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DRUG SHORTAGES IN HOSPITAL PHARMACIES: CAUSES AND MITIGATION STRATEGIES

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Abstract

This short review gathers published evidence on drug shortages affecting hospital pharmacies, and it reports no new data. It sets out how shortages are defined, the manufacturing, economic and regulatory causes described in the literature, and the consequences for patients, staff and budgets, with particular attention to sterile injectables, anticancer drugs and antibiotics. Mitigation strategies used inside hospitals are compared, including inventory management, therapeutic substitution, compounding and ethical allocation, alongside national and international policy responses. The literature agrees on the main causes and harms, but definitions differ between countries, most studies are surveys or case descriptions, and few measure patient outcomes or test which responses work best.

1. INTRODUCTION

Few things disrupt a hospital pharmacy as quickly as a drug that cannot be obtained. A wholesaler's message that a product is unavailable may arrive on a Friday afternoon, with no date for resupply, and the pharmacist then has to decide what to tell the wards, which patients take priority and what can be used instead. Shortages of this kind have been described for decades, but they became a standing feature of hospital practice in the early 2010s, when reports from the United States documented a sharp rise in the number of products affected [1, 2]. Similar experience has been reported from Europe, Canada and many lower-income countries [3, 4, 5].

Experienced hospital pharmacists often say that a significant fraction of their week goes on supply problems, work that has to be done on top of clinical duties and that brings no obvious reward when it goes well.

The problem is not confined to rare or obsolete products. Many shortages involve old, inexpensive generic drugs that hospitals depend on every day, among them sterile injectables, electrolytes, local anaesthetics, opioids and cytotoxic agents [6, 7]. Because these drugs are cheap and have several manufacturers on paper, the market was assumed to be robust. In practice a fault at one plant can remove most of the national supply within weeks, and there is little spare capacity to fill the gap. Pharmacists spend considerable time managing this, a burden that is seldom visible to those who do not work in supply. The reliance on cheap sterile products is itself part of the story, since hospitals use them in vast quantities and cannot easily switch to a different dosage form without retraining staff and altering pump libraries.

This review summarises the published literature on shortages from the standpoint of the hospital pharmacy. It draws on surveys, case descriptions, policy reports and reviews, and it does not present new data. After a short look at definitions and scale, it covers the causes put forward by manufacturers, regulators and pharmacists, the effects on care and cost, the practical strategies that hospitals use, and the policy measures proposed at national and international level. The closing section sets out the weaknesses of the evidence and areas that need more work. Evidence is grouped by theme in table 1, and the distribution of those themes is shown in fig. 1. Statements about size or cost are limited to findings that several sources report.

Table 1: Published findings on causes, effects and management of hospital drug shortages

Topic	Reported finding	Ref.
Sterile injectables manufacturing quality	Shortages linked to quality failures at few plants with limited spare capacity.	[6, 8]
Low-price generics market economics	Thin margins discourage redundancy and favour market exit or consolidation.	[4, 9]
Supply-chain structure stakeholder interviews	Manufacturers, wholesalers and pharmacists each name different causes.	[10, 11]
Oncology drugs pharmacist surveys	Many centres changed patient care because of chemotherapy shortages.	[12, 13]
Anaesthetic agents national survey	Shortages of routine agents affected care in most responding departments.	[14, 15]
Substitution medication safety	Unfamiliar products and pump settings raise the risk of dosing errors.	[7, 16]
Antibacterials trends 2001 to 2013	Many commonly used agents affected, with consequences for prescribing.	[17, 18]
Response team ASHP guidelines	Designated team, risk assessment, communication and documentation recommended.	[19, 20]
Ethical allocation committee frameworks	Transparent criteria and cross-disciplinary review proposed for scarce drugs.	[21, 22]
Compounding and import sterile standards	Alternative routes need quality controls and clear labelling.	[23]
Notification rules 28 countries	Wide range of national measures, few evaluated for effect.	[24, 25]

