Deprescribing medications that may increase the risk of hepatic encephalopathy: A qualitative study of patients with cirrhosis and their doctors

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Abstract

Background and aims: Multiple medications are associated with an increased risk of incident hepatic encephalopathy. Despite this known risk, medications such as opioids, benzodiazepines, gabapentin/pregabalin, and/or proton pump inhibitors are increasingly prescribed to persons with cirrhosis. Deprescribing is a promising intervention to reduce the burden of hepatic encephalopathy. Given that deprescribing has not been trialed in cirrhosis, we evaluated the barriers and facilitators to safe and successful deprescribing in cirrhosis.

Methods: We conducted, transcribed, and analyzed semi-structured interviews using qualitative methodology with 22 subjects. This included eight patients with cirrhosis and recent use of opiates, benzodiazepines, gabapentin/ Lyrica, and/or proton pump inhibitors as well as 14 providers (primary care, transplant surgery, transplant hepatology). Interviews explored opinions, behaviors, and understanding surrounding the risks and benefits of deprescribing.

Results: Major provider-specific barriers included deferred responsibility of the deprescribing process, knowledge gaps regarding the risk of hepatic encephalopathy associated with medications (e.g. proton pump inhibitors) as well as the safe method of deprescription (i.e. benzodiazepines), and time constraints. Patient-specific barriers included knowledge gaps regarding the cirrhosis-specific risks of their medications and anxiety about the recurrence of symptoms after medication discontinuation. Patients uniformly reported trust in their provider's opinions on risks and wished for more comprehensive education during or after visits. Providers uniformly reported support for deprescription resources including pharmacist or nurse outreach.

Conclusion: Given knowledge of medication risks related to hepatic encephalopathy in patients with cirrhosis, deprescribing is universally seen as important. Knowledge gaps, inaction, and uncertainty regarding feasible alternatives prevent meaningful implementation of deprescription. Trials of protocolized pharmacy-based deprescribing outreach and patient-facing education on risks are warranted.

Keywords

Hepatic encephalopathy, medication deprescribing, benzodiazepines, opiates

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Key Summary

Summarize the established knowledge on this subject

1. Hepatic encephalopathy (HE) is a morbid complication of cirrhosis.
2. The risk of HE may be increased by psychoactive medications and proton pump inhibitors.
3. Deprescribing is felt to be a promising approach to HE prevention.

What are the significant and/or new findings of this study?

1. Patients are unaware of how their medications influence the risk of HE.
2. Patients are willing to follow physician recommendations regarding deprescribing but are afraid of worsening symptoms.
3. Physicians do not feel comfortable deprescribing opioids or benzodiazepines.
4. Physicians do not feel responsible or equipped with the resources for deprescribing.

Introduction

Hepatic encephalopathy (HE) is a common and devastating complication of cirrhosis. HE occurs in up to 40% of patients with cirrhosis, diminishes health-related quality of life (HRQOL)[1 3] and increases both hospitalizations[4] and mortality.[4 6] Several classes of commonly prescribed medications influence the risk of HE episodes.[7 9] These include benzodiazepines, gamma-aminobutyric acid (GABA)-ergics, opioids, and proton-pump inhibitors (PPIs).[7 9]

While patients with cirrhosis often have genuine indications for these medications, there are two problems. First, the risk-benefit of such medications changes for those with or at high-risk for HE. Second, there has been a recent and marked increase in prescriptions for medications linked to HE such as benzodiazepines, GABA-ergics, and PPIs.[9] From 2008-2014, we found that, among US Medicare enrollees with cirrhosis, the share of person-years with prescriptions for benzodiazepines, gabapentin, opioids, and PPIs rose by 242%, 210%, 124%, and 33%, respectively.[9] Safely deprescribing such medications is part of effective HE management.[10]

Deprescribing is the deliberate process of discontinuing medications by the healthcare team with the intention of reducing risk or improving health outcomes.[11] In the general population, the vast majority of patients believe their medications are necessary but would stop if instructed. Deprescription for patients with cirrhosis, however, is hampered by a lack of data. Patient and provider attitudes/knowledge of its risks and benefits are unknown. The infrastructure for implementing safe deprescribing, particularly for benzodiazepines where there is a risk of severe withdrawal, is similarly lacking. Herein, we performed a qualitative study to characterize both prescriber and patient opinions and knowledge regarding the use and adverse effects of medications that influence the risk of HE in patients with cirrhosis.

Methods

Subject recruitment

We conducted a prospective qualitative study that aimed to recruit patients and providers for recorded semi-structured interviews between June-September 2019. First, we screened all appointments at the University of Michigan hepatology clinics for patients who had a history of decompensated cirrhosis and had an active prescription for benzodiazepines, gabapentin/ pregabalin, opioids, or PPIs. Second, we used a stratified purposeful sampling approach to recruit clinicians including hepatologists, liver transplant surgeons, hospitalists, and primary care providers, non-randomly selecting participants thought to be representative of the intended patient or provider population. All interviews were conducted in-person or by phone, recorded, and transcribed verbatim by a transcription service. Written, informed consent was obtained from each patient in this study. This study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. This study was approved by the University of Michigan Ethical Review Board on 5/2/2019 (HUM00161296).

