

Drug shortages as a medication-safety problem: clinical impact, therapeutic substitutions, and mitigation strategies

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Abstract: Drug shortages have become a recurrent feature of modern pharmacotherapy and should be conceptualised as a medication-safety problem rather than a purely logistical supply issue. I synthesised PubMed-indexed evidence (search and verification date: 10 February 2026) spanning scoping reviews, systematic reviews, pharmacovigilance analyses, observational outcome studies, and policy analyses to evaluate clinical consequences of shortages, safety risks from therapeutic substitutions, and mitigation strategies at clinical and system levels. The evidence indicates that shortages frequently involve high-consequence drug classes (generic sterile injectables, antibiotics, oncology agents) and generate harm through delayed/omitted therapy, forced substitution with unfamiliar agents or concentrations, and increased system complexity. Patient-important outcome signals include higher mortality during the US norepinephrine shortage in septic shock care (absolute risk increase 3.7%; adjusted OR 1.15) and worsened oncology outcomes during an intravenous etoposide shortage (increased hospitalisation and shorter progression-free survival). Pharmacovigilance studies demonstrate that shortages are associated with adverse drug reactions, medication errors, disease worsening, and serious outcomes including deaths or life-threatening events, with replacement drugs commonly implicated. Mitigation strategies with the strongest practical support are structured therapeutic interchange protocols led by pharmacists and stewardship teams (notably antimicrobial stewardship for antibiotic shortages), standardised order sets and concentration controls, active monitoring for substitution-related ADRs and errors, and transparent prioritisation frameworks for scarce curative therapies. India/LMIC evidence highlights that prolonged public-sector stock-outs and variable availability of essential medicines shift patients towards private procurement and informal substitution, requiring governance, procurement and distribution reforms alongside local inventory and digital visibility tools. Overall, shortage preparedness should be integrated into medication-safety programmes with explicit contingency pathways, audit of shortage-driven adverse events, and system-level supply resilience policies.

Keywords: Drug shortages, medicine safety, pharmacotherapy, therapeutic substitutions

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Introduction

Drug shortages have shifted from episodic inconvenience to a recurrent systems problem that can directly undermine medication safety and patient outcomes. In practice, I have found that “shortage management” is often treated as an operational inconvenience for pharmacy supply teams; however, the downstream clinical reality is closer to a latent safety threat that propagates into prescribing, dispensing, administration, monitoring, and patient counselling. Contemporary reviews describe drug shortages as a complex health-care crisis that disproportionately affects widely used generic injectable medicines—particularly anaesthesia agents, antibiotics, analgesics, nutrition/electrolytes, and chemotherapy—where a small number of manufacturers and limited surge capacity amplify fragility (1). The literature also emphasises manufacturing quality and production disruptions, alongside market dynamics, as recurrent proximal drivers (1,2).

From a medication-safety perspective, a shortage is not merely “a medicine is unavailable”. It is, more precisely, a forced deviation from standard-of-care medication pathways. Deviations can occur at multiple decision points—whether by delaying treatment, substituting a different agent, changing route or formulation (e.g., IV to oral), using unfamiliar concentrations, rationing doses, compounding, or altering monitoring intensity. In the drug shortage era, the clinical effects are increasingly documented across economic, clinical, and humanistic domains, although evidence quality varies across drug classes and settings (3,4).

A scoping review of medication shortages and patient outcomes found that most published studies describe adverse economic, clinical and humanistic outcomes, including increased out-of-pocket costs, drug errors, adverse events and mortality, while also noting that some substitutions can be clinically equivalent in select contexts when carefully managed (4). This tension underpins the central safety challenge: some substitutions are acceptable (and occasionally necessary), but the process of substitution—often under time pressure, with incomplete local protocols—creates predictable risk.

In this umbrella-style narrative synthesis, drug shortages are treated explicitly as a medication-safety problem. My aim is to synthesise evidence on: (i) the clinical impact of shortages on patient outcomes and safety, (ii) therapeutic substitution risks and where harms concentrate, and (iii) mitigation strategies spanning patient-level, institutional stewardship, and system-level policy levers, with an India/LMIC-relevant perspective grounded in verifiable evidence.