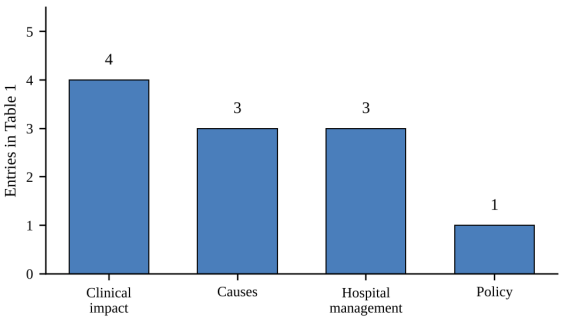


Fig. 1: Number of entries in table 1 by theme

A note on terms may help readers from different backgrounds. In some countries the word shortage refers only to a formal national notice by a regulator, whereas in hospital practice it refers to any interruption that affects the ability to supply a patient. Both usages appear in the studies cited, and they are not interchangeable. Local shortages, caused by a supplier failing to deliver to one hospital, may never appear in a national list. Readers comparing studies should therefore check which meaning each uses before

drawing conclusions about frequency or severity across countries.

2. DEFINITIONS AND SCALE

No single definition of a drug shortage is used everywhere. The American Society of Health-System Pharmacists defines one as a supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent [19, 20]. European regulators distinguish shortages that affect a whole country from those that affect individual pharmacies, and a qualitative study among European stakeholders found wide differences in definitions, which hamper comparison [26]. The World Health Organization has likewise noted that national definitions vary in the length of interruption and the degree of impact required [27]. Without an agreed definition, a hospital that reports ten shortages in one country may be describing something different from a hospital that reports ten in another, and policy comparisons become shaky.

Counting methods also differ, so numbers must be read with care. American data, compiled from reports to a drug information service, showed new shortages climbing to a peak in 2011 and then declining, although the total number of active shortages remained high in later years [1, 2]. Studies of specific groups of drugs show persistence: shortages of drugs used in emergency departments rose steadily over the first fifteen years of the century, and antibacterial shortages affected a large share of the agents in common use [18, 28]. Systematic reviews of the literature confirm that most published work comes from North America, with growing contributions from Europe [29, 30]. Lists compiled by regulators, wholesalers, professional bodies and hospitals capture different events, so the picture depends on whose list is consulted. Hospital-level shortages are almost certainly undercounted in every national figure.

Duration varies widely. Many shortages resolve within a few months, yet a substantial number last a year or more, and some products never return [1]. Long shortages are especially troublesome for hospitals, which must move from emergency measures to settled alternatives that are safe for staff to use. Surveys in several countries have found that nearly all hospital pharmacies had managed at least one shortage in the previous year, and that critical products such as anaesthetic agents and chemotherapy were among those affected [7, 13, 14]. Each extension forces a second round of work, because the interim solution adopted in week one rarely suits month six.

The kinds of products affected are fairly consistent across reports. Sterile injectables account for the largest share, followed by oral products of low cost and long history, and a smaller number of vaccines, biologics and speciality agents [1, 28]. Within injectables, electrolytes, anaesthetics, analgesics, antibiotics and cytotoxic drugs recur from year to year. Therapeutic importance varies from products with many alternatives to those with none, and a shortage is far more serious in the second case. Reports therefore try to separate shortages of critical drugs from those with easy substitutes, although the criteria for calling a drug critical are not uniform. Hospitals typically build their own lists of critical items, based on clinical risk, number of suppliers and volume of use [18, 20].

Lower-income countries face a different version of the problem. Shortages there are often linked with weak procurement systems, funding gaps and dependence on imports, and they affect basic essential medicines such as antibiotics and insulin, not just sterile generics [3, 5]. Reports from these settings are scarcer and less detailed. The global nature of ingredient manufacturing means that a disruption in one region is often felt in others, a point made forcefully when a pandemic disrupted transport and production [31, 32]. Donor-funded programmes and pooled procurement have helped in some cases, although long-term resilience depends on domestic manufacturing and sound logistics.

3. CAUSES OF SHORTAGES

Manufacturing and quality problems are the most commonly cited cause of shortages of sterile injectables. These products are hard to make, need dedicated facilities and are

vulnerable to contamination, particulate matter and failures in filling lines. Analysis of generic sterile injectables by regulators found that shortages were closely linked to quality failures at a small number of plants, with the number of manufacturers for many products being small [6]. When a facility is closed for remediation, others can seldom increase output quickly enough, because capacity is already stretched. A government review of the shortage problem has described that low prices and thin margins weaken the incentive to invest in manufacturing quality and spare capacity, which adds to the fragility [8]. The same analysis also noted that when a manufacturer exits the market for commercial reasons, the effect on supply is permanent and not temporary, which compounds the effect of the quality issues [6, 9]. Remediation after an inspection failure commonly takes many months, during which the affected products stay unavailable.

