# The Drug Shortage Era: A Scoping Review of the Literature 2001–2019

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**Drug shortages continue at crisis levels in the United States, with no end in sight. Extensive research in disparate areas has been conducted to explore the impact that shortages have on patients and the healthcare system. We conducted a scoping review to categorize existing work in order to identify opportunities for further research. We considered peer-reviewed and non-peer-reviewed articles involving non-vaccine, human drug shortages in the United States published in English between January 2001 and May 2019. In total, 430 papers were charted according to the following categories: causes, impacts on care, health outcomes, costs, management, prevention, and federal government response. Of these, 112 papers considered causes; 199 discussed effects, 158 considered management strategies, and 140 discussed prevention. We provide a resource to navigate the vast literature on drug shortages in the United States, identifying areas in need of further research. This review highlights the widespread negative effects that drug shortages have on patients, providers, and health system costs in the United States. Evidence of their ramifications should be sufficient to justify policy change. Future work should move from characterizing the problem to working toward solutions to reduce the impact, occurrence, and effects of shortages.**

Drug shortages have become the norm in the American health system. Although shortages have occurred on occasion for decades, over 200 drugs have been short each year from 2010 to 2018.[1,2] The median shortage lasts over a year, and large segments of the market have been affected.[1,3,4] Nearly all hospitals experience drug shortages, and providers regularly treat patients with alternative agents and potentially suboptimal therapies.[5–7] Entire cohorts of physicians and pharmacists have been educated in a time when shortages are common and some first-line medications are unavailable. These shortages have put patients at risk of poor health outcomes and led to major health system costs.[8,9]

Numerous papers have discussed aspects of the crisis, and it can be difficult to navigate the growing body of literature. A comprehensive list of the literature is challenging to obtain, and authors may unknowingly be repeating research that has already been completed. Studies have been published in many outlets, and papers are often targeted to a particular therapeutic area. Yet, the dynamics that contribute to shortages cross therapeutic lines, and policies intended to address shortages should likely be implemented more broadly. It may be challenging for decision makers to know the extent of the impact of shortages and for researchers to find productive directions for future work.

The US Food and Drug Administration (FDA) Drug Shortage Task Force Report from October 2019 recommended "creat[ing] a shared understanding of the impact of drug shortages and the contracting practices that may contribute to them."[10] This paper provides a framework to do so by characterizing the existing research on drug shortages. It classifies the available literature into major areas, including the effects of shortages and why they occur, to give stakeholders a common ground of what is already known. Researchers may better target new drug shortage research where gaps in the literature exist.

In this paper, we present a comprehensive survey of the literature published since 2001 about drug shortages in the United States. We use a scoping review framework to survey the wide range of analyses and identify gaps for further research. We classify articles into several areas, including research related to the characteristics of drug shortages, why they occur and persist, their effects, how they are managed, what the government has done, and how they may be prevented. Using this classification, we identify directions for future research. This paper offers researchers the opportunity to focus the scarce research resources into areas that need further investigation.

## METHODS

The analysis was conducted according to a standard scoping review framework and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Scoping Reviews (PRISMA-ScR) guidance.[11,12]

### Data sources and searches

To identify papers, we searched four electronic databases (PubMed, Scopus, Web of Science, and Embase) using the terms (drug AND shortage) OR (medicine AND shortage) for papers published in English starting in 2001. The initial search was conducted in May 2018, and the final refresh occurred in May 2019. An example of the full query for PubMed is available in the **Supplementary Materials**. The online search was augmented with other publications in our collections, and the reference list of each included article was reviewed to identify other papers.

