003-4819-79-4-555](https://doi.org/10.7326/0003-4819-79-4-555)
19. Shlaes, D. M., Gerding, D. N., John, J. F., Craig, W. A., Bornstein, D. L., Duncan, R. A., ... Marr, J. J. (1997). Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: Guidelines for the prevention of antimicrobial resistance in hospitals. *Clinical Infectious Diseases*, 25(3), 584–599. DOI: [10.1086/513766](https://doi.org/10.1086/513766)
20. MacDougall, C., & Polk, R. E. (2005). Antimicrobial stewardship programs in health care systems. *Clinical Microbiology Reviews*, 18(4), 638–656. DOI: [10.1128/CMR.18.4.638-656.2005](https://doi.org/10.1128/CMR.18.4.638-656.2005)
21. Fishman, N. (2006). Antimicrobial stewardship. *The American Journal of Medicine*, 119(6, Suppl 1), S53–S61. DOI: [10.1016/j.amjmed.2006.04.003](https://doi.org/10.1016/j.amjmed.2006.04.003)
22. Owens, R. C. (2008). Antimicrobial stewardship: Concepts and strategies in the 21st century. *Diagnostic Microbiology and Infectious Disease*, 61(1), 110–128. DOI: [10.1016/j.diagmicrobio.2008.02.012](https://doi.org/10.1016/j.diagmicrobio.2008.02.012)
23. Ohl, C. A., & Luther, V. P. (2011). Antimicrobial stewardship for inpatient facilities. *Journal of Hospital Medicine*, 6(Suppl 1), S4–S15. DOI: [10.1002/jhm.881](https://doi.org/10.1002/jhm.881)
24. Leekha, S., Terrell, C. L., & Edson, R. S. (2011). General principles of antimicrobial therapy. *Mayo Clinic Proceedings*, 86(2), 156–167. DOI: [10.4065/mcp.2010.0639](https://doi.org/10.4065/mcp.2010.0639)
25. Doron, S., & Davidson, L. E. (2011). Antimicrobial stewardship. *Mayo Clinic Proceedings*, 86(11), 1113–1123. DOI: [10.4065/mcp.2011.0358](https://doi.org/10.4065/mcp.2011.0358)
26. Radyowijati, A., & Haak, H. (2003). Improving antibiotic use in low-income countries: An overview of evidence on determinants. *Social Science & Medicine*, 57(5), 733–744. DOI: [10.1016/S0277-9536\(02\)00418-5](https://doi.org/10.1016/S0277-9536(02)00418-5)
27. Morgan, D. J., Okeke, I. N., Laxminarayan, R., Perencevich, E. N., & Weisenberg, S. (2011). Non-prescription antimicrobial use worldwide: A systematic review. *The Lancet Infectious Diseases*, 11(9), 692–701. DOI: [10.1016/S1473-3099\(11\)70054-8](https://doi.org/10.1016/S1473-3099(11)70054-8)
28. Charani, E., Edwards, R., Sevdalis, N., Alexandrou, B., Sibley, E., Mullett, D., ... Holmes, A. (2011). Behavior change strategies to influence antimicrobial prescribing in acute care: A systematic review. *Clinical Infectious Diseases*, 52(1), 1–10. DOI: [10.1093/cid/cir101](https://doi.org/10.1093/cid/cir101)



- Diseases*, 53(7), 651–662. DOI: [10.1093/cid/cir445](https://doi.org/10.1093/cid/cir445)
29. Davey, P., Brown, E., Fenelon, L., Finch, R., Gould, I., Hartman, G., ... O'Neill, B. (2005). Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews*, (4), CD003543. DOI: [10.1002/14651858.CD003543.pub2](https://doi.org/10.1002/14651858.CD003543.pub2)
 30. Cooke, F. J., & Holmes, A. H. (2007). The missing care bundle: Antibiotic prescribing in hospitals. *International Journal of Antimicrobial Agents*, 30(1), 25–29. DOI: [10.1016/j.ijantimicag.2007.03.003](https://doi.org/10.1016/j.ijantimicag.2007.03.003)
 31. Petti, C. A., Polage, C. R., Quinn, T. C., Ronald, A. R., & Sande, M. A. (2006). Laboratory medicine in Africa: A barrier to effective health care. *Clinical Infectious Diseases*, 42(3), 377–382. DOI: [10.1086/499363](https://doi.org/10.1086/499363)