Economics sits behind the manufacturing story. Prices of old generic injectables are low and driven down by competitive tendering, group purchasing and, in Europe, national cost-containment measures. Low margins discourage investment in redundant capacity and encourage firms to exit the market or consolidate [4, 6]. A report on root causes prepared for the American regulator concluded that the market does not reward manufacturers for reliability, since buyers rarely know or pay for the quality of the supply chain, and that this is a central reason shortages recur [9]. Parallel trade, in which products are exported from low-price to high-price countries, has been cited in Europe as a further source of local gaps [4, 11]. Buyers, for their part, are rarely able to tell a reliable supplier from an unreliable one when both quote the same price.

Supply-chain structure contributes. Active ingredients are made in a few countries, often in a handful of plants, and the finished product may pass through several firms before reaching a wholesaler. Just-in-time inventory practices, adopted to reduce cost, leave little buffer when a delay occurs. Interviews with pharmaceutical companies and wholesalers in Finland and with stakeholders in four European countries show that each actor sees different causes, with manufacturers pointing to demand forecasts and quotas, wholesalers to delivery problems, and pharmacists to poor communication [10, 11]. Information is a recurring weakness: hospitals often learn of a problem late, and the cause is not always disclosed. Better visibility of the upstream chain, down to the source of the active ingredient, is repeatedly proposed as a remedy, though companies regard such details as commercially sensitive [9].

Sourcing of raw materials deserves separate mention. A single plant may supply the active substance to many finished-product manufacturers, so a fault there spreads to every product that depends on it. Concentration of ingredient production in a small number of countries leaves the system exposed to export restrictions, trade disputes and local disasters, and the first months of the pandemic showed how quickly this exposure can translate into hospital shortages of sedatives, neuromuscular blockers and other critical-care drugs [31, 32]. Shortages that arise from the ingredient stage take longer to correct than those caused by a filling line problem, because new sources need qualification by regulators and by the manufacturer. The message from reviews is that visibility of the chain is as important as capacity [33].

Demand-side factors and regulation matter too. Sudden surges in use, for example when a competing product is withdrawn and customers move to the alternative, can exhaust stock quickly. Regulatory actions to protect patients, such as recalls and import restrictions, can themselves create gaps, although they are necessary [2, 34]. Natural disasters and the interruption of transport have caused major shortages of intravenous fluids and other products. The broad conclusion of the reviews is that most shortages have several causes at once, and single-cause explanations are rarely adequate [33, 34]. Seasonal demand can also tip a fragile supply into shortage, as with antibiotics in winter.

Discontinuation for commercial reasons is a quiet but frequent source. When a firm judges a product unprofitable, it may stop making it

with limited notice, and if no other firm takes over, the product disappears. Notification requirements for companies are intended to give regulators and hospitals earlier warning, but compliance and enforcement vary between countries [24, 25]. A requirement for longer notice before withdrawal, together with the option for regulators to arrange continued supply, has been suggested as a remedy, although in practice it is difficult to compel a firm to keep producing an unprofitable item. Public registers of planned withdrawals would at least make the information available to buyers.

4. CLINICAL AND ECONOMIC CONSEQUENCES

The most serious effects fall on patients. A scoping review of medication shortages and patient outcomes found reports of delayed or cancelled treatment, use of less effective alternatives, more adverse events and, in some cases, deaths, although the methods were mostly descriptive [29]. The best known examples come from oncology. Shortages of established chemotherapy agents forced clinicians to choose between delaying treatment and using regimens with less evidence, and surveys of oncology pharmacists found that a majority had faced a shortage that changed patient care [12, 13]. Children with cancer were particularly exposed when a drug with no equal substitute disappeared [35]. Even when the end result is a delay of only days, patients and families experience anxiety about whether treatment will be as effective.