### Article selection

We considered peer-reviewed and non-peer-reviewed gray literature that focused on shortages of non-vaccine, human drug products. Gray literature included reports from the government and major organizations as well as

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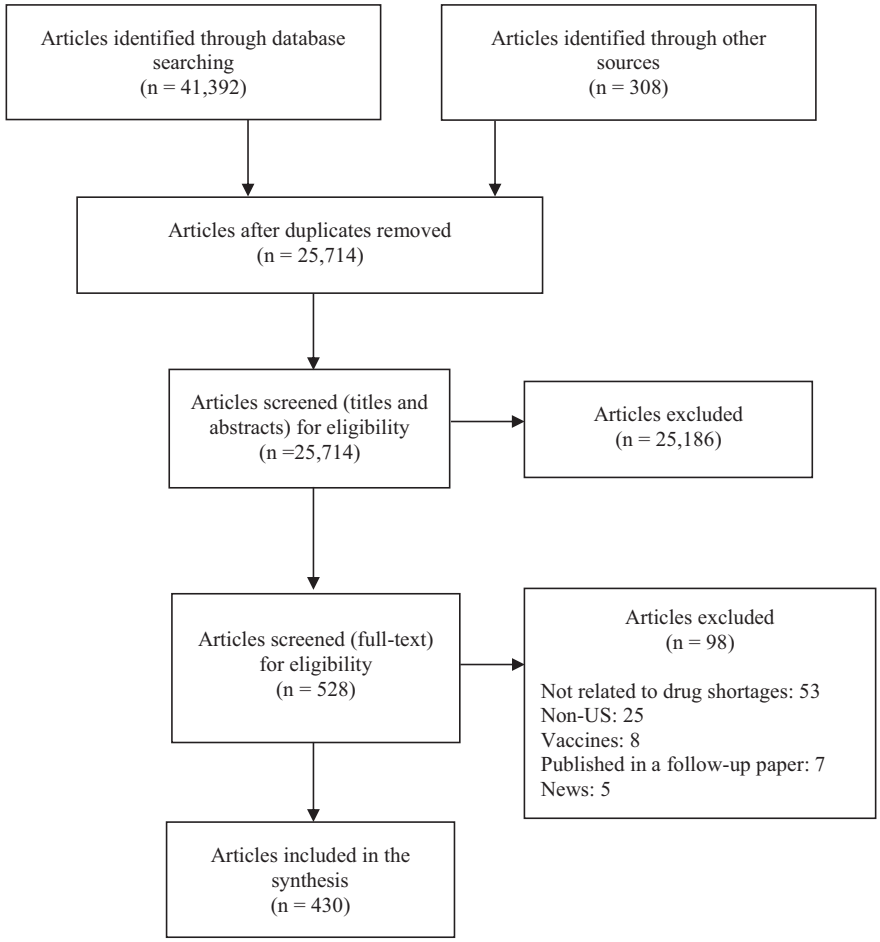


**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Scoping Reviews (PRISMA-ScR) diagram.

conference proceedings. Although drug shortages are a global problem, to narrow the scope, we focused on shortages in the United States. Papers related to vaccines were also excluded because these shortages have been better studied and have different market dynamics than other drugs.[13]

In the initial screen of the identified articles, a single researcher reviewed the title and abstract of each paper to filter out irrelevant literature and duplicates. The exclusion criteria were: unrelated to drug shortages, based primarily on non-US data, focused on vaccines, or news articles. We also excluded conference presentations that were later published as full papers. To calibrate the screening process, a second research staff member reviewed the decisions for ~ 100 articles, and discrepancies were resolved through discussion. If the paper did not clearly meet the exclusion criteria based on the title and abstract review, it was remained eligible for inclusion. The full-text paper of each remaining eligible paper was read by one researcher to determine its relevancy. If an article was excluded at the full-text screening stage, a second research staff member read the article to confirm the exclusion criteria were met. The remaining articles were included in the synthesis.

### Data extraction

For each included article, key information was compiled including: publication year; journal; drug or type of drug considered; focus; and source of data. Each article was also classified according to topic areas (e.g., causes and effects) and categories within each area (e.g., type of cause). The synthesis was conducted using a cascading process, and the lists of areas and categories were updated as more articles were reviewed.