Methods

For this study literature searching and reference verification were performed on 10 February 2026 using PubMed as the primary database, with Google Scholar reserved for items lacking a PubMed record (none were required for the final set). We used combinations of the following search terms: “drug shortage” AND (medication error OR adverse event OR substitution OR therapeutic interchange OR patient outcome OR mortality), “drug shortage” AND (oncology OR chemotherapy OR norepinephrine OR antibiotic), and “medicine shortages” AND (India OR essential medicines OR stock-outs). Authors prioritised systematic reviews, scoping reviews, high-quality observational studies with clinical endpoints, pharmacovigilance analyses, and policy analyses indexed in PubMed. For each included reference, we verified bibliographic metadata (authors, title, journal, year, volume/issue, pages or article number) and recorded the PMID and DOI (where available) directly from the PubMed record.

Given heterogeneity in definitions (shortage, stock-out), settings (hospital, community), and outcomes (errors, ADEs, mortality, costs), we structured the Results around (i) mechanisms of safety risk and (ii) higher-risk clinical domains supported by stronger empirical evidence. Authors report quantitative estimates only when clearly available from the cited paper’s abstract or PubMed record excerpts.

Results

Drivers and where shortages concentrate

Multiple overviews converge on the observation that shortages frequently involve generic sterile injectables, where low margins, limited manufacturer redundancy, constrained production capacity, and quality-related manufacturing disruptions can rapidly lead to national or regional scarcity (1,2). In such markets, even a single plant disruption can propagate into global supply constraints because alternative manufacturers may already be operating at high capacity and may require regulatory lead time to upscale (1,2). Contemporary descriptions of the “drug shortage era” note that extensive research spans causes, impacts on care and outcomes, costs, management and prevention, supporting the conclusion that shortages can be sufficiently harmful to justify policy change, while also highlighting persistent evidence gaps (3).

The salient medication-safety implication is that shortages are not random: they tend to strike medicines used in acute care, anaesthesia, critical care, infectious diseases, and

oncology—settings where route changes and dose conversions are common and where therapeutic windows may be narrow. Consequently, safety risk concentrates in environments that already tolerate little pharmacotherapy variance (1,5).

How shortages create medication-safety risk

It is suggested that the shortage-to-harm pathway into three dominant mechanisms supported across the evidence base.

First, shortages cause delay, omission, or rationing of indicated therapy. In contexts where time-to-treatment matters (e.g., septic shock vasopressors; chemotherapy schedules), delay or regimen alteration can plausibly worsen outcomes, and this is supported by observational outcome studies described below (7,13).

Second, shortages force therapeutic substitution and non-standard regimen construction. In practice, this includes switching to unfamiliar alternatives, changing concentrations or formulations, or shifting IV to oral routes due to supply constraints. Even when the alternative drug is clinically acceptable, substitution introduces risk via dosing errors, monitoring mismatches, and reduced clinician familiarity (4,5).

Third, shortages increase system workload and process complexity, which can create downstream error opportunity. Hospital-level shortage responses commonly require urgent protocol updates, rapid education, EHR order-set modifications, and pharmacy compounding or procurement workarounds. This “extra work” is not a neutral adaptation; it re-allocates attention and increases cognitive load at the same time as clinical teams manage sicker patients (1,3,5).

The scoping review by Phuong and colleagues reports that shortages are predominantly associated with adverse outcomes across economic, clinical and humanistic domains, including increased drug errors and adverse events, while acknowledging that equivalence is sometimes reported when substitutions are closely managed (4). This duality suggests a safety framing: substitution can be clinically justified, but substitution management is the safety-critical intervention.