Anaesthesia and critical care have been affected as well. When propofol supplies were interrupted, hospitals had to change to alternative agents with different pharmacology, and warnings were issued about the risks that accompanied the change [15]. A national survey of Canadian anaesthetists reported that most had experienced shortages of agents in routine use and that a large proportion had observed an effect on care [14]. Emergency medicine physicians have described similar difficulties with drugs required in resuscitation and rapid sequence intubation, where substitutes are not always available or familiar [16, 28]. These accounts show how shortages can touch every area of hospital care, not only specialties in which expensive drugs are used.

Substitution brings its own hazards, and medication errors are among the best documented. Staff must work with a drug or concentration they do not usually use, with doses and infusion rates that are unfamiliar, and with labels and pumps programmed for another product. Hospital surveys reported that shortages were linked with increased risk of error, including wrong-dose events, and that pharmacists spent much of their time on mitigating work [7, 16]. Shortages of antibiotics prompt the use of broader-spectrum or more toxic drugs, which has implications for resistance and for adverse effects, and these downstream costs rarely reach the formal accounts [17, 18]. Pharmacists stress that the safest response is often to limit the number of changes and to make each one visible to all staff at the same time.

Financial effects are tangible. Surveys of health systems estimated that managing shortages cost large amounts in additional labour and in the purchase of more expensive alternatives or of products from the grey market, where price gouging and doubts over authenticity have been reported [1, 7]. The hospital pays more for the same therapeutic result, and the extra staff time spent calling suppliers, reviewing protocols and updating systems is a hidden cost. A shortage can also shift consumption towards costlier branded products, raising pharmacy expenditure well beyond the item that disappeared [7, 34]. Studies of cost are mainly based on estimates and surveys, and few follow costs prospectively in a single institution.

Pharmacy workload is a further measurable effect. In national surveys, pharmacy directors reported that managing shortages took many staff hours each week, that the amount of time had grown over the years, and that it displaced clinical activities such as ward review [2, 7]. Tasks include contacting suppliers, searching for alternatives, updating the electronic record, relabelling, writing communications and training staff. Smaller hospitals with fewer pharmacists feel the strain most, since they have less capacity to absorb the work and less buying power with

wholesalers. These burdens are seldom included in estimates of the cost of a shortage, so published figures probably understate the true economic effect [1, 7].

Staff and morale suffer too. Pharmacists describe the constant uncertainty and the ethical strain of deciding who receives a scarce drug as a source of stress, and some report moral distress when they must ration. These effects are less often measured than costs but are mentioned repeatedly in qualitative studies. Support from colleagues, clear institutional policy and an ethics committee that shares the burden are reported to ease this strain, and are inexpensive to arrange compared with the cost of staff turnover. Surveys that include questions on well-being would put numbers on a problem now known mainly from anecdote.

5. MITIGATION STRATEGIES IN HOSPITAL PHARMACY

Professional guidance has been available for more than a decade and sets out a structured approach. The American guidelines recommend that hospitals designate a team, usually led by pharmacy, to assess each shortage, estimate its likely impact, identify alternatives, communicate with clinicians and document decisions [19, 20]. A key element is rapid, clear communication, because the front-line staff who administer drugs must know what has changed and how the substitute differs. Hospitals that treat shortages as routine operational events, with standard procedures and not improvisation, are described as better placed to protect patients [1, 20]. Such guidance is voluntary, however, and is based mostly on expert consensus. Its elements are collected in table 1, and the spread of that material across categories is illustrated in fig. 1. Hospitals without a formal team often find that responsibility drifts to whoever answers the telephone, and decisions are then recorded poorly or not at all.

Not every shortage deserves the same response, and teams that try to give each one a full review quickly run out of time. A short risk rating helps to sort them. The usual questions are whether alternatives exist, how many suppliers remain, how heavily the drug is used and which patient groups depend on it, with children, patients in intensive care and those on cancer treatment given particular attention [19, 20]. A shortage with an easy substitute and a quick expected recovery can be handled through purchasing and a brief notice to prescribers. One that affects a drug with no alternative calls for the full team, written criteria for use and regular updates. The same lists of critical products are also useful for judging where stock is thin before a shortage begins [18]. A review date should be set for each rating, since a shortage that began as minor can become serious as stock runs down, and the original assessment then needs to be repeated.

