shpa

+ MEDICINE SHORTAGES IN AUSTRALIA

A snapshot of shortages in Australian hospitals

———
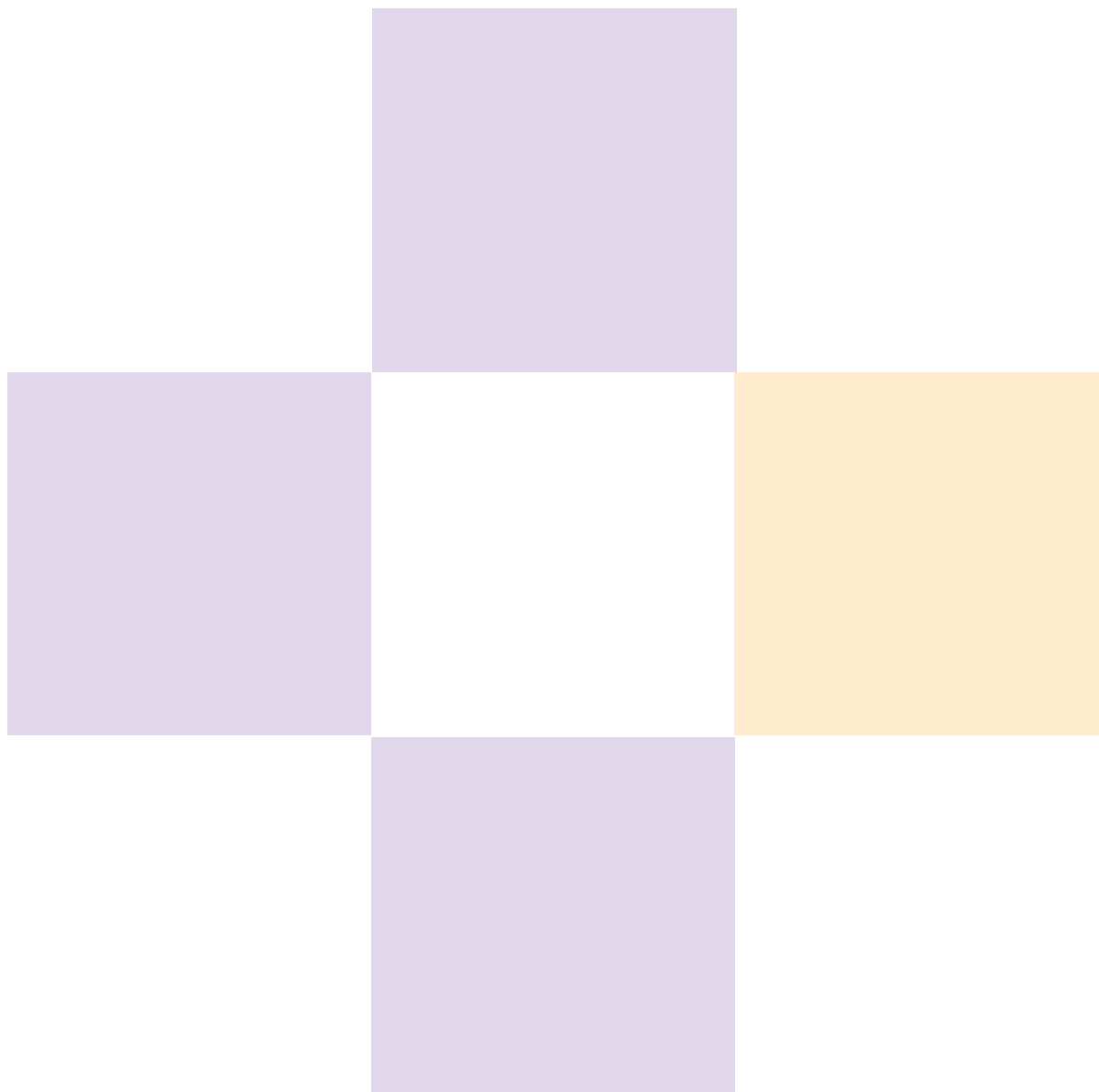
June 2017

Table of Contents

About SHPA

The Society of Hospital Pharmacists of Australian (SHPA) is the national membership organisation for pharmacists, pharmacist technicians and pharmacy interns working in hospitals and other healthcare settings, with more than 4,400 members across Australia. SHPA's members are progressive advocates for clinical excellence, passionate about patient care and committed to evidence-based practice.

SHPA is committed to facilitating the safe and effective use of medicines. SHPA supports pharmacists to meet medication and related service needs, so that both optimal health outcomes and economic objectives are achieved for Australians, as individuals, for the community as a whole and for healthcare facilities within our systems of healthcare.