The initial areas were: causes; health effects; costs; guidance; mitigation strategies; and prevention strategies. The process began with no categories within areas. Papers were first reviewed by one researcher to determine whether they were associated with areas and categories within the areas (i.e., for each: yes or no). As new areas and categories were identified, articles that had been previously reviewed were re-reviewed to evaluate whether they were associated with the new areas and categories. After all of the articles were reviewed, the areas and categories were finalized. All articles were fully reviewed a second time to check their alignment with area and category. There is not a registered protocol, although additional detail is available by request to the corresponding author.

### Data synthesis and analysis

The final categories and counts of associated articles are presented in narrative form in the text and in **Table 1**. The references for the papers classified in each area, category, and subcategory are presented in tables in the **Supplementary Materials**. Because articles can be associated with multiple categories, the count of articles associated with an overarching category may be less than the sum of the counts of the individual categories. The distributions of papers by publication year, journal, and therapeutic/practice area are shown in figures in the text and the **Supplementary Materials**.

## SYNTHESIS

### Article characteristics

There were 41,700 articles that met the initial search criteria. After duplicates between databases and articles from other

**Table 1 Count of articles by area and category**

| Area | Category | *n* |
|---|---|---|
| Types of papers | Overviews | 33 |
| | Specific providers | 8 |
| | Reviews of specific areas | 27 |
| | Perspectives, editorials, viewpoints, and commentaries | 66 |
| | Surveys | 54 |
| | Shortage prevalence and characteristics at a particular time | 48 |
| | Shortage prevalence and characteristics over time | 56 |
| Causes | Total | 112 |
| | Proximate | 69 |
| | Economic factors | 64 |
| | Capacity and inventory dynamics | 55 |
| | Regulatory | 36 |
| Effects | Total | 199 |
| | Delivery of care | 156 |
| | Health outcomes | 120 |
| | Labor and costs | 77 |
| Management strategies | Total | 158 |
| | Guidance or tools | 78 |
| | Examples | 91 |
| Prevention strategies | Total | 140 |
| | Reducing the impact of disruptions or potential shortages | 101 |
| | Increasing supply chain resiliency | 72 |
| | Decreasing risk of disruptions | 49 |
| | Increasing attractiveness to produce drug | 43 |
| Federal government response to shortages | Total | 26 |
| | Overviews | 16 |
| | Reports | 11 |
| | Events | 7 |

sources were removed, the titles and abstracts of 25,714 articles were screened for eligibility. Review of the full-text was done for 528 articles; 430 articles were included in the final analysis. The process is presented in a PRISMA-ScR diagram in **Figure 1**. The number of papers corresponding to each area and category is given in **Table 1**.

Publication years are presented in **Figure 2**. There were 34 articles published before 2011 and 44 articles, on average, each year from 2011 to 2018. One hundred sixty-seven journals published at least one article.

### What types of papers have been published?

Many papers presented overviews about drug shortages (33 papers; **Table S1**). Some were targeted toward specific providers (8 papers), and others presented reviews of specific areas (27 papers). There have also been many published perspectives and opinion pieces (66 papers). Fifty-four papers reported survey results. Few surveys included patients or industry experts as respondents (2 and 4 papers, respectively). Forty-eight papers reported the characteristics of shortages at a particular time, and 56 presented data on shortages over time. Many were based on data from the University of Utah Drug Information Service and the FDA.[1,14,15] Papers that presented counts of shortages generally considered a national context, although not all hospitals may experience a given shortage.[16] Papers frequently focused on shortages in particular practice (e.g., critical care, 20 papers) or therapeutic areas (e.g., oncology, 68 papers).

### What causes shortages?

There are many factors that may contribute to drug shortages (**Table S2**). In total, 112 papers evaluated or reported one or more causes. They can be categorized in the following areas: proximate (69 papers); economic factors (64 papers); capacity and inventory dynamics (55 papers); and regulation (36 papers).

In many cases, the root causes of shortages are unknown or unreported[17] because of the proprietary nature of drug manufacturing. Companies must notify the FDA when medically necessary drugs are expected to be short but are not required to report the specific issue.[18] Although perspectives have been published that discuss possible underlying causes and market failures,[19] better data will be necessary to work on solutions. Industry partnerships will be critical in conducting such analyses.