Evidence of harm with patient-important outcomes

Mortality signal during the US norepinephrine shortage

One of the clearest links between shortage conditions and patient-important outcomes comes from the 2011 national shortage of norepinephrine in the US. In a retrospective cohort study of 26 hospitals from the Premier Healthcare Database (n=27,835 adults with septic shock), hospital-level shortage quarters were associated with changes in vasopressor practice and higher mortality (7). Norepinephrine use declined from 77.0% pre-shortage to 55.7% during the shortage, while phenylephrine was the most common alternative (baseline 36.2%, maximum 54.4%) (7). The study reported in-hospital mortality of 39.6% during shortage quarters versus 35.9% during normal quarters, an absolute risk increase of 3.7% (95% CI 1.5%–6.0%), with an adjusted odds ratio of 1.15 (95% CI 1.01–1.30) (7). The accompanying editorial argues that the norepinephrine experience illustrates potential harm from national shortages of generic sterile injectables, reinforcing the medication-safety salience of supply chain instability for first-line acute-care drugs (8).

This evidence is not proof that the substitute vasopressor itself caused mortality differences; it represents a plausible causal chain where shortage-driven practice variation co-occurs with worse outcomes, including potential confounding by unmeasured severity or reinforcement of suboptimal alternatives. Nonetheless, the presence of a mortality signal at population scale makes shortages difficult to dismiss as purely logistical.

Pharmacovigilance evidence: adverse drug reactions and medication errors

Pharmacovigilance analyses provide complementary evidence that shortages can be associated with clinically significant harm, including serious outcomes.

A retrospective study using the French National Pharmacovigilance Database extracted shortage-related reports from 1985 through end-2019 and included 462 cases after selection (9). The study noted increasing cases from 2004 to 2019 and described both adverse drug reactions (ADRs) and medication errors. Disease worsening was observed in 15.9% of cases, often related to lack of efficacy of the replacement drug; half of cases were considered serious; and death and/or life-threatening situations were reported in 5.8% (9). Medication errors were identified in 51 cases (11%), mostly at the administration step and involving a human factor (9). These data are important because they show harm signals that are plausibly linked to the processes of substitution and administration during shortage events.

The CIRUPT prospective study (French pharmacovigilance network) collected notifications involving shortage drugs between 1 January 2020 and 30 June 2021 and reported 224 included cases (10). These involved mainly ADRs (59%) and medication errors (23%), with 29% serious cases (10). The authors further report that shortages were associated with ADRs related to replacement drugs in 59% of cases, drug inefficacy in 18%, and aggravation of underlying disease in 11% (10). Notably, the study observed that in 82% of cases the shortage drug was subject to information delivered to health professionals by the national medicines safety agency, yet harms still occurred (10). This finding is central to mitigation strategy design: communication is necessary but insufficient.

Together, these pharmacovigilance studies anchor the claim that drug shortages are not merely administrative problems; they can manifest as identifiable medication-safety events, including serious harm and death, in real-world reporting systems (9,10).

Intensive care sedation shortages: process change with unanticipated harms

Shortage-driven changes can yield harms even when classical prescribing error rates do not rise. In a retrospective chart review examining sedation and analgesia prescribing during a national shortage of fentanyl and injectable benzodiazepines in a paediatric ICU, Hughes et al compared January–February 2011 vs January–February 2012 and found no statistically significant difference in prescribing error rates (33 errors/169 orders vs 39 errors/179 orders; $p=0.603$) (6). However, unintended extubations per 100 ventilator days increased from 0.15 to 1.13 ($p<0.001$) during the shortage period (6). While the study cannot establish causality, it demonstrates that substitutes and altered sedation pathways may affect broader clinical process outcomes that matter to patients (unintended extubation), even if the narrow metric of dose-appropriateness errors appears stable.

Therapeutic substitution domains and mitigation implications

I now summarise substitution-driven risks and mitigation needs in domains where evidence suggests high consequence.

Antibiotic shortages and stewardship-mediated substitution

A systematic review of antibiotic drug shortages (studies from 2000–July 2023; 74 included studies, predominantly high-income countries) provides a structured view of causes and clinical effects (11). Piperacillin–tazobactam was the most frequently reported shortage drug (21/74 studies; 28.4%), and many reported antibiotics were in the WHO “Watch” category (27/54; 51%) (11). The review identifies manufacturing disruptions—such as active pharmaceutical ingredient and raw material supply problems—as a frequent cause (11). Reported clinical implications included increased length of stay, treatment failure after inferior alternatives, and negative impacts on antimicrobial stewardship programmes; robust economic analyses were described as unavailable (11). Importantly, the review reports that successful mitigation strategies were often driven by hospital antimicrobial stewardship (AMS) and infectious diseases teams (11).