Medicine shortages in Australia

Discussion of the results of SHPA's medicines shortages prevalence study April 2017

Introduction

Major shortages of frequently used intravenous antimicrobials in hospitals have increasingly become a source of concern and uncertainty for many hospital pharmacy departments around the country. While vancomycin and metronidazole shortages were reported in the news media in late 2016, SHPA members advise that medicines shortages are far broader and more frequent than reported publicly.

According to feedback from members; pharmacy directors and procurement officers regularly experience considerable difficulties procuring important antimicrobials for intravenous use including: vancomycin, metronidazole, acyclovir, meropenem, azithromycin, ceftazidime, daptomycin, fluconazole, ampicillin, amoxicillin. These medicines are used to treat life-threatening bacterial, viral and fungal infections.

Shortages of intravenous antimicrobials threaten to force hospitals to depart from well-established hospital treatment protocols and established Therapeutic Guidelines. SHPA is concerned that a need to adjust treatment protocols depending upon medicine availability presents a significant 'quality use of medicines' risk.

Hospital pharmacists are increasingly spending large amounts of time contacting multiple suppliers in order to pay a higher price for a delayed delivery of key medicines. An analysis by the Premier Healthcare Alliance in the United States found medicines shortages cost hospital budgets a minimum of US$200 million annually through the forced purchasing of expensive alternatives to essential medicines; the additional labour resourcing to source alternatives was estimated to be US$216 million per annum. This directly impacts patient care by diverting precious staff time and reducing pharmacists' capacity to provide clinical services, creating a need to prioritise prescribing of key antimicrobial medicines for patients, and impacting hospital medicine budgets.

The manufacture and distribution of medicines in Australia play an important role in our well-regulated health care system. However, notification of shortages is voluntary, and anecdotal evidence indicates information provision from manufacturers and wholesalers is poor. To assess supply notifications and measure the impact of shortages, SHPA has undertaken a prevalence study of medicine shortages as experienced in Australian pharmacy departments.

Methodology

SHPA undertook a point of prevalence survey of medicine shortages experienced by members in hospitals across Australia to demonstrate their extent and impact on hospital pharmacy and clinical practice, as well as the timeliness and quality of information provided to clinicians from regulators, sponsors and wholesalers.

The online Medicines shortages prevalence survey was conducted on Tuesday 4 April 2017. The Directors of Pharmacy at all Australian hospital pharmacy departments were invited to complete a survey and state which medicines were unavailable for ordering on that day, and how it affected the care they provided for patients. In addition, the survey was promoted in the SHPA member e-newsletter and to healthcare stakeholders. All participation was voluntary.

Participants (who included procurement officers as well as hospital pharmacists) had until midnight Friday 9 April to complete the online survey which allowed up to 30 entries. Once received, all information was de-identified, compiled and analysed in Microsoft Excel. All entries were compared to a list of known medicines shortages, and grouped by therapeutic group as well as brand name (medicine product name) and active ingredient, to identify true shortages rather than examples of standard brand substitution.

Respondents were asked how they were notified of the shortage, their action in response to the shortage, any cost or patient impact, and any timeframe given for when the product would be available. Free text comments on the impact of medicines shortages and possible stockpiling were also recorded. SHPA downloaded data from the Therapeutic Goods Administration (TGA)'s Medicines Shortages Initiative website (https://www.tga.gov.au/medicine-shortages-information-initiative) on 4 April in order to compare publicly reported shortages to shortages recorded in the survey.

For the purposes of the study all shortages were classified as a medicine that a hospital planned to order for use with patients but was unable to. This is in line with the formal definition by the International Pharmaceutical Federation as 'a drug supply issue requiring a change. It impacts patient care and requires the use of an alternative agent.'

Key results

One thousand five hundred and seventy-seven (1,577) entries of medicine shortages were recorded across approximately 280 healthcare providers, which included public (72.9%), private (17.8%) and not-for-profit (9.3%) health service facilities and generally proportional geographic spread across Australia. Sixty-seven per cent of respondents were in metropolitan locations. There was also good representation of health service facilities of different sizes (Chart 1).

Key findings:
- 100% of respondents said they had experienced a medicine shortage in the preceding 12 months.
- 95% of respondents recorded at least one medicine shortage on 4 April.
- Across all respondents, a total of 1,577 entries were recorded, comprising 365 different commercial products across 154 different active ingredients (see Appendix 1: List of medicine shortages by active ingredient).
- Entries covered a wide range of medicine classes; the most frequent recorded shortages were antimicrobials (20%), then anaesthetics/analgesia (12%), cardiology (10%), endocrinology (10%), chemotherapy (9.5%) and neurology (9%) medicines.
- Of the 365 different medicine product shortages reported in the survey, only 54 (14.8%) were reported on TGA's Medicines Shortage Initiative website on 4 April.
- Information provided on the TGA website on 4 April did not align with reported hospital experience indicating the 'date of supply' information was largely inaccurate.