### What effects do shortages have?

Drug shortages can have far-reaching consequences, and 199 papers reported their effects. These can be classified into 156 papers on the delivery of care (**Table S3**); 120 papers about health outcomes (**Table S4**); and 77 papers related to labor and costs (**Table S5**).

Among the papers that discussed the delivery of care, many focused on treatment changes (114 papers) or delays and cancellations (34 papers). Of the 120 papers that reported health outcomes, 50 were retrospective or observational studies, and 17 reported medication errors that resulted because of a shortage. The cost-related papers considered the effects of shortages on the costs of drugs (50 papers); labor required to manage shortages (25 papers); and other treatment-related costs (12 papers). Overall institutional cost changes (12 papers) were also reported.

Many of the reports about the effects of shortages were based on survey data. These indicated substantial impact (e.g., over 1,000 near misses, errors, and adverse events were reported in a 2010 Institute for Safe Medication Practices survey[20]), although the true effects are not known and likely under-reported. The most recent data from a centralized reporting system on errors is from 2003–2004.[21] It is difficult to determine the full impact of a particular shortage in part because surveys tended to ask whether practices had changed rather than the magnitude of the effect. For example, 70% of surveyed infectious disease physicians reported they changed prescribing in the past 2 years because of a shortage[22]; it is not known for how many patients or how frequently these changes occurred. Two exceptions presented the magnitude of oncology drug shortages. One estimated

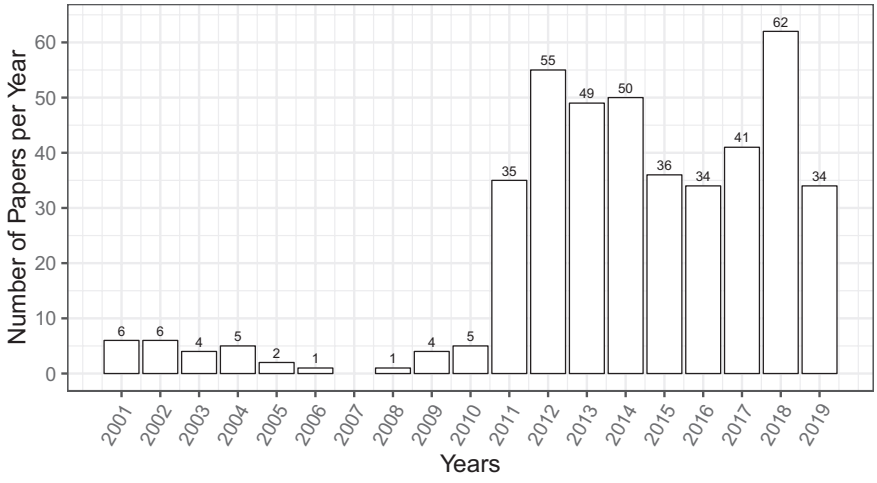


**Figure 2** Distribution of papers by year of publication.

that 550,000 people were affected by a shortage in 2011, and another reported that drug utilization did not substantially change for many short drugs 2004–2011.[23,24] Papers rarely reported shortages by patient demographics.

National estimates suggest that the cost to manage shortages is hundreds of millions of dollars each year.[9,25,26] A recent estimate reported the labor cost alone is US $359 million annually.[9] These cost estimates are increasing, and this may be due to the increasing number of active shortages, which doubled between 2014 and 2010 when an earlier major labor survey was conducted.[25,27] There is also an increasing use of automation and informatics systems in hospitals.[28] These automated systems are not easily adaptable when changes are needed for a shortage; even a simple switch from a vial to a syringe can require over 50 hours of informatics time.

### How are shortages managed?

Health systems have actively worked to reduce the effects of shortages on patients, and 158 papers considered management strategies. These include 78 papers that presented guidance or tools to help providers and 91 papers that reported examples (**Table S6**). In particular, the current American Society of Health-System Pharmacists management guidelines present a process that includes operational and therapeutic assessments, analysis of the impact of a shortage, planning, communication, and implementation.[28] Other reports provide guidance for particular therapeutic or practice areas (40 papers) as well as ethical dilemmas (25 papers). Management examples include strategies to conserve the short drug (57 papers), acquire additional units (37 papers), communicate effectively (30 papers), and manage inventory (19 papers).