From a medication-safety standpoint, antibiotic substitution is complex because equivalence depends on infection source, susceptibility, toxicity profile, renal function and local resistance patterns. Shortage-driven escalation (e.g., broader-spectrum substitutes) can also generate delayed harm via resistance pressure. Therefore, AMS-driven protocols and close monitoring are not optional extras; they are core safety controls during antibiotic shortages (11).

Oncology shortages: regimen disruption, altered outcomes, and ethical allocation

Oncology provides high-stakes examples where shortage-driven changes can plausibly affect survival. A Hematology/Oncology Pharmacy Association survey of 68 US organisations (December 2019–July 2020) reported that 63% of institutions experienced one or more drug shortages per month, with a 34% increase in 2019 compared with 2018 (12). Treatment delays, reduced doses, or alternative regimens were reported by 75% of respondents; difficult-to-obtain agents included vincristine, vinblastine, intravenous immunoglobulin, leucovorin, and Bacillus Calmette–Guérin (12). Respondents reported increased risk of medication errors and adverse outcomes, and clinical research disruption (12). While survey data are not outcome data, they quantify the scale of frequent shortage exposure in oncology practice and underscore how shortages propagate into regimen changes.

More direct outcome evidence is seen in the Ontario intravenous etoposide shortage (2018–2020). In a natural experiment framework, Browne et al evaluated extensive-stage small-cell lung cancer patients treated pre-shortage vs during shortage and reported adjusted associations with worsened outcomes during shortage exposure: increased hospitalisation (OR 2.30, 95% CI 1.01–5.24; $P=0.047$) and shorter progression-free survival (hazard ratio 1.79, 95% CI 1.19–2.68; $P=0.005$) (13). This study provides a concrete example of how shortage-driven substitution (IV to oral etoposide regimens, irinotecan regimens, or oral monotherapy) can be associated with measurable harms (13).

For Bacillus Calmette–Guérin shortages in non-muscle invasive bladder cancer, evidence-based strategies have been discussed, including alternative intravesical chemotherapy and modification of maintenance schedules, reflecting a framework of risk-stratified substitution and dose-sparing strategies when constrained by supply (14). These approaches illustrate a broader mitigation principle: in shortage settings, ethically defensible algorithms should prioritise patients most likely to benefit, while ensuring regimen changes reflect the best available evidence rather than ad hoc practice variation.

This brings ethical allocation and transparency into medication safety. While not shortage-specific, disaster medicine principles emphasise planned, structured approaches for scarce resource triage, grounded in ethical principles and a continuum from conventional to contingency to crisis standards (21). Shortage governance, in my view, should operationalise similar principles: define “contingency prescribing” in advance, document criteria, and support clinicians and pharmacists with defensible, standardised decision tools (21).

Patient experience and disclosure as safety work

Drug shortages also generate humanistic outcomes that matter for safety through shared decision-making and consent. In a patient-perspective survey framed around an anaesthesia drug shortage scenario (neostigmine shortage), Hsia et al reported that 76.2% of respondents wanted to be told about the shortage if substitute drug combinations had slight differences in side effects (95% CI 70.5%–81.3%) (20). The proportion wanting to delay surgery increased as substituted drug side effects were portrayed as increasing (20). This evidence supports a practical point: shortage-driven substitutions may trigger patient preferences that affect scheduling, adherence, and trust. Patient communication is therefore part of safety mitigation, not merely an ethical add-on.

A practical summary table of shortage-driven substitutions and mitigation strategies

The table below summarises representative high-risk shortage-driven substitutions documented in the included evidence base and translates them into mitigation actions. I emphasise that substitutions should not be viewed as “automatic swaps”; the safety work lies in structured protocols, monitoring, and communication.