Discussion

In light of the data collected, medicine shortages remain a substantial problem for public and private hospitals across Australia with significant implications for patient care, staff resourcing and expenditure.

An unforeseen limitation of SHPA's data collection tool was that survey respondents were only able to submit a maximum of 30 medicine shortages; in some instances, respondents had more medicine shortages to report but were not able to practicably do so. A limitation on accurately projecting the extent of medicine shortages is the difficulty of counting how many hospitals utilise a hospital pharmacy service, or are supported by community pharmacies. Similar to hospitals, hospital pharmacies differ considerably in size and organisation and both centralised pharmacy and outsourced pharmacy arrangements are common. However, the high response rate and large number of shortages recorded indicated a significant problem exists across hospital pharmacies.

From late 2016, Australian media attention regarding this issue focused on shortages of key antimicrobials such as intravenous metronidazole and vancomycin which are used to treat life-threatening infections. The Medicines shortages prevalence survey indicated that antimicrobials remain a major concern, as they comprised half of the ten most common shortages (Table 2), and were the medicine class respondents most frequently attempted to stockpile. However, although supply of antimicrobials remains particularly problematic, shortages impact the breadth of medicines supply. More than 60% of reported shortages were for medicines other than antimicrobials. The next most prevalent class of medicines shortages were anaesthetics/analgesics which accounted for 14% of the 1,577 entries, a rate consistent with international evidence of ongoing anaesthetic shortages.

Nationally, the lack of accurate information available regarding medicine shortages exacerbates the problems inherent in the complex supply chain of a vital product. By far, the most common way in which procurement officers realised a medicine was in shortage was when their hospital's ordering system displayed the medicine was 'out of stock' or 'on back order'. This retrospective advice does not allow for health service facilities, in particular prescribers and pharmacists, to proactively plan for disruptions and provide optimal patient care.

The data collected shows hospital pharmacists are required to respond to medicine shortages on a daily basis, resulting in a range of actions including using emergency stock; alternative brands and formulations available in Australia; and stockpiling and using the TGA's Special Access Scheme (SAS) to obtain alternatives from overseas. This supports SHPA's understanding that hospital pharmacists have developed sophisticated and administratively burdensome 'workarounds' to mitigate medicines shortages, which are costly in terms of staff time and hospital expenditure, in order to minimise the impact on patient care as much as possible.

SHPA recommends that greater attention be paid to the need for proactive notification of medicine shortages to reduce the staff time spent and expenditure allocated by individual hospitals in response to a systemic problem.

The results collected highlight a number of specific concerns:

Significant impact on clinical care

More than 32% of the actions taken in response to medicines shortages have a direct impact on patient care through either the substitution of a less efficacious medicine, change in the route of administration due to a different formulation or a lack of alternatives for treatment (Table 3).

Using a less efficacious medicine means taking more time to treat the same condition, thus potentially increasing the length of a hospital admission and subsequent cost to the taxpayer. Using less efficacious medicines may also mean exposing patients to medicines with more adverse effects which will also incur extra costs to monitor and treat; both of these workarounds may negatively impact patient quality of life during care episodes.

A key principle of medicines safety is to always use the least invasive route, for example, switching the patient from an oral antibiotic as soon as practicably possible from intravenous antibiotics, as the invasive nature of injectable intravenous medicines carry a secondary risk of local site infections. Changing the route of administration to address a lack of a medicine therefore is also wrought with patient risk, especially where patients are forced to use more invasive routes of administration where oral dose forms are in shortage. Patients may not be aware of the reason for their treatment revision.

Frequent shortages of antimicrobials

Antimicrobials made up half of the most commonly reported shortages (Table 2) and accounted for almost 40% of all the individually reported medicines product shortages and over 20% of all unique medicine product shortages. The most common response to this

shortage was the use of emergency/constrained stock (28.3%). The next most frequent responses all had the potential to negatively impact on both patient care and antimicrobial stewardship practices, with 10.1% switching to a different dose form/strength, 8.2% using second or third line medicines and 6.4% reporting 'no alternatives' for treatment.

These responses to antimicrobial medicine shortages carry inherent problems for pharmacy practice. A significant risk with using second and third line medicines is undoing antimicrobial stewardship efforts with respect to educating doctors, particularly junior doctors, about best practice antimicrobial prescribing and the preferred first line antimicrobials for infectious diseases. The threat of widespread antimicrobial resistance is well documented.

Antimicrobial medicines were also reported as the most likely to be stockpiled. Stockpiling of essential resources can negatively affect the capability of less well-resourced facilities to obtain essential medicines when required, most commonly regional and rural services.