### How can shortages be prevented?

In total, 140 papers presented or discussed potential strategies to prevent shortages (**Table S7**). Many were proposed in the context of specific types of shortages (e.g., generic injectable drugs). Strategies aimed to reduce the impact of disruptions (101 papers); increase the resiliency of pharmaceutical supply chains (72 papers); decrease the risk of disruptions (49 papers); and increase the attractiveness to produce the drug (43 papers).

Researchers at the FDA reported that investments in quality systems would be critical to stemming shortages.[29,30] Improved transparency may incentivize improvements in quality.[29] Recent papers noted that drug manufacturing sites could be evaluated as part of national security or essential infrastructure.[31,32] Industry respondents recommended connecting the organization's internal goals, metrics, or incentives to shortage prevention.[33] Few papers have analyzed the potential effects of prevention strategies or have evaluated the effects of those that have been implemented.

### How has the government responded?

The federal government has taken steps to reduce shortages (**Table S8**). These have been detailed in overviews (16 papers) and reports from the Government Accountability Office (GAO) and the FDA (11 papers). Several summits and meetings have been held to discuss causes and potential solutions (7 papers, **Table S1**). In 2011, President Obama issued an Executive Order to direct the FDA to address shortages, and, in 2012, the US Food and Drug Administration Safety and Innovation Act (FDASIA) was passed to require manufacturers to notify the FDA 6 months prior to a shortage of a medically necessary drug.[18,34] The FDA reported that many shortages have been prevented, including 145 in 2017, although many persist.[35] In 2018, the FDA formed a task force to study solutions to prevent drug shortages.[36] Currently, the FDA cannot require manufacturers to maintain redundancy, to implement other business continuity measures, or to produce a drug. If market-based solutions are unable to resolve shortages, further legislation may be necessary.

## FUTURE DIRECTIONS

By all measures, research on drug shortages is active and ongoing. Nonetheless, the classification process led to several open questions. Although the effects of shortages are expansive they are not fully known. There are several papers related to the prevalence and characteristics of shortages, yet few consider shortage magnitude; it would be useful to quantify shortages by their severity or the

proportion of supply affected. There are opportunities to analyze how frequently changes are made to the delivery of care and the types of patients who are affected. This could include reporting counts of the number of substitutions, doses affected, and suboptimal treatments provided due to shortages, in aggregate as well as for specific subpopulations or regions. It would be a major step forward if we could answer: how many people typically receive a drug that is short, and how many people are harmed because of its shortage?

This is challenging because there is not a national database on health outcomes or shortage effects. The existing databases focus rather on shortage characteristics and durations.[14,15] In the absence of this infrastructure, researchers have suggested that the impact of shortages on patients and the healthcare system may be under-reported.[37,38] Many papers that present patient harm are case studies or reports from a single center.[39,40] There are far fewer multicenter analyses of health outcomes. Additional research into overall harms may be more relevant. Two examples of this done well are the studies on the shortage of norepinephrine in patients with septic shock and mechlorethamine in pediatric patients with Hodgkin's lymphoma.[8,41] Shortages may not affect all hospitals and patients equally,[42] and limited research has been conducted on disparities in care. There are opportunities to evaluate how shortages affect vulnerable populations, including people who are uninsured. Research is also limited for the geriatric and outpatient populations.

Some estimates of the costs of shortages are becoming dated, and limited work has been done on the indirect costs of shortages. Although the risks of poor health outcomes should be reason enough to prompt action, continuing to quantify costs due to shortages may help stakeholders justify interventions.