Shortage context (representative)	Typical substitution or work-around	Key safety risks introduced	Recommended mitigation strategies (clinical)	Recommended mitigation strategies (system-level)
Norepinephrine shortage in septic shock	Increased use of alternative vasopressors (e.g., phenylephrine)	Practice variation under time pressure; potential mismatch with guideline-based first-line therapy; observed higher in-hospital mortality during shortage quarters (7)	Pre-built “shortage sepsis vasopressor” order sets; pharmacist-led therapeutic interchange with haemodynamic monitoring plan; explicit criteria for when alternatives are acceptable	Multi-supplier procurement and buffer stock for first-line critical medicines; early shortage notification and regional mutual aid between hospitals (1,8)
Sedative/opioid shortages in paediatric ICU	Alternative sedatives/analgesics; revised sedation algorithms	Unfamiliar dosing/conversions; process harms despite stable prescribing error rates; increased unintended extubations observed during shortage period (6)	Standardised conversion charts; nursing and physician education; mandatory pharmacist review for initiation/titration; monitoring for withdrawal/oversedation; evaluate downstream outcomes (e.g., extubations)	Protect ICU essential medicines list with minimum par levels; central pharmacy oversight of shortage substitutions and standard concentrations (1,6)
Drug shortages detected via pharmacovigilance (broad classes)	Replacement drugs; altered therapy pathways; administration process changes	ADRs from replacement drugs; medication errors at administration step; serious events and deaths reported (9,10)	High-alert medication double-checks during substitution periods; enhanced ADR surveillance; “stop and verify” prompts for concentration/route changes	National/regional pharmacovigilance signals integrated into shortage governance; regulator communications plus local controls, recognising that information alone is insufficient (10)
Antibiotic shortages (e.g., piperacillin–tazobactam)	Alternative agents often requiring broader spectrum or different monitoring	Treatment failure with inferior alternatives; longer length of stay; negative impacts on AMS programmes (11)	AMS-led substitution algorithms; infection-site and resistance-informed choices; renal dosing/monitoring protocols; de-escalation plans once supply returns	Diversify API/raw material supply and manufacturing resilience; hospital forecasting and purchase agreements guided by stewardship priorities (11)
Oncology drug shortages (frequent, multi-agent)	Treatment delays; dose reductions; alternate regimens; omission when no alternatives	Increased risk of medication errors; disrupted clinical trials; regimen compromise reported by practitioners (12)	Multidisciplinary shortage tumour board; standardised therapeutic interchange; documentation and patient counselling; prioritisation algorithms	National oncology shortage guidance; coordinated procurement; transparency in allocation criteria for scarce curative agents (12,21)
Intravenous etoposide shortage in ES-SCLC	IV-to-oral etoposide regimens; irinotecan-based regimens; oral monotherapy	Increased hospitalisation and worse PFS during shortage period (13)	Shortage-specific pathway with explicit equivalence assumptions and monitoring; early toxicity and effectiveness review; shared decision-making about trade-offs	Regional/national contingency planning for cancer drug supply; mechanisms to avoid protracted shortages of essential injectables (13)

Shortage context (representative)	Typical substitution or work-around	Key safety risks introduced	Recommended mitigation strategies (clinical)	Recommended mitigation strategies (system-level)
BCG shortage for NMIBC	Intravesical chemotherapy alternatives; modified maintenance schedules	Risk of recurrence/progression if suboptimal alternatives or dosing schedules are used	Evidence-based substitution and dose-sparing schedules; risk stratification; clear patient counselling	Sustainable manufacturing and procurement planning for biologics; national guidance harmonisation to reduce “postcode” practice variation (14)
Essential medicines stock-outs in India (system-level)	Patients seek medicines elsewhere (private sector), or go without	Interrupted care; affordability barriers; variable availability and prolonged stock-outs reported across states (16)	Facility-level stock monitoring with escalation; standard therapeutic interchange lists aligned to essential medicines; patient counselling and refill planning	Strengthen procurement and distribution management; inventory management systems and governance reforms to reduce stock-outs (16)
Magnesium sulphate availability gaps in India (selected districts)	Suboptimal or inconsistent use; variable concentrations (25% vs 50%)	Stock-outs and variable formulations can contribute to dosing errors and inconsistent practice (17)	Standardise concentration availability and dosing protocols; training and checklists for obstetric emergencies	Essential obstetric medicine supply assurance; logistics and procurement strengthening for district and primary facilities (17)
Private pharmacies and substitution practices in Odisha	Patients choose private pharmacies for better stock; substitutions reported	Informal substitution and advice may increase risk if not governed by protocols	Encourage standard counselling and documentation; improve referral linkages; clarify scope of substitution	Strengthen regulatory oversight; align public-sector drug availability to reduce forced reliance on private stock and unregulated substitution (18)