Common use of the Special Access Scheme (SAS)

In the data the Federal Government's SAS was regularly recorded as a key means of addressing shortages, despite its different purpose and the significantly increased procurement costs it incurs. Twenty per cent of the most common shortages prompted use of the SAS, which would potentially impact on hospital budgets given the higher procurement costs of sourcing medicines internationally (Table 4), the most common use of the scheme. Use of the SAS increased costs in 93% of cases across all medicines, and 100% of the time when the SAS was used to procure antimicrobials (Chart 6).

In addition to increased expenditure, procuring medicines from overseas that are not registered in Australia often means medicine product labelling and packaging are not up to Australian standards, do not feature English, or do not have Product Information or Consumer Medicines Information documents. This presents a challenge to both consumers and pharmacists in their pursuit of optimal medication safety and Quality Use of Medicines.

Unreliability of notifications

A persistent problem reported by respondents was the poor quality and low frequency of medicine shortage notifications from stakeholders. The survey results show procurement officers were made aware of 70% of medicines shortages only when they attempted to order the medicine using their electronic ordering system (Chart 3). This notification is too late to allow efficient medicine management. Minimal information was also provided by suppliers on hospital ordering systems regarding when medicines would again be available (Chart 4).

The government-supported mechanism for notification is the TGA's Medicine Shortage Initiative (MSI) website which relies on voluntary notification from suppliers, and sometimes pharmacists. Of the 365 different medicine products reported as unavailable in SHPA's survey, only 54 (14.8%) were listed on the TGA MSI website on the date of the survey. Not only were many medicines shortages not reported on the website, but the data that was published was not current or accurate in many cases.

Conclusion

The issue of medicine shortages is not a new one, however SHPA members report that it is often considered by hospital management, government and pharmaceutical suppliers as an administrative inconvenience rather than a clinical concern. The data collected in this survey indicates that shortages have a clinical impact as well as absorbing considerable pharmacy staff time and medicines budgets.

SHPA believes the data collected in this survey should encourage greater consideration of strategic approaches to reducing the impact of shortages, notably the requirement for greater notification from manufacturers or wholesalers. This would require legislative change as the issue of an Australian Register of Therapeutic Goods (ARTG) number contains no implicit requirement to ensure supply, or notify inability to supply, to the Federal Government.

In practice, the burden of managing widespread medicine shortages is currently being borne by individual pharmacy departments across the country. A systemic approach to both supply and notification has the potential to substantially improve efficiency and increase hospitals' capacity to support optimal patient care. As medicines shortages continue to increase in Australia and overseas this would address a growing pressure on hospitals.

Looking forward, an investigation into the economic impact of medicine shortages, both in the cost of purchasing higher priced foreign medicines, and opportunity cost of clinical pharmacy resources used in procurement workarounds, would be valuable data to enable a comprehensive picture of the costs of shortages.

Due to the serious implications of inadequate supply, manufacturers and wholesalers have a responsibility to inform the Australian community when they are unable to supply medicines they are registered to provide. Given the increasing complexity of the international medicines marketplace and the varying reliability of global supply chains it may be reasonable to accept interrupted supply is inevitable. In this case, notification is the obligation of the social license granted to the medicines industry given their important role in healthcare. SHPA is confident that a commitment to timely notification would return a significant dividend for Australians, both in patient care and in the effective use of limited hospital resources.

References

Aubusson, K. (2017). 'Patients will die if they don't fix this': Hospitals rationing, stockpiling first-line antibiotics amid drug shortage. *Sydney Morning Herald*. [online] Available at: http://www.smh.com.au/national/health/patients-will-die-if-they-dont-fix-this-hospitals-rationing-stockpiling-firstline-antibiotics-amid-drug-shortage-20161209-gt7wyd.html

Australasian Society for Infectious Diseases (2017) ASID calls for a National Drug Shortage Strategy to prevent patient suffering and development of antibiotic-resistant infections. [online] Available at: https://www.asid.net.au/documents/item/1337

Australian Commission on Safety and Quality in Health Care (2016) *AURA 2016: first Australian report on antimicrobial use and resistance in human health*. Sydney: ACSQHC

Economist Intelligence Unit Ltd (2017) Cancer medicines shortages in Europe: Policy recommendations to prevent and manage shortages. *The Economist Healthcare*. Available at http://www.eiu.com/graphics/marketing/pdf/ESMO-Cancer-medicines-shortages.pdf

International Pharmaceutical Federation (2013) *Report of the international summit on medicines shortage*, the Hague, the Netherlands: International Pharmaceutical Federation

International Pharmaceutical Federation (2017) *Reporting medicines shortages: Models and tactical options*, the Hague, the Netherlands: International Pharmaceutical Federation

Johnson, S (2017) Hospitals forced to stockpile and ration antibiotics as Australia faces an 'unbelievable' national shortage. [online] Daily Mail Australia. Available at: http://www.dailymail.co.uk/news/article-4021312/Australia-faces-unbelievable-antibiotics-shortage-expert-says-people-die.html