Managing shortages at health systems continues to be difficult. Providers generally have little notice before a shortage occurs,[6] and projected resolution dates are often unavailable or underestimated.[43] Although many hospitals have management plans, many report wanting to improve their processes.[44] There are opportunities to improve projections, increase collaborations between institutions, and develop further guidance for treatments in times of shortage. Further research may be necessary to develop informatics systems that are flexible to supply disruptions.[45]

Few analyses exist on the potential effects of policies to prevent shortages. Other disciplines may be able to add insight in this area, including economists, industrial engineers, and psychologists. Further analyses on the effects of group purchasing organizations, new ventures, such as Civica Rx,[46] and other supply chain partners would also likely be worthwhile.

In general, there has been limited work from the perspective of manufacturers. Open questions include the cost-effectiveness of quality improvement measures and ways to improve business continuity. There is nearly no transparency about manufacturing practices and supply chain decisions, and it is clear that the pharmaceutical industry must be involved in preventing shortages.

Finally, patients may be largely unaware that shortages occur.[47] This unfamiliarity may make shared decision making difficult and limit public support for policies intended to reduce shortages.

### Limitations

We reviewed over 40,000 papers, with only one researcher conducting the initial filtering step. It is possible that relevant articles may have been missed in the initial screening. To mitigate this, we reviewed the reference lists of all included papers and supplemented the initial papers with relevant citations. In addition, because the dynamics of shortages have changed over time, it is important to consider the context in which each article was written. Earlier papers provide important context but should not be considered representative of present-day conditions.

## CONCLUSIONS

Drug shortages in the United States are a public health crisis. This paper offers the first comprehensive review of the available literature on drug shortages to provide a framework for a shared understanding of the causes, effects, and strategies. Shortages continue to occur in high numbers, and it is clear that they have led to major health concerns and increased costs. Researchers have reported numerous errors associated with shortages and several deaths. Collectively, health systems spend millions of hours and hundreds of millions of dollars annually to manage shortages. Taken as a whole, the literature is clear that shortages have negatively affected the delivery of care, and the breadth of research should be sufficient to justify substantial legislative or market change. We recognize the efforts of many to mitigate shortages, but continued efforts and research are needed to identify ways to reduce their effects. We recommend directions for further study and call on stakeholders to take potentially bold steps to prevent shortages. Open questions remain, but the most pressing is simply—when will the era of drug shortages end?

## SUPPORTING INFORMATION

Supplementary information accompanies this paper on the *Clinical Pharmacology & Therapeutics* website (www.cpt-journal.com).

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## CONFLICT OF INTEREST

The University of Utah has a contract with Vizient to provide information about drug shortages. The amount represents < 5% of the overall budget. Erin Fox has received the following support: for providing continuing education on drug shortages (partial travel support from: JCPP, AAMC, Mayo Clinic Dept. of Anesthesia, European COST, University of Illinois, ACCP, University of Iowa, American Society of Anesthesiologists, APSF, Massachusetts Society of Health System Pharmacists, Idaho Society of Health System Pharmacists, MHA Business Summit, Infusion Nurses Society, POHMS, Oklahoma Society of Health System Pharmacists, Cleveland Clinic Abu Dhabi); complimentary registration (ISPE); for facilitating meeting about drug shortages: partial travel support (NASEM). All other authors declared no competing interests for this work.