Inventory and purchasing measures come first. Pharmacies can raise safety stock for critical products, although stockpiling can worsen a shortage by pulling supply from other hospitals, and guidelines caution against hoarding [19]. Dual sourcing of key products, contracts that require suppliers to disclose risks, and use of several wholesalers reduce dependence on a single channel. Regular review of a list of critical drugs, ranked by clinical importance and number of suppliers, shows where vulnerability lies. Some hospitals join regional networks to share stock in emergencies, a practice that works best when agreements are in place before a crisis. The balance between preparedness and fairness to other hospitals is delicate, and guidance suggests purchasing at normal levels unless a clear clinical reason exists.

Therapeutic substitution is the commonest clinical response. A pharmacy and therapeutics committee approves alternatives in advance wherever it can, with dose conversion tables, compatibility information and notes on monitoring. Changes should be built into the electronic prescribing system and smart pumps so that staff see the new product and concentration, not the old one, since mismatches between pump library and product are a known hazard [16, 20]. Where alternatives are limited, route conversion from intravenous to oral therapy, longer dosing intervals or smaller volumes can stretch supplies, provided that clinical criteria are clear. The key point is that these are clinical decisions that need prescriber

agreement and not purely supply decisions. Pharmacists often prepare one-page summaries for each shortage so that nurses and doctors see key differences in one place.

In-house preparation and outsourcing offer another route. Hospitals with suitable facilities may compound a product from bulk ingredient or import a foreign-licensed equivalent, and both approaches have been used during shortages of injectables and fluids. Compounding must follow the relevant standards for sterile preparations, since quality problems in the product made by the pharmacy would simply replace one risk with another [23]. Importation raises labelling, language and regulatory issues, and clinicians need an explanation of differences in strength or packaging. These routes cost more and take longer than purchasing a licensed product, so they suit situations where a shortage is long and no clinical substitute exists. Documentation of the source, batch and beyond-use date of every such product protects patients and the hospital alike.

When supply cannot meet demand, allocation becomes an ethical question. Frameworks proposed for hospitals suggest that decisions be made by a committee with clinical, pharmacy and ethics input, that criteria be transparent and based on likelihood of benefit, and that patients not be disadvantaged on grounds such as social standing [21]. For life-saving paediatric cancer drugs, an ethical framework developed through a consensus process proposed principles for choosing among children and for communicating with families [22]. Such tools are valuable because without them allocation falls to individual clinicians at the bedside, which is both inconsistent and distressing. Documented allocation decisions can later be reviewed and improved.

Information and forecasting systems are underused. A pharmacy that knows its consumption by unit and by month can estimate how long stock will last and decide quickly when to restrict use. Alerts from regulators and wholesalers give early notice, and national notification schemes aim to make this routine [9, 24]. Local dashboards that show days of stock on hand for critical drugs, linked to the purchasing system, allow earlier action. The guidelines place emphasis on prompt, honest communication with prescribers, including when the pharmacy does not know the end date, since clinicians prefer to plan around uncertainty than to be surprised [19, 20]. Sound information is cheap compared with the cost of emergency purchasing.

Staff education and monitoring close the loop. Hospitals that audit errors linked with substitution, review near misses and share lessons across wards can reduce the harm associated with unfamiliar products. Dashboards that display current shortages and the approved alternatives help prescribers, and regular reports to the medicines safety committee keep leaders informed. Few of these measures have been formally evaluated, so their value rests on expert opinion and local experience more than on trial data [19, 29]. Training sessions based on real near misses are often better received than general lectures, because staff recognise the situations described. Short briefings at handover are another low-cost option.

6. POLICY AND REGULATION

Governments and regulators have started to act. In the United States, a task force examined root causes and proposed measures including greater transparency about manufacturing quality, contracts that reward reliability and incentives for mature quality systems [9]. European authorities have issued guidance requiring marketing authorisation holders to notify shortages and have set up mechanisms for coordinated responses [24]. A comparison of 28 European and Western Asian countries found a wide range of measures, among them mandatory notification, export restrictions, stockpiling requirements and public lists, though few had been evaluated for effect [25]. The speed at which such measures take effect is uncertain, and manufacturers have argued that disclosure rules add administrative burden without addressing the underlying economics.