Jones, Davis & Looke (2017) Death from untreatable infection may signal the start of the post-antibiotic era. *Medical Journal of Australia*; 206 (7) 292-293

Society of Hospital Pharmacists of Australia (2013) Standards of Practice for Clinical Pharmacy Services, *Journal of Pharmacy Practice and Research*; 43 (2) supplement

Swan, N (2017) Drug shortages. [online] ABC Radio National. Available at: http://www.abc.net.au/radionational/programs/healthreport/drug-shortages/8411502

Therapeutic Guidelines (2017) *Therapeutic Guidelines*. [online] Therapeutic Guidelines. Available at: https://tgldcdp.tg.org.au/etgcomplete

Ventola, C. L. (2011) The Drug Shortage Crisis in the United States: Causes, Impact, and Management Strategies. *Pharmacy and Therapeutics*, *36*(11), 740–757.

United States Government Accountability Office (2014) *Drug Shortages - Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability*. Government Accountability Office. Washington.

Woodhead, M. (2017) Alarm as antibiotic of last resort runs out. [online] Australian Doctor. Available at: https://www.australiandoctor.com.au/news/latest-news/last-resort-antibiotics-running-out

World Health Organisation (2016) Medicines shortages. WHO Drug Information; 30(2) Geneva: Switzerland. Available at http://www.who.int/medicines/publications/druginformation/WHO_DI_30-2_Medicines.pdf?ua=1

Tables

Table 1: Health Service Facility Site Peer Groups

Principal referral hospitals	19%
Public acute group A / Public acute group B hospitals	20%
Public acute group C / Public acute group D hospitals	13%
Private acute group A / Private acute group B hospitals	9%
Private acute group C / Private acute group D hospitals	4%
Children's / Women's / Combined Women's and children's	6%
Psychiatric hospital	9%
Same day hospital	9%
Sub- and non-acute hospitals (Public or private rehabilitation)	11%

Table 2: Most commonly reported medicine shortages

Vancomycin	9.4%
Metronidazole	9.2%
Norfloxacin	5.7%
Remifentanil	4.5%
Glyceryl trinitrate	3.0%
Fentanyl	2.9%
Aciclovir	2.6%
Dantrolene	2.2%
Tranexamic acid	2.2%
Azithromycin	2.2%

Table 3. Most commonly reported medicine shortages by therapeutic group

Antimicrobials	20.5%
Anaesthesia/Analgesia	12.0%
Cardiology	10.3%
Endocrine	10.3%
Chemotherapy	9.4%
Neurology	9.0%
Psychotropics	6.0%
Blood disorders	4.3%
Gastrointestinal	3.8%
Anti-inflammatory	2.6%
Vaccine	2.1%
Antiemetics	1.7%
Other	8.1%

Table 4: What action did you take because of the shortage?

Borrowing stock from another pharmacy	1%
Use second/third line medicines	6%
Use an alternative medicine of equal efficacy	7%
I have no alternatives	12%
Procuring stock through SAS	13%
Switch to a different dose form/strength	15%
Using emergency stock	20%
Using an alternative brand	26%

Table 5: Action taken for most common medicines shortages

Procuring stock through SAS	20.2%
Use an alternative medicine of equal efficacy	6.5%
Using an alternative brand	17.8%
Use second/third line medicines	5.7%
Using emergency stock	31.0%
Switch to a different dose form/strength	10.9%
Borrowing stock from another pharmacy	1.1%
I have no alternatives	6.8%

Table 6. Did this action increase costs?

Yes	51%
No	37%
N/A	13%

Charts

Chart 1. Health services by peer group

Health Service Facility Site Peer Groups

- Principal referral hospitals
- Public acute group A / Public acute group B hospitals
- Public acute group C / Public acute group D hospitals
- Private acute group A / Private acute group B hospitals
- Private acute group C / Private acute group D hospitals
- Children's / Women's / Combined Women's and children's
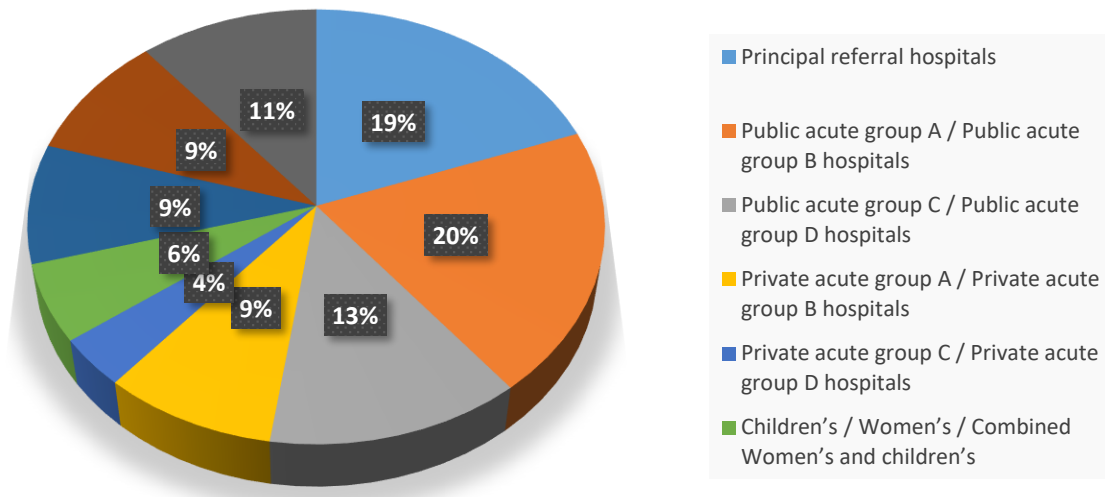
Chart 2. Pharmacist action per medicine shortage