 32. Archibald, L. K., & Reller, L. B. (2001). Clinical microbiology in developing countries. *Emerging Infectious Diseases*, 7(2), 302–305. DOI: [10.3201/eid0702.010232](https://doi.org/10.3201/eid0702.010232)
 33. Reller, L. B., Weinstein, M., Jorgensen, J. H., & Ferraro, M. J. (2009). Antimicrobial susceptibility testing: A review of general principles and contemporary practices. *Clinical Infectious Diseases*, 49(11), 1749–1755. DOI: [10.1086/647952](https://doi.org/10.1086/647952)
 34. Christ-Crain, M., Jaccard-Stolz, D., Bingisser, R., Gencay, M. M., Huber, P. R., Tamm, M., & Müller, B. (2004). Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: Cluster-randomised, single-blinded intervention trial. *The Lancet*, 363(9409), 600–607. DOI: [10.1016/S0140-6736\(04\)15591-8](https://doi.org/10.1016/S0140-6736(04)15591-8)
 35. Bouadma, L., Luyt, C.-E., Tubach, F., Cracco, C., Alvarez, A., Schwebel, C., ... Wolff, M. (2010). Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): A multicentre randomised controlled trial. *The Lancet*, 375(9713), 463–474. DOI: [10.1016/S0140-6736\(09\)61879-1](https://doi.org/10.1016/S0140-6736(09)61879-1)
 36. Kumar, A., Roberts, D., Wood, K. E., Light, B., Parrillo, J. E., Sharma, S., ... Cheang, M. (2006). Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Critical Care Medicine*, 34(6), 1589–1596. DOI: [10.1097/01.CCM.0000217961.75225.E9](https://doi.org/10.1097/01.CCM.0000217961.75225.E9)
 37. Dellinger, R. P., Levy, M. M., Carlet, J. M., Bion, J., Parker, M. M., Jaeschke, R., ... Vincent, J.-L. (2008). Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. *Critical Care Medicine*, 36(1), 296–327. DOI: [10.1097/01.CCM.0000298158.12101.41](https://doi.org/10.1097/01.CCM.0000298158.12101.41)
 38. Okeke, I. N., Klugman, K. P., Bhutta, Z. A., Duse, A. G., Jenkins, P., O'Brien, T. F., ... Laxminarayan, R. (2005). Antimicrobial resistance in developing countries. Part II: Strategies for containment. *The Lancet Infectious Diseases*, 5(9), 568–580. DOI: [10.1016/S1473-3099\(05\)70217-6](https://doi.org/10.1016/S1473-3099(05)70217-6)
 39. Pittet, D., Hugonnet, S., Harbarth, S., Mourouga, P., Sauvan, V., Touveneau, S., & Perneger, T. V. (2000). Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *The Lancet*, 356(9238), 1307–1312. DOI: [10.1016/S0140-6736\(00\)02814-2](https://doi.org/10.1016/S0140-6736(00)02814-2)
 40. Bantar, C., Sartori, B., Vesco, E., Heft, C., Saúl, M., Salamone, F., & Oliva, M. E. (2003). A hospitalwide intervention program to optimize the quality of antibiotic use: Impact on prescribing practice, antibiotic consumption, cost savings, and bacterial resistance. *Clinical Infectious Diseases*, 37(2), 180–186. DOI: [10.1086/375818](https://doi.org/10.1086/375818)
 41. Apisarnthanarak, A., Danchaivijitr, S., Khawcharoenporn, T., Limsrivilai, J., Warachan, B., Bailey, T. C., & Fraser, V. J. (2006). Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clinical Infectious Diseases*, 42(6), 768–775. DOI: [10.1086/500955](https://doi.org/10.1086/500955)
 42. Carling, P., Fung, T., Killion, A., Terrin, N., & Barza, M. (2003). Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infection Control & Hospital Epidemiology*, 24(9), 699–706. DOI: [10.1086/502278](https://doi.org/10.1086/502278)