1. Government Accountability Office (GAO). GAO-16-595: drug shortages: certain factors are strongly associated with this persistent public health challenge <https://www.gao.gov/products/GAO-16-595> (2016).
2. Identifying the root causes of drug shortages and finding enduring solutions <https://healthpolicy.duke.edu/sites/default/files/atoms/files/duke-fda_drug_shortages_presentation_slides__0.pdf> (2018).
3. Hassig, T.B., McKinzie, B.P., Fortier, C.R. & Taber, D. Clinical management strategies and implications for parenteral nutrition drug shortages in adult patients. *Pharmacotherapy* **34**, 72–84 (2014).
4. Hosseini, R. *et al*. Factors associated with the incidence of oncology drugs shortages in the United States (2001–2017). *Value Health* **21**, S372 (2018).
5. American Hospital Association. AHA survey on drug shortages <https://www.aha.org/system/files/content/11/drugshortagesurvey.pdf> (2011).
6. Hantel, A., Siegler, M., Hlubocky, F., Colgan, K. & Daugherty, C.K. Prevalence and severity of rationing during drug shortages. *JAMA Intern. Med.* **179**, 710–711 (2019).
7. Kehl, K.L. *et al*. Oncologists' experiences with drug shortages. *J. Oncol. Pract.* **11**, e154–e162 (2015).
8. Vail, E. *et al*. Association between US norepinephrine shortage and mortality among patients with septic shock. *J. Am. Med. Assoc.* **317**, 1433–1442 (2017).
9. Vizient Drug shortages and labor costs <https://www.vizientinc.com/-/media/documents/sitecorepublishingdocuments/public/vzdrugshortageslaborcost_fullreport.pdf> (2019).
10. US Food and Drug Administration (FDA). FDA drug shortages task force drug shortages: root causes and potential solutions <https://www.fda.gov/media/132059/download> (2019).
11. Arksey, H. & O'Malley, L. Scoping studies: towards a methodological framework. *Int. J. Soc. Res. Methodol. Theory Pract.* **8**, 19–32 (2005).
12. Tricco, A.C. *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann. Intern. Med.* **169**, 467–473 (2018).
13. Ridley, D.B., Bei, X. & Liebman, E.B. No shot: US vaccine prices and shortages. *Health Aff.* **35**, 235–241 (2016).
14. American Society of Health-System Pharmacists (ASHP). ASHP current drug shortages <https://www.ashp.org/drug-shortages/current-shortages> (2019).
15. US Food and Drug Administration (FDA). FDA drug shortages <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm> (2019).
16. Banerjee, R., Thurm, C.W., Fox, E.R. & Hersh, A.L. Antibiotic shortages in pediatrics. *Pediatrics* **142**, e20180858 (2018).
17. Mazer-Amirshahi, M. *et al*. U.S. drug shortages for medications used in adult critical care (2001–2016). *J. Crit. Care* **41**, 283–288 (2017).
18. US Food and Drug Administration Safety and Innovation Act (FDASIA). Public Law 112–144 <https://www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf> (2012).
19. Gatesman, M.L. & Smith, T.J. The shortage of essential chemotherapy drugs in the United States. *N. Engl. J. Med.* **365**, 1653–1655 (2011).
20. Institute for Safe Medication Practices (ISMP). ISMP Drug shortages: National Survey Reveals High Level of Frustration, Low Level of Safety. ISMP Medicat. Saf. Alert! <http://www.ismp.org/resources/special-issue-drug-shortages-national-survey-reveals-high-level-frustration-low-level> (2010).
21. De Oliveira, G.S., Theilken, L.S. & McCarthy, R.J. Shortage of perioperative drugs: implications for anesthesia practice and patient safety. *Anesth. Analg.* **113**, 1429–1435 (2011).
22. Gundlapalli, A.V., Beekmann, S.E., Graham, D.R. & Polgreen, P.M. & Members of the Emerging Infectious Network. Antimicrobial agent shortages: the new norm for infectious diseases physicians. *Open Forum Infect. Dis.* **5**, 1–5 (2018).
23. IMS Institute for Healthcare Informatics. Drug shortages: a closer look at products, suppliers and volume volatility <https://www.puncturemovie.com/wp-content/themes/Romix/pdfs/ihii-drug-shortage-report.pdf> (2011).
24. Alpert, A. & Jacobson, M. Impact of oncology drug shortages on chemotherapy treatment. *Clin. Pharmacol. Ther.* **106**, 415–421 (2019).