For the medicine shortage you reported, what action did you take as a result? (n=1577)
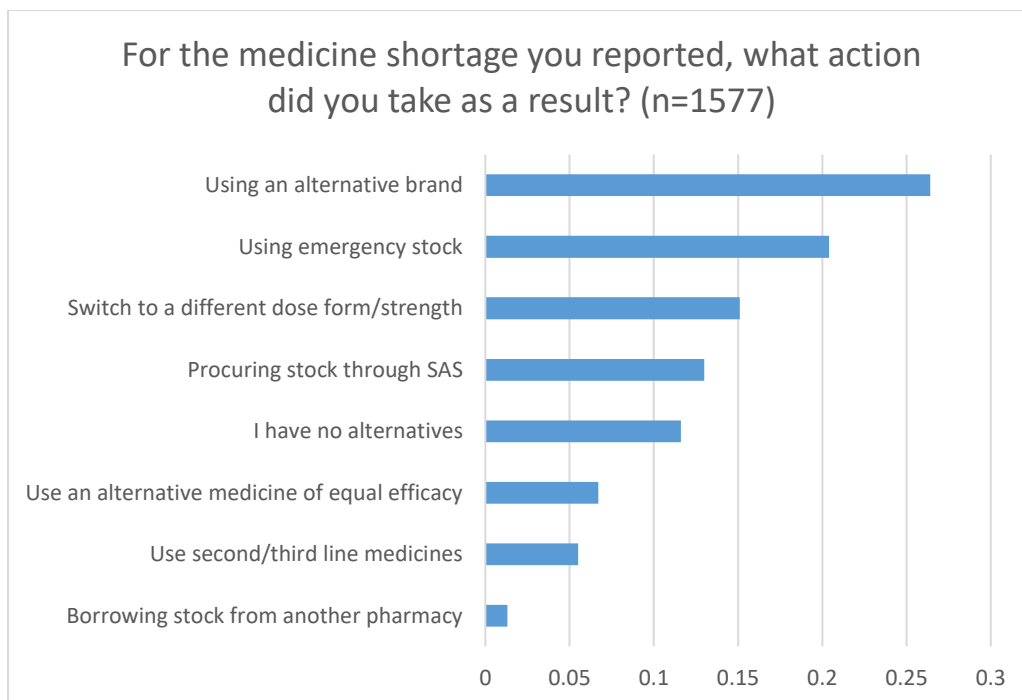
Chart 3. Methods of notification of medicine shortages

For the medicine shortage you reported, how were you made aware? (n=1577)
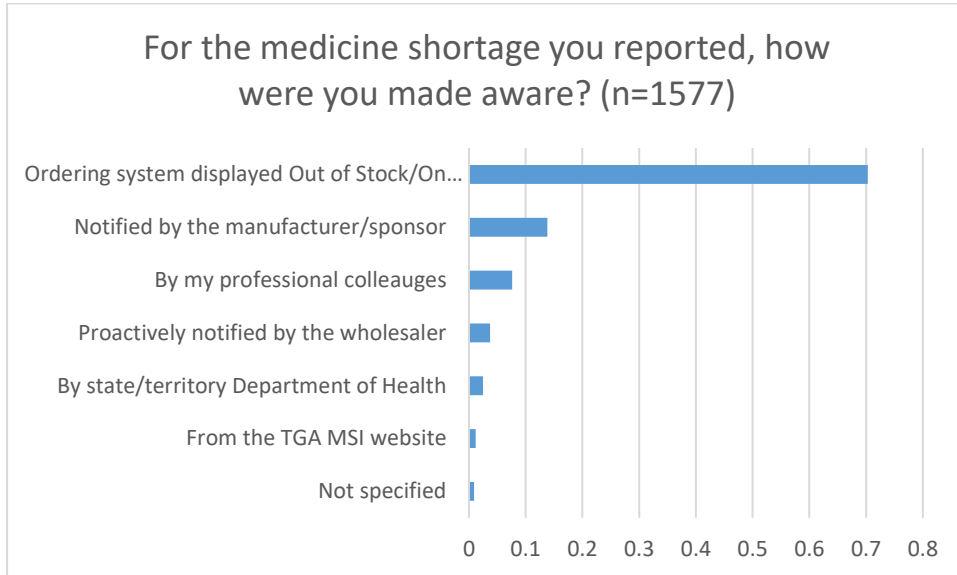
Chart 4. Notification of expected availability for reported shortage

