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Original Article

Understanding the role of antibiotic-associated adverse events in influencing antibiotic decision-making

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Abstract

Objective: To (1) understand the role of antibiotic-associated adverse events (ABX-AEs) on antibiotic decision-making, (2) understand clinician preferences for ABX-AE feedback, and (3) identify ABX-AEs of greatest clinical concern.

Design: Focus groups.

Setting: Academic medical center.

Participants: Medical and surgical house staff, attending physicians, and advanced practice practitioners.

Methods: Focus groups were conducted from May 2022 to December 2022. Participants discussed the role of ABX-AEs in antibiotic decision-making and feedback preferences and evaluated the prespecified categorization of ABX-AEs based on degree of clinical concern. Thematic analysis was conducted using inductive coding.

Results: Four focus groups were conducted ($n = 15$). Six themes were identified. (1) ABX-AE risks during initial prescribing influence the antibiotic prescribed rather than the decision of *whether* to prescribe. (2) The occurrence of an ABX-AE leads to reassessment of the clinical indication for antibiotic therapy. (3) The impact of an ABX-AE on other management decisions is as important as the direct harm of the ABX-AE. (4) ABX-AEs may be overlooked because of limited feedback regarding the occurrence of ABX-AEs. (5) Clinicians are receptive to feedback regarding ABX-AEs but are concerned about it being punitive. (6) Feedback must be curated to prevent clinicians from being overwhelmed with data. Clinicians generally agreed with the prespecified categorizations of ABX-AEs by degree of clinical concern.

Conclusions: The themes identified and assessment of ABX-AEs of greatest clinical concern may inform antibiotic stewardship initiatives that incorporate reporting of ABX-AEs as a strategy to reduce unnecessary antibiotic use.

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Introduction

Approximately 50% of all hospitalized patients receive at least one antibiotic during their hospitalization.[1] Although antibiotics have life-saving potential, they can also cause harm. Antibiotic-associated adverse events (ABX-AEs), harms due to exposure to an antibiotic, are common with prior studies showing that 20% of hospitalized patients receiving antibiotics develop at least one ABX-AE, 20% of which occur due to non-clinically indicated antibiotic prescriptions.[2–4] A myriad of ABX-AEs can occur, including drug toxicities, *Clostridioides difficile* infection, and antimicrobial resistance. The consequences of these ABX-AEs can range from increased costs and inconvenience due to additional testing (e.g., serial electrocardiograms to monitor QTc interval while on a fluoroquinolone) and prolonged hospitalization to permanent end-organ dysfunction and death.[2–8]

The incidence and burden of ABX-AEs may be overlooked, at least in part due to the lack of feedback about the occurrence of ABX-AEs to prescribers, aside from specific events such as *C. difficile* infection.[9] Under-recognition of ABX-AEs is problematic because it may bias provider decision-making toward the perceived benefit of antibiotic therapy over the risk of ABX-AEs. Increasing awareness of the occurrence of ABX-AEs through a

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feedback mechanism may not only improve antibiotic prescribing practices by changing perceptions of the risks of antibiotic therapy, but also increase early recognition of ABX-AEs and decrease the severity of ABX-AEs. To develop an effective method of feedback, a deeper understanding of how ABX-AEs factor into clinical decision-making and how clinicians prefer to receive feedback regarding ABX-AEs is needed.

The objectives of this study were (1) to understand the role of ABX-AEs in decision-making when prescribing antibiotics, (2) to identify which ABX-AEs are of greatest clinical concern to clinicians, and (3) to understand clinician preferences for receiving feedback about ABX-AEs.

Methods

Study design, sample, and recruitment

Virtual focus groups of approximately 1-hour duration were conducted from May 2022 to December 2022 with medical and surgical clinicians (i.e., house staff physicians, attending physicians, and advanced practice providers [APPs]) who had prescribing privileges at Johns Hopkins Hospital (JHH), a 1,091-bed academic medical center.