25. Kaakeh, R. *et al*. Impact of drug shortages on U.S. health systems. *Am. J. Health Pharm.* **68**, 1811–1819 (2011).
26. Cherici, C.*et al*. Navigating drug shortages in American healthcare: a premier healthcare alliance analysis <https://www.heartland.org/publications-resources/publications/navigating-drug-shortages-in-american-healthcare-a-premier-healthcare-alliance-analysis> (2011).
27. Reed, B.N. *et al*. The impact of drug shortages on patients with cardiovascular disease: causes, consequences, and a call to action. *Am. Heart J.* **175**, 130–141 (2016).
28. Fox, E.R. & McLaughlin, M.M. ASHP guidelines on managing drug product shortages. *Am. J. Health Pharm.* **75**, 1742–1750 (2018).
29. Woodcock, J. & Wosinska, M. Economic and technological drivers of generic sterile injectable drug shortages. *Clin. Pharmacol. Ther.* **93**, 170–176 (2013).
30. Dill, S. & Ahn, J. Drug shortages in developed countries - reasons, therapeutic consequences, and handling. *Eur. J. Clin. Pharmacol.* **70**, 1405–1412 (2014).
31. Council on Science and Public Health. Drug Shortages: Update (2-A-18) <https://www.ama-assn.org/councils/council-science-public-health/prescription-drugs-csaph-reports> (2018).
32. Mazer-Amirshahi, M. & Fox, E.R. Saline shortages — many causes, no simple solution. *N. Engl. J. Med.* **378**, 1472–1474 (2018).
33. ISPE report on the ISPE drug shortages survey <https://ispe.org/sites/default/files/initiatives/drug-shortages/2013-ISPE-drug-shortages-survey-report.pdf> (2013).
34. Obama, B.Executive order 13588 – reducing prescription drug shortages <https://obamawhitehouse.archives.gov/the-press-office/2011/10/31/executive-order-13588-reducing-prescription-drug-shortages> (2011).
35. US Food and Drug Administration (FDA). FDA report on drug shortages for calendar year 2017 <https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM610662.pdf> (2017).
36. Gottlieb, S.Statement by FDA Commissioner Scott Gottlieb, M.D., on formation of a new drug shortages task force and FDA's efforts to advance long-term solutions to prevent shortages <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm613346.htm> (2018).
37. Chan, L.-N. Iatrogenic malnutrition: a serious public health issue caused by drug shortages. *J. Parenter. Enter. Nutr.* **37**, 702–704 (2013).
38. McLaughlin, M.M., Lin, J., Nguyen, R., Patel, P. & Fox, E.R. Unavailability of outpatient medications: examples and opportunities for management. *J. Pharm. Technol.* **33**, 83–86 (2017).
39. Corrigan, M. & Kirby, D.F. Impact of a national shortage of sterile ethanol on a home parenteral nutrition practice: a case series. *J. Parenter. Enter. Nutr.* **36**, 476–480 (2012).
40. Patel, S., Liedtke, M., Ngo, D. & Medeiros, B.C. A single-center experience of the nationwide daunorubicin shortage: substitution with doxorubicin in adult acute lymphoblastic leukemia. *Leuk. Lymphoma* **54**, 2231–2235 (2013).
41. Metzger, M.L., Billett, A. & Link, M.P. The impact of drug shortages on children with cancer–the example of mechlorethamine. *N. Engl. J. Med.* **367**, 2461–2463 (2012).
42. Bhat, S., Roberts, R. & Devlin, J.W. Posted versus actual drug shortages. *Am. J. Health Pharm.* **69**, 1363–1364 (2012).
43. McLaughlin, M.M., Pentoney, Z., Skoglund, E. & Scheetz, M.H. Projections for antiinfective drug shortages and time to actual resolution. *Am. J. Health Pharm.* **71**, 2074–2078 (2014).
44. Holmes, O.W. & Hughes, P.J. Drug shortage management in Alabama hospital pharmacies. *Innov. Pharm.* **4**, (2013).
45. Vanek, V.W. *et al*. A call to action for optimizing the electronic health record in the parenteral nutrition workflow. *Am. J. Health Pharm.* **75**, 1400–1420 (2018).
46. Council on science and public healthDrug shortages: 2019 update (2-A-19) <https://www.ama-assn.org/system/files/2019-05/a19-csaph2.pdf> (2019).
47. Frosch, Z.A.K. *et al*. Cancer drug shortages: awareness and perspectives from a representative sample of the US population. *Cancer* **124**, 2205–2211 (2018).