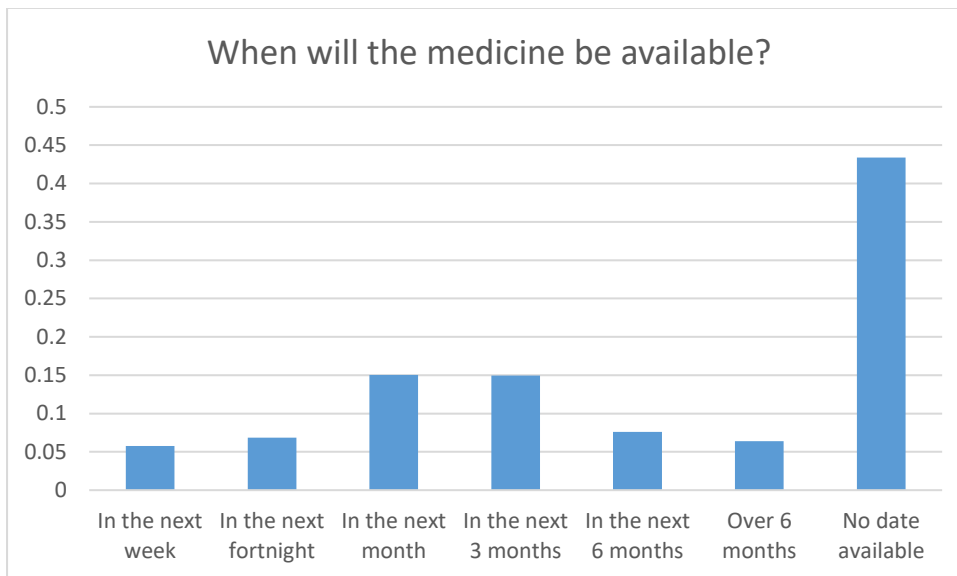When will the medicine be available?

Chart 5. Incurring increased costs on antimicrobials versus all shortages
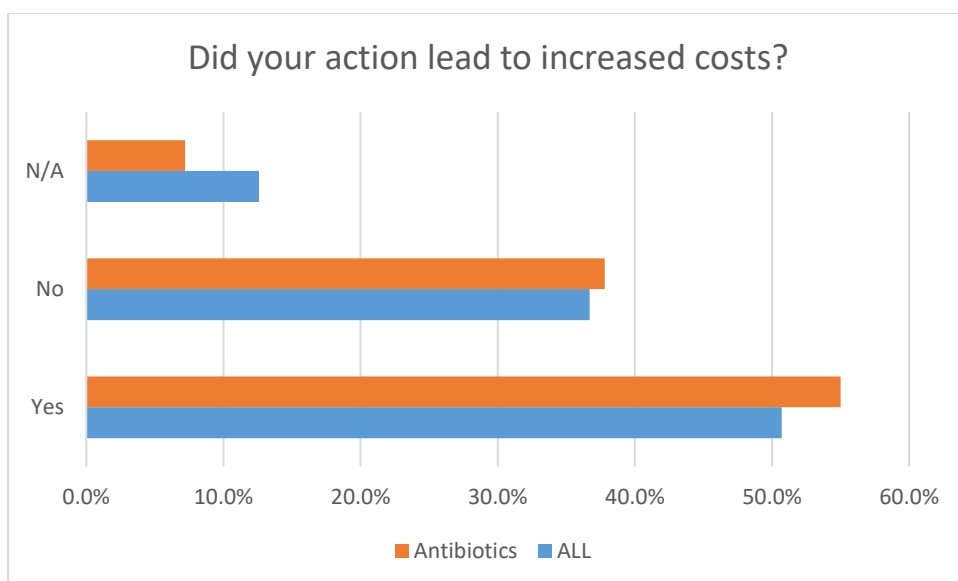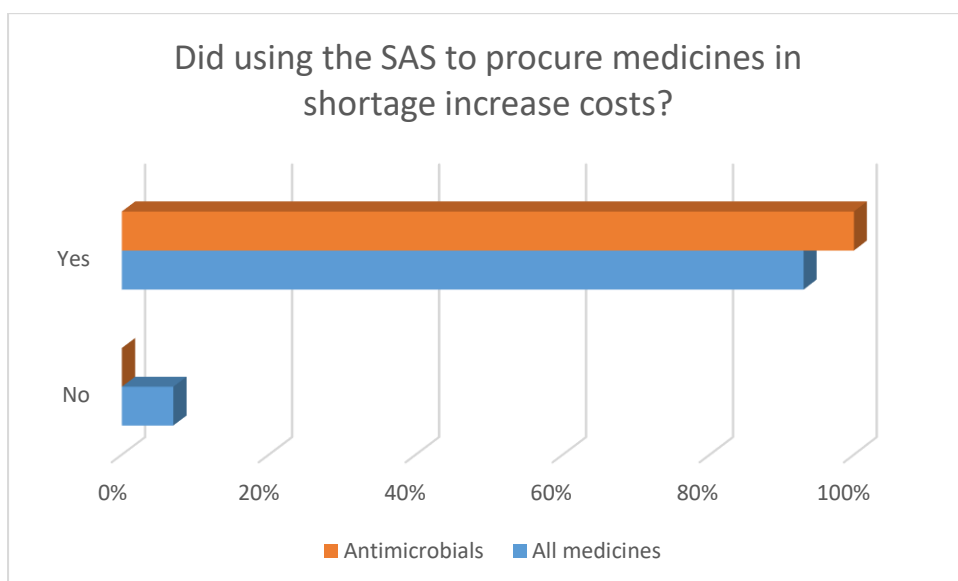

Chart 6. Incurring increased costs using the SAS to obtain antimicrobials versus all shortages

Appendix 1: List of medicine shortages by active ingredient

Vancomycin	Midazolam
Metronidazole	Ciprofloxacin
Norfloxacin	Nicotine
Remifentanil	Octreotide
Glyceryl trinitrate	Phenytoin
Fentanyl	Sildenafil
Aciclovir	Cephalexin
Dantrolene	Chlorhexidine gluconate
Tranexamic acid	Epirubicin
Azithromycin	Imipramine
Hepatitis B vaccine	Nystatin
Etoposide	Telmisartan
Zoledronic acid	Cocaine
Benztropine	Pyridoxine
Meropenem	Biperiden
Dinoprostone	Carbimazole
Mupirocin	Methylprednisolone
Trifluoperazine	Mirtazapine
Dexamethasone/framycetin/gramicidin	Risperidone
Indomethacin	Testosterone
Gabapentin	Allopurinol
Dexamethasone	Atropine
Piperacillin/tazobactam	Cefepime
Meningococcal vaccine	Cephazolin
Isoprenaline	Fosinopril/HCT
Bupivacaine/fentanyl	Hydromorphone
Heparin products	Isosorbide mononitrrate
Dexmedetomedine	Melphalan
Oestradiol	Ondansetron
Fluconazole	Paracetamol
Ligocaine	Prochlorperazine
Pantoprazole	Valaciclovir
Tramadol	Amantadine
Hyoscine hydrobromide	Ampicillin
Ketamine	Aprepitant
Lamotrigine	Benzocaine/adrenaline/zinc
Pancreatic enzymes	Candesartan/HCT
Calcium folinate	Cefoxitin
Candesartan	Clotrimazole
Spironolactone	Dipyridamole/aspirin
Vasopressin	Dothiepin
Diptheria & tetanus vaccine	Entecavir
Disulfiram	Estradiol
Oxaliplatin	Flucloxacillin

Fosinopril		Dopamine
Gemcitabine		Dornase alfa
Ketorolac		Doxorubicin
Levetiracetam		Esomeprazole
Metaraminol		Famciclovir
Metoprolol		Ferrous sulphate
Morphine		Flumazenil
Pitressin		Fluorouracil
Pramipexole		Fluphenazine
Propantheline		Flutamide
Propofol		Framycetin
Quinapril		Hyoscine butylbromide
Ranitidine		Ibuprofen
Ribavirin		Lorazepam
Simvastatin		Macrogol 3350-Electorlytes
Sumatriptan		Methotrexate
Adenosine		Mycophenolate
Adrenaline		Nandralone
Amoxicillin		Oseltamavir
Amphotericin		Oxazepam
Anakinra		Oxytocin
Anidulafungin		Phosphate
Atorvastatin		Pioglitazone
BCG vaccine		Potassium chloride
Bifidobacterium bifidim-lactobacillus acidopholis		Probanthine
Bivalirudan		Raloxifene
Bupivacaine		Ramipril
Calcipotriol		Reteplase
Carbachol		Rocuronium
Cimetidine		Tacrolimus
Desferrioxamine		Tinidazole
Diphtheria-Tetanus-Pertussis-Poliovirus vaccine		Topiramate
		Valsartan
		Voriconazole

Medicines are listed in order of prevalence of shortage. Duplicates may appear due to the combination of active ingredients in products.