International bodies add a wider perspective. The World Health Organization has described approaches to preventing and managing shortages of essential medicines, including better forecasting, improved information

sharing and review of procurement rules, and has pointed to the need for common terms [27]. Reviews emphasise that shortages are a global problem requiring cross-border cooperation, because ingredients are traded worldwide and local solutions cannot fix a global weakness [5, 33]. The experience of the pandemic reinforced calls for geographical diversification of manufacturing and greater domestic capacity for critical products [31, 32]. Harmonised terminology would ease the sharing of data and help avoid duplication of effort between regions.

Many proposals remain untested. Mandatory buffer stocks, price floors for essential generics and mutual recognition of imported products are discussed frequently, with strong views on each. Critics note that forcing stock holding adds cost, that price floors can distort markets, and that notification rules are only as good as their enforcement [4, 25]. The sensible conclusion from the policy literature is that no single measure is sufficient, that incentives for reliability must be built into purchasing, and that early warning given to hospitals is among the most useful and least costly steps. Hospital pharmacists, who see the results of policy at first hand, are seldom consulted when new rules are written. Evidence from other sectors, such as food and energy, is sometimes borrowed, but pharmaceuticals differ in their regulation and in the harm caused by substitution.

Hospital pharmacists have a role in policy as well as practice. They hold information about local effects, contribute to national reporting systems and can press for procurement contracts that include supply guarantees. Professional bodies have called for pharmacist involvement in shortage planning at every level. Participation in national working groups, systematic reporting of local shortages and sharing of how alternatives were managed all feed into a better collective response, and cost little beyond staff time. Their input is particularly valuable when reviewing proposed legal requirements, since they know which obligations are workable at the level of a busy dispensary. Their view also helps regulators see how national rules play out at the bedside.

7. LIMITATIONS AND FUTURE DIRECTIONS

The evidence has clear limits. Most published work consists of surveys with modest response rates, narrative accounts from single hospitals and policy commentaries, and few studies compare outcomes with and without a shortage. Definitions and data sources differ so widely that numbers from different countries cannot be pooled, a limitation highlighted in reviews of the field [26, 30]. Studies of patient outcomes are rare and often confounded, because patients who receive an alternative differ in other ways. Publication from lower-income countries is sparse, which skews the view towards the circumstances of wealthy health systems [5, 29]. As a result, firm statements about what works are hard to justify and recommendations lean heavily on expert opinion.

Several priorities follow. Common definitions and reporting standards would let shortages be counted and compared. Prospective studies that follow patients through a shortage, with measures of error, clinical outcome and cost, would tell hospitals which responses deserve investment. Evaluations of policies, such as notification rules or stock requirements, are needed before they are copied elsewhere [25]. Finally, research on the experiences of staff, and on ethical allocation in practice, would help to support decisions that are currently left to individual judgement [21, 22]. Collaboration between hospitals and regulators on data sharing could make some of this work achievable at modest cost.

8. CONCLUSION

Shortages of hospital drugs are a persistent, multifactorial problem. The literature points to quality failures in sterile manufacturing, weak market incentives, concentrated supply chains and poor information flow as the main drivers, and it documents harm in the form of delayed treatment, substitution errors and added cost [4, 6, 9]. Oncology, anaesthesia and anti-infective therapy have been affected most often, and children are at particular risk when a product has no equal substitute [13, 18, 35]. That pattern has held across countries and over time, which supports treating it as a stable feature of the supply system.

Hospital pharmacies can reduce, but not remove, the harm. Structured shortage teams, advance approval of alternatives, careful change of prescribing systems and pumps, transparent allocation rules and clear communication form the core of recommended practice [16, 19, 20, 21]. Lasting improvement depends on policy that rewards reliable supply and gives hospitals early notice. The evidence base remains largely descriptive, and well-designed studies of outcomes and of the policies themselves are the next step [25, 29, 30]. Hospitals can help by documenting their experience in a form that others can learn from.

9. ABBREVIATIONS

ASHP-American Society of Health-System Pharmacists, EMA-European Medicines Agency, FDA-Food and Drug Administration, IV-Intravenous, P&T-Pharmacy and therapeutics (committee), USP-United States Pharmacopeia, WHO-World Health Organization, EU-European Union, MAH-Marketing authorisation holder

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All the authors have contributed equally.

12. CONFLICT OF INTERESTS

Declared none

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