India and LMIC perspective: stock-outs, private-sector substitution, and feasibility of digital mitigation

While much published shortage literature is US- or Europe-centric, LMIC evidence highlights that “shortage” frequently manifests as recurrent stock-outs in public-sector supply chains, with strong implications for safety, continuity of care and substitution behaviour.

In an India-focused systematic review of essential medicines availability and utilisation, Wadhwa et al found inadequate availability across states, with availability varying from 17% to 51% across major states and stock-outs reported from 4 to 14 weeks, linked to governance and procurement differences across states (16). Although this literature is often framed as access and utilisation, the medication-safety implications are immediate: prolonged stock-outs force abrupt discontinuation, patient-led substitution, and procurement from variable-quality private sources, all of which can elevate error risk.

Drug availability studies also demonstrate how variable formulation availability can complicate safe administration. In North Karnataka, Katageri et al found that magnesium sulphate availability varied across facility types and that stock-outs were reported in the preceding six months, alongside variability in concentration formulations across public and private facilities and variable dosing schedules (17). In maternal emergencies where magnesium sulphate is time-critical, such heterogeneity can plausibly contribute to dosing errors and inconsistent use (17).

In Odisha, Kalita et al's large-scale analysis shows how private pharmacies fill care gaps: 17% of households sought outpatient care from private pharmacies; 90% of pharmacies reported providing medical advice; and 26% reported substituting prescribed drugs (18). Private pharmacies had better stocks of essential drugs than public primary-care facilities, and patients cited convenience and better drug stocks as reasons for choosing pharmacies (18). From a safety lens, this indicates that public-sector stock-outs can shift medicine use into a less regulated substitution ecosystem, increasing the need for policy responses that address both public supply resilience and private-sector governance.

Finally, it is worth to consider the feasibility of digital and managerial mitigations in LMIC environments. A Cochrane mixed methods systematic review assessed mobile-device strategies for stock notification and commodity tracking and concluded that evidence is sparse, with only one controlled before-after study (very low certainty) for effects on commodity availability; however, descriptive studies across African and Asian countries (including India and Pakistan) show common aims of making stock-level data visible to managers for corrective action (15). Importantly, the review notes that some broader health-system issues—such as national-level drug shortages—cannot be mitigated by primary-care-level digital interventions alone (15). This is consistent with my framing: digital stock dashboards can reduce local “blindness” and improve responsiveness, but they cannot manufacture drugs; therefore, supply resilience requires upstream procurement and manufacturing solutions (15,16).

To situate these findings in broader LMIC practice, authors note that chronic disease programme reports from Uganda and South Africa describe how drug stock-outs can undermine routine care delivery and patient experience (19,20). Although not “drug shortage research” in the narrow sense, these studies reinforce that in settings where stock-outs are frequent, medication safety must include continuity-of-supply as a foundational component of chronic disease management (19,20).

Discussion

Authors interpret the evidence base as supporting three conclusions relevant to medication/pharmacotherapy journals.

First, drug shortages have matured into a measurable medication-safety risk with documented associations with serious harm and patient-important outcomes. The norepinephrine shortage study provides rare large-scale outcome evidence of higher in-hospital mortality during shortage periods, co-occurring with substitution to phenylephrine (7). Pharmacovigilance studies—both retrospective and prospective—show that shortages can be associated with serious ADRs, medication errors, disease worsening, and a non-trivial proportion of deaths or life-threatening events (9,10). Oncology evidence, including a shortage-driven natural experiment in etoposide supply, demonstrates clinically meaningful outcome decrements (hospitalisation and progression-free survival) (13).