Recruitment e-mails were disseminated by departmental and divisional administrators at JHH. Potential participants indicated their availability by contacting the study coordinator (T.N.H.) or via the online tool "YouCanBookMe," and focus groups were scheduled based on availabilities of the potential participants.[10] Initially, participants received $25 Amazon gift cards as compensation, but due to low recruitment, participants in the final focus group session received $50 Amazon gift cards.

Data collection

Three main topics were covered during each focus group session using a focus group guide to direct data collection (Supplemental Appendix A). Participants were asked to discuss their clinical experiences with ABX-AEs and the role ABX-AEs play in their decision-making when prescribing antibiotics and their opinions regarding the utility of feedback regarding ABX-AEs and preferences for how feedback should be delivered. Participants were shown a list of ABX-AEs, which were categorized into prespecified groups based on degree of clinical concern (i.e., "mildly concerning," "moderately concerning," or "very concerning") (Supplemental Appendix B). They were asked to vote on their preferred categorization of each ABX-AE and discuss their reasoning, as well as to suggest additional ABX-AEs that they believed were of clinical importance. Categories were prespecified by the research team to facilitate consideration of ABX-AE categorizations within the allotted time. Points of interest noted during a focus group session that were not specified in the focus group guide were explored further in subsequent focus groups.

Focus groups were moderated by J.P.C., an infectious diseases physician with experience in antibiotic stewardship, with input from S.M.G., an experienced qualitative researcher. Focus group discussions were audio-recorded with permission from all participants and transcribed verbatim by a professional transcription service with identifiers removed.

This study was approved by the Johns Hopkins University School of Medicine Institutional Review Board. Oral consent was obtained from each participant at the start of each focus group session.

Data analysis

Transcripts were analyzed using NVivo 12.0 (QSR International, Burlington, MA). Transcripts were coded inductively in an iterative manner during the period in which focus groups were conducted. Coding of the initial transcript was used to develop a codebook, which was refined with coding of subsequent transcripts. The coding scheme was reviewed with the entire research team after each transcript was coded. All transcripts were coded by two independent reviewers (J.P.C. and T.N.H.), and discrepancies in coding were resolved by consensus. Codes were used to conduct thematic analysis.

Results

A total of 4 focus groups, lasting between 45 and 75 minutes, were conducted with 3 to 5 participants per session. Among the 15 total participants, the majority were female (93.3%), White (46.7%), Asian (40.0%), and non-Hispanic (73.3%) (Table 1). There was a relatively equal amount of house staff physicians, attending physicians, and APPs who participated. Providers from 7 different specialties participated with the most common specialty being general internal medicine (40.0%).

Themes

We identified 6 major themes related to the role ABX-AEs play in clinical decision-making, clinical concern for ABX-AEs, or preferences regarding feedback.

The risk of ABX-AEs during initial prescribing influences the antibiotic prescribed rather than the decision of whether to prescribe

The risk of ABX-AEs was reported as an important component of clinical decision-making when initially prescribing antibiotics. However, the risk of ABX-AEs often does not influence the decision to prescribe an antibiotic or not, but rather influences the choice of a specific agent. In many situations, the clinical indication is felt to trump the risk of possible ABX-AEs, particularly if the patient's clinical status appears to be deteriorating, even if there is no definitive evidence of an infection. As one house staff physician noted, "I'm thinking less of potential adverse events associated with antibiotics and more . . . if they need 48 hours of broad spectrum until we sort of settle things out and have a better idea about what is causing their underlying pathology."

Instead, as one APP described, clinicians tend to " . . . think more in the question of not [whether] to prescribe but what to prescribe" when considering the risk of ABX-AEs. As another APP described, " . . . we've got a wide range of choices [in antibiotics] that we try to whittle down to one that has the least [side] effects." The specific side effect profiles of the antibiotics are carefully considered in conjunction with the patient's clinical history to select an agent that is believed to confer the least risk to the patient. For example, one attending physician noted, " . . . I do check for a history of *C. diff* just to kind of sway my decision for an antibiotic or another."

The occurrence of an ABX-AE leads to reassessment of the clinical indication for antibiotic therapy

Once an ABX-AE has occurred, clinicians repeat the risk-benefit analysis to decide how the antibiotic regimen should be managed. At the crux of the repeat analysis is reevaluation of the indication for therapy. As one APP noted, " . . . you weigh the severity of the

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Table 1. Demographics of focus group participants

Characteristic	Total Participants ($N = 15$)
Female – No. (%)	14 (93.3)
Race – No. (%)	
White	7 (46.7)
Asian	6 (40.0)
Black	1 (6.7)
Other	1 (6.7)
Ethnicity – No. (%)	
Non-Hispanic	11 (73.3)
Unknown	4 (26.7)
Clinical Role – No. (%)	
House Staff Physician*	6 (40.0)
Advanced Practice Provider	5 (33.3)
Attending Physician	4 (26.7)
Clinical Specialty – No. (%)	
General Internal Medicine	6 (40.0)
Cardiology	2 (13.3)
Pulmonary/Critical Care	2 (13.3)
General Surgery	1 (6.7)
Surgical Critical Care	1 (6.7)
Neurology	1 (6.7)
Pediatrics	1 (6.7)

*House staff physicians included senior residents and fellows; no interns participated in this study.

infection, like how much they really need that [specific] antibiotic and then what other antibiotic options there are. Sometimes . . . that's the only option and you just have to kind of push through . . . "

However, there is greater scrutiny of the indication for therapy during this repeat risk-benefit analysis, and clinicians may choose to stop antibiotic therapy completely if the indication is questionable. As another APP described, "we would . . . potentially stop the antibiotic and evaluate . . . , it depends on how strong the indication is . . . " This situation is illustrated in a hypothetical case shared by an attending physician: " . . . for a COPD exacerbation . . . perhaps I'm more concerned with this being driven by an inflammatory process . . . I would certainly just discontinue [antibiotics]."

The impact of an ABX-AE on other management decisions is as important as the direct harm of the ABX-AE

Clinicians use various indicators that capture the degree of direct harm from the ABX-AE to determine their level of concern about an ABX-AE. For some AEs, different thresholds of laboratory values may be an indicator of severity and change the degree of clinical concern. For example, an APP noted how the degree of thrombocytopenia changes their level of concern: "less than 75,000 [platelets] I would say mild but if it's less than . . . 25,000 I would say moderate." The development of clinical symptoms also raises clinical concern, as described by a house staff physician discussing hepatotoxicity: "I think liver failure is very concerning, and then maybe moderately concerning would be encephalopathy and bleeding, and then mild is just a bump in LFTs [liver function tests]."

Additionally, an ABX-AE can significantly impact other management decisions, which was equally important as direct harm in determining the degree of clinical concern. For instance, a cardiac APP noted, " . . . [hepatoxicity is] very concerning because you have to start holding some medications . . . You can't give a statin. You can't give your amiodarone. These are drugs you depend on." A surgical critical care APP provided another example: "If they're thrombocytopenic, then we have to not give prophylactic subcutaneous heparin that can cause . . . sequelae . . . [such as] DVTs [deep vein thrombosis]." The potential for additional harms cascading downstream from the initial ABX-AE further heightens clinicians' concerns about the ABX-AE.

ABX-AEs may be overlooked because of limited feedback regarding the occurrence of ABX-AEs

Participants reported that currently there is little to no feedback regarding the occurrence of ABX-AEs, aside from cases of *C. difficile* infection. Although some clinicians reported receiving occasional feedback from their team pharmacist, the lack of a formal feedback method has resulted in instances where clinicians were not aware of the consequences of their prescribing decisions until well after the event occurred. One house staff physician recalled, "We had a patient who developed DRESS [drug reaction with eosinophilia and systemic symptoms] . . . and they presented it on noon conference and I was like, 'oh, my God, this is the patient that I had seen,' but I would have not known that she had developed DRESS from the medication if I wasn't informed [at the conference]." The difficulty in clinicians seeing the consequences of their prescribing decisions is at least partly driven by rotation of clinicians on teams. " . . . For people who rotate on different services, we don't have a lot of continuity with patients, so we don't see what happens when we leave," remarked another house staff physician.

Clinicians are receptive to feedback regarding ABX-AEs but are concerned about it being punitive

Clinicians were generally open to receiving feedback about ABX-AEs and believed that it would provide educational value and help with their future clinical decision-making, as well as increase vigilance for ABX-AEs. One house staff physician described how feedback may help them realize " . . . here was a warning sign of something to monitor for or a symptom that was representative of something that may have happened . . . " However, others noted that there may be limitations to the effectiveness of feedback, such as a house staff physician who remarked, "if it [an ABX-AE] occurred while pursuing standard of care, [it would] not necessarily [be] something that would change my practice . . . "

Since some ABX-AEs will occur even in the context of appropriate antimicrobial therapy in patients without any clear risk factors for the AE, clinicians did raise concerns that feedback could be used punitively despite adhering to best practices. Concerns about benchmarking against peers were also raised. As one attending physician warned, "it can start to become a benchmark or metric that a provider needs to meet, and I think that has to be taken into [account] really carefully, lest it becomes something . . . punitive rather than educational." Participants noted that contextualizing ABX-AEs (e.g., comparing ICU providers to ICU providers), focusing on feedback of preventable ABX-AEs (e.g., ABX-AE due to non-clinically indicated antibiotics), and having ABX-AEs manually verified prior to feedback

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being delivered would help maximize educational value while limiting perceptions of feedback being punitive.

Feedback must be curated to prevent clinicians from being overwhelmed with data

Clinicians were also concerned about being inundated with data regarding ABX-AEs, which may limit the effectiveness of feedback, since, as one house staff physician pointed out, "It might become too much data and I would weed it [all feedback] out." Clinicians were particularly concerned about the reporting of "mildly concerning" ABX-AEs since they are more common and often don't result in severe consequences. As another house staff physician noted, " . . . it's hard to imagine getting a bunch of e-mails about like diarrhea and not having a trade-off there with . . . alarm fatigue." Furthermore, clinicians expressed a preference to receive information only about AEs that were likely attributable to the antibiotic, since there are many cases such as when " . . . you have an ICU patient who's coming in with multi-system organ failure, and there's going to be a lot of things on that list that might cause whatever adverse event we saw down the line." Clinicians additionally requested that feedback be delivered in a manner that was non-interruptive and less frequent to limit the amount of data being received. However, despite the concerns about being overwhelmed with data, clinicians did express interest in having patient-level data to review, since it would help " . . . put things in context more easily, since . . . I would . . . remember that patient, remember that case," as one attending physician noted.

Categorization of ABX-AEs based on degree of clinical concern

Participants generally agreed with the prespecified categorizations of ABX-AEs based on degree of clinical concern, although there was some variability in the categorization of ABX-AEs prespecified as being moderately concerning (Fig. 1). The ABX-AEs that were deemed most concerning were drug rash with eosinophilia and systemic symptoms syndrome, anaphylaxis, Steven-Johnson syndrome, neuropathy, severe *C. difficile* infection, and nephrotoxicity requiring dialysis. Participants noted difficulty in categorizing some of the ABX-AEs that were prespecified as "moderately concerning" since these ABX-AEs may vary greatly in the degree of severity (e.g., liver enzyme elevation just above the upper limit of normal vs liver enzyme elevation five times the upper limit of normal vs acute liver failure).

Additionally, participants suggested several other ABX-AEs that they believed were clinically significant and for which they thought feedback would be valuable. Suggested ABX-AEs included ototoxicity, serotonin syndrome, drug fever, tendinopathy, aortic aneurysm/dissection, thrush/vulvovaginal candidiasis, and electrolyte abnormalities, as well as antimicrobial resistance.

Discussion

In this study, we gained insight into the role ABX-AEs play in clinical decision-making when prescribing antibiotics, the ABX-AEs that are of greatest concern to clinicians, and clinician preferences regarding feedback. These findings may help inform the development and implementation of an effective method for ABX-AE feedback, which is needed given the frequency and consequences of ABX-AEs.

Our findings indicate that despite ABX-AEs commonly occurring in clinical practice, clinicians may under-recognize incident ABX-AEs that occur due to their prescribing decisions.[2–4] A major factor contributing to this issue cited by clinicians was the lack of continuity of care with patients in the inpatient setting due to rotating providers on clinical teams, compounded by the lack of feedback regarding these events. Although some clinicians reported receiving occasional feedback about ABX-AEs, typically from pharmacy colleagues, the feedback is unstructured and is unlikely to capture many of the ABX-AEs that occur.

A structured feedback mechanism regarding the occurrence of ABX-AEs would likely increase awareness of the occurrence of ABX-AEs since clinicians generally appeared receptive to such feedback.[9] As noted by several participants, this increased awareness may meaningfully change a clinician's future prescribing patterns and increase their vigilance for the occurrence of ABX-AEs. Thus, this form of feedback would potentially provide antibiotic stewardship programs (ASPs) with an additional tool to encourage the rationale use of antibiotics and improve antibiotic safety, paralleling the effects of *C. difficile* feedback interventions on decreasing inappropriate antibiotic use and incident *C. difficile* infections.[11,12] However, to ensure clinician engagement, it will be necessary to address concerns regarding being inundated with data and data being used in a punitive manner when developing and implementing a feedback mechanism.

Although increased recognition of the occurrence of ABX-AEs may shift the initial risk-benefit analysis when prescribing closer to the null rather than biased toward the benefits, it is necessary to also be cognizant of potential unintended consequences. Given perceptions that the indication for antibiotic therapy invariably trumps the risk of ABX-AEs when initially prescribing, rather than discouraging the use of antibiotics, increased awareness may simply lead to a shift in the specific agents that are prescribed based on specific AEs that have recently occurred. Antibiotic stewardship programs will need to navigate this issue as they strive to balance core stewardship principles with increased concerns regarding ABX-AEs, while also being mindful of how various specialties may prioritize different ABX-AEs in their decision-making.[13] Additionally, increased transparency regarding the occurrence of ABX-AEs may have medicolegal implications, although this specific concern was not voiced by participants.[14]

While ABX-AE feedback is a promising tool that ASPs may use to improve prescribing patterns and improve antibiotic safety, additional work is needed to translate it into clinical practice. Most importantly, identification of ABX-AEs currently relies on manual chart review, and further studies are needed to develop and validate approaches to identifying ABX-AEs in a systematic and reproducible manner, such as through electronic surveillance, to ensure accurate capture of the burden of ABX-AEs.[13] Additionally, further qualitative work is required in different contexts to assess if there are differences in provider perceptions and preferences that may impact the effectiveness of such an intervention. Finally, a feedback tool will need to be developed and piloted to assess clinician engagement with the intervention, as well as the impact on clinical outcomes.

Although this study offers important insight into a topic that has not previously been well explored using robust qualitative methods, the study has limitations. As with any qualitative study, our results are not meant to be generalizable but rather provide insights that could not be obtained through a quantitative study. Although clinicians from a variety of specialties and clinical roles participated in the study, the participants' views may not reflect those of other clinicians in our institution since we had a relatively small sample size of voluntary participants with most being female and white or Asian; however, despite the sample size, thematic saturation was reached. Additionally, pharmacists were

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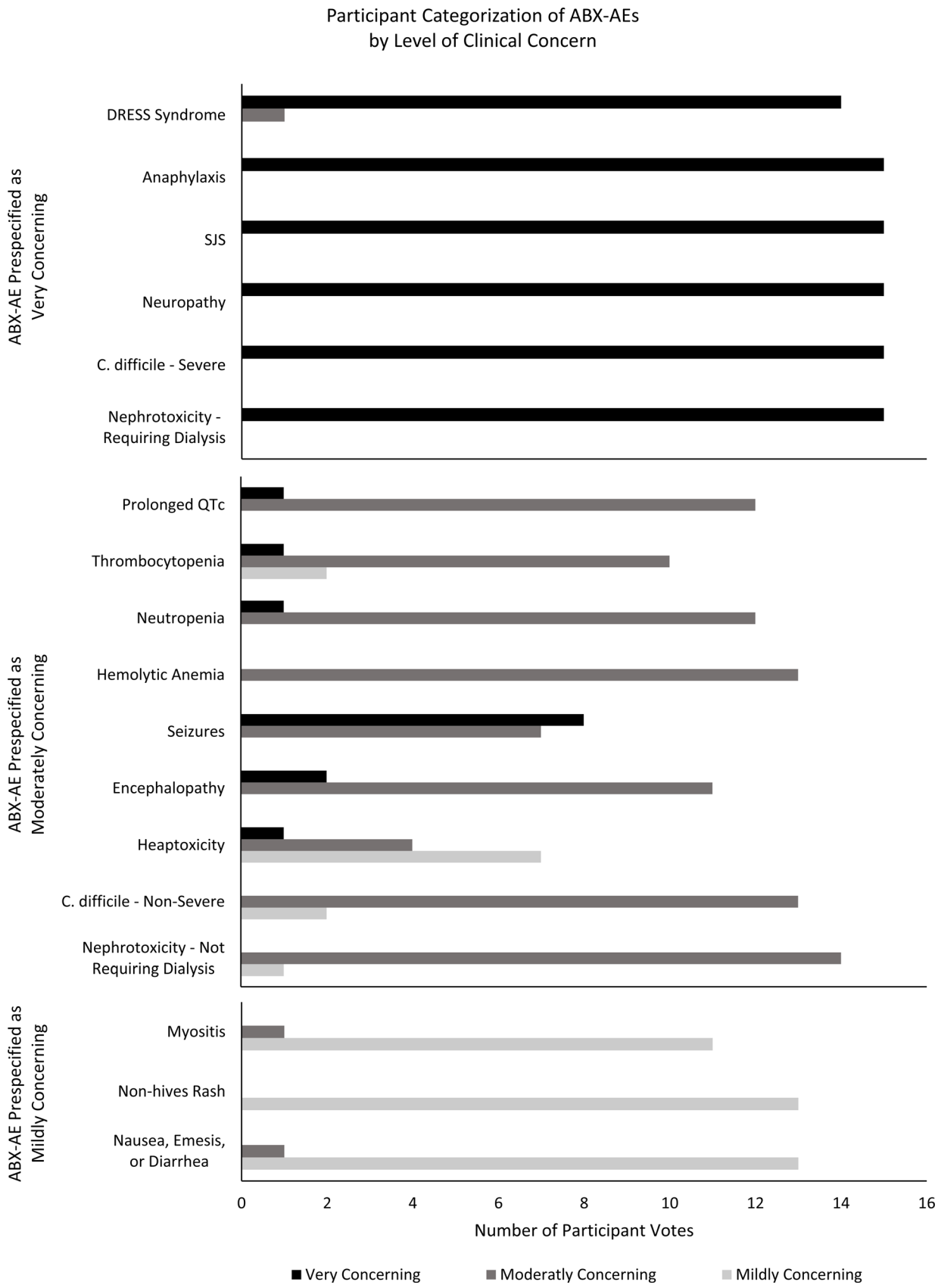

Figure 1. Participant categorization of Antibiotic-Associated Adverse Events (ABX-AEs) by level of clinical concern. Abbreviations: DRESS = Drug Reaction with Eosinophilia and Systemic Symptoms; SJS = Steven-Johnsons Syndrome; C. difficile = *Clostridium* difficile; QTc = Corrected QT interval.

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not included in this study as they are not the intended target audience for feedback about ABX-AEs (i.e., prescribers), but they may have additional insights into the clinical decision-making process when antibiotics are prescribed. Further, there may be some bias in participant responses due to factors such as pre-categorization of ABX-AEs based on degree of clinical concern, as well as social desirability bias given the nature of focus groups. Finally, specific criteria were not proposed for each of the prespecified ABX-AEs, which likely contributed to heterogeneity in assessments by clinicians for ABX-AEs prespecified as "moderately concerning."

In conclusion, this study provides a deeper understanding of the role of ABX-AEs in clinical decision-making when prescribing antibiotics, the ABX-AEs of greatest clinical concern, and clinician feedback preferences. These insights may help in the development and implementation of ABX-AE feedback methods to improve prescribing practices and enhance patient safety.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ash.2024.2

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Competing interests. All authors report no conflicts of interest relevant to this article.

References

1. Magill SS, Edwards JR, Beldavs ZG, *et al.* Prevalence of antimicrobial use in US Acute Care Hospitals, May–September 2011. *JAMA* 2014;312:1438. doi: 10.1001/jama.2014.12923
2. Tamma PD, Avdic E, Li DX, Dzintars K, Cosgrove SE. Association of adverse events with antibiotic use in hospitalized patients. *JAMA Intern Med* 2017;177:1308. doi: 10.1001/jamainternmed.2017.1938
3. Same RG, Hsu AJ, Cosgrove SE, *et al.* Antibiotic-associated adverse events in hospitalized children. *J Pediatr Infect Dis Soc* 2021;10:622–628. doi: 10.1093/jpids/piaa173
4. Hagiya H, Kokado R, Ueda A, *et al.* Association of adverse drug events with broad-spectrum antibiotic use in hospitalized patients: a single-center study. *Intern Med* 2019;58:2621–2625. doi: 10.2169/internalmedicine.2603-18
5. Shehab N, Patel PR, Srinivasan A, Budnitz DS. Emergency department visits for antibiotic-associated adverse events. *Clin Infect Dis* 2008;47:735–743. doi: 10.1086/591126
6. Lin RY, Nuruzzaman F, Shah SN. Incidence and impact of adverse effects to antibiotics in hospitalized adults with pneumonia. *J Hosp Med* 2009;4. doi: 10.1002/jhm.414
7. Macy E, Contreras R. Adverse reactions associated with oral and parenteral use of cephalosporins: a retrospective population-based analysis. *J Allergy Clin Immunol* 2015;135:745–752.e5. doi: 10.1016/j.jaci.2014.07.062
8. Lovegrove MC, Geller AI, Fleming-Dutra KE, Shehab N, Sapiano MRP, Budnitz DS. US emergency department visits for adverse drug events from antibiotics in children, 2011–2015. *J Pediatr Infect Dis Soc* 2019;8:384–391. doi: 10.1093/jpids/piy066
9. Bauer KA, Kullar R, Gilchrist M, File TM. Antibiotics and adverse events: the role of antimicrobial stewardship programs in 'doing no harm'. *Curr Opin Infect Dis* 2019;32:553–558. doi: 10.1097/QCO.0000000000000604
10. Free Online Scheduling Tool – YouCanBookMe. Accessed August 16, 2023. https://youcanbook.me
11. Benoist H, De La Blanchardière A, Flatres A, Isnard C, Thibon P, Saint-Lorant G. Effect of a prospective audit with intervention and feedback on Clostridioides difficile infection management. *Int J Clin Pharm* 2020;42:923–930. doi: 10.1007/s11096-020-01050-z
12. Baur D, Gladstone BP, Burkert F, *et al.* Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:990–1001. doi: 10.1016/S1473-3099(17)30325-0
13. Barreto EF, Mueller BA, Kane-Gill SL, Rule AD, Steckelberg JM. β-Lactams: the competing priorities of nephrotoxicity, neurotoxicity, and Stewardship. *Ann Pharmacother* 2018;52:1167–1168. doi: 10.1177/1060028018783984
14. Sohn D. Negligence, genuine error, and litigation. IJGM. Published online February 2013:49. doi: 10.2147/IJGM.S24256