Interviews

A semi-structured interview guide was developed with the purpose of assessing the barriers, facilitators, and methods to overcoming challenges to deprescribing (Supplementary Material). The interview guide was developed by the study team according to the theoretical domains framework[9] and workshopped with experts in qualitative methodology. Patients and providers were asked open-ended interview questions by a single interviewer. The interviewer also documented detailed notes during all interviews, to be used in the event of poor audio quality.

During the interview, we sought to better understand patients' and providers' understanding of the risks, consequences, and prevention of HE, knowledge of the medications being explored, and experience with these medications. Patients were asked to recall any personal experiences involving these medications as well as discuss any provider education given regarding their uses. Similarly, we asked providers to describe their practice for prescribing these medications as well as the education that they provide to their patients during prescription. Both patients and providers were asked to provide feedback on barriers, facilitators, and potential methods to deprescribing.

Qualitative analytic approach

All interviews were recorded, transcribed verbatim, deidentified and analyzed systematically[12 15] using an inductive approach that replicates well-established qualitative methodology.[12 15] When analyzing the transcripts, our research team employed a three-step group coding process that was informed by experts in qualitative analysis. The three steps were: (a) developing the codebook, (b) coding (open and axial), and (c) determining themes and relationships. The codebook was developed by conducting a thorough review of transcripts to identify recurrent concepts and generate preliminary codes.[12 15] The codebook was continuously refined and expanded in an iterative process to reflect emerging themes throughout the data collection and analysis phases.[10] The coding team developed open codes using six interviews separately on the NVivo software platform.[16] Axial coding categories (see Tables 1 and 2) were developed and we completed an inter-rater reliability exercise designed to ensure the consistent interpretation of each code. Once optimal agreement was achieved (kappa coefficient >0.60), the remainder of the coding was completed by a single coder. Once recurring themes and relationships were identified and characterized using

exemplary quotes, a conceptual model displaying our theory of the primary barriers was developed (Figure 1).

Results

We interviewed a total of 22 individuals. We contacted 19 providers, five declined (four primary care doctors, one hepatologist), and interviewed seven hepatologists (median experience 4 years, range 2-30), two transplant surgeons (12 and 13 years of experience), and five primary care physicians (median 5 years experience, range 3-15). We contacted 15 patients, two declined, and transcribed eight interviews. The patients were 50% female, average 52 ± 16 years old, and one (12.5%) had a college degree. The etiology of liver disease was alcohol-related in four (50%) patients and nonalcoholic fatty liver disease in two (25%) patients. The mean model for end-stage liver disease sodium (MELD-Na) was 13±4 and 75% had prior episodes of overt HE. The proportion of patients receiving prescriptions for gabapentin/pregabalin, opioids, PPIs, or benzodiazepines were 37.5%, 100%, 87.5%, and 62.5%, respectively. Of the eight patients interviewed, eight (100%), five (62.5%), eight (100%), and seven (87.5%) patients reported that they did not recall prior counseling on the risks (as they relate to HE) of gabapentin/pregabalin, opioids, PPIs, and benzodiazepine, respectively. Four (50%) patients had prior experience with deprescribing that was either self-initiated or initiated by their provider.

Overarching patient-reported themes

In Table 1 we characterize the major themes that emerged from transcripts of patient interviews. In general, patients report following doctors' orders and adhering to all prescribed medications. One of the main drivers of this behavior was the belief that their prescribers adequately weighed the risks and benefits on an on-going basis, “I let him be in charge. I trust him in what he's doing and saying.” Patients reported dismay when doctors disagreed about the risk/benefits of medications and did not communicate to resolve conflicts. However, if the hepatologist suggested significant risks of decompensation from one of their medications, patients would be willing to discontinue, for example saying “I'd stop 'em all in a heartbeat,” or “But if somebody told me that, 'Hey, that gabapentin is not making your liver-doing it any favors,' okay, let's get rid of it.” Most patients interviewed did not understand why they were prescribed PPIs.

> I really didn't need to be on that... It seemed like they just had a protocol that they followed. Then they just prescribed those drugs no matter what.
>
> I was prescribed on that from basically day one of my diagnosis to prevent varices or acid reflux that could cause varices, I guess.

Table 1. Themes from patients.

Code	Theme	Exemplar quote(s)
Behavioral regulation	Patients uniformly follow doctors' orders	“But being on a transplant list, I do realize that those rights teeter. There's a fine line.”
		“Oh. I would listen to the doctor