Second, substitution is the pivot point where medication safety is either preserved or lost. The same substitution can be safe in principle and unsafe in practice. Safety depends on protocols, dose conversion tools, monitoring plans, and the integration of pharmacists and stewardship teams into rapid response. The antibiotic shortages review is instructive in that it identifies AMS-driven strategies as prominent successful responses (11). Similarly, ICU and oncology experiences show that shortage periods require systematic operationalisation of therapeutic interchange, not ad hoc substitutions (6,12).

Third, communication and information dissemination are necessary but insufficient. The CIRUPT study observed that most shortage drugs were associated with professional communications from the national agency, yet harms still occurred (10). This implies that shortage governance must include active controls at the point of care: standardised order sets, concentration standardisation, “high-alert” double-checks, and enhanced monitoring for known substitution risks. Patient communication is part of this control system, as patients often want disclosure and may choose to delay elective care depending on perceived substitution risk (20). This study view disclosure as a safety intervention because it improves alignment

between therapy changes and patient preferences and may reduce downstream non-adherence or distrust.

From a policy and implementation perspective, It is suggested that a layered mitigation strategy, aligning to a “conventional–contingency–crisis” continuum used in disaster resource frameworks (21). Under conventional conditions, health systems should maintain buffer stocks for high-consequence medicines and ensure procurement redundancy for generic injectables and essential oncology agents (1,2). In contingency mode (anticipated shortages), institutions should activate structured shortage pathways—therapeutic interchange protocols, EHR updates, pharmacist-led review—and pre-define which substitutions are acceptable with what monitoring. In crisis mode (no safe equivalent), transparent rationing principles and prioritisation algorithms become ethically and clinically necessary, particularly in curative oncology and critical care (12,21).

The India/LMIC evidence reinforces that shortage mitigation cannot be exclusively hospital-centric or technology-centric. When public-sector medicine availability is low and stock-outs are prolonged, patients inevitably seek alternatives, often via private pharmacies where substitution practices are common (16,18). Therefore, improving public procurement and distribution management, harmonising state procurement mechanisms, and strengthening inventory systems are medication-safety interventions at population scale (16). Digital inventory tracking may improve visibility and local management but cannot solve national-level supply deficits without upstream reforms (15).

Limitations

This review is constrained by heterogeneity in shortage definitions, the predominance of high-income country evidence in some domains, and a reliance on observational designs for many outcome signals. Even strong studies (e.g., norepinephrine shortage and septic shock mortality) remain vulnerable to residual confounding and cannot isolate which component of shortage response (substitution choice, dosing, monitoring, delays) drove observed harms (7). Pharmacovigilance studies identify safety signals but are subject to reporting bias and limited denominators (9,10). Survey literature provides breadth on prevalence and perceived harms but is not outcome adjudication (12). India/LMIC evidence often arises from access and health systems research rather than shortage-specific safety endpoints, requiring cautious translation into medication-safety recommendations (15,16,18–20). I have therefore prioritised claims supported directly by the cited sources and avoided extrapolating beyond the available evidence.

Conclusion

Authors conclude that drug shortages should be treated as a medication-safety problem with demonstrable associations with patient harm, including mortality signals in acute care and clinically meaningful outcome changes in oncology. Safety risk concentrates in forced deviations from standard medication pathways, particularly therapeutic substitution under time pressure. Effective mitigation requires a layered approach: stewardship-led therapeutic interchange protocols, pharmacist integration, enhanced monitoring, and patient communication at the clinical level; and procurement resilience, manufacturing redundancy, transparency, and ethical allocation frameworks at system level. In India and other LMIC contexts, recurrent stock-outs and private-sector substitution practices extend the shortage problem into questions of governance, equity, and continuity of care, making procurement and supply-chain reform a central medication-safety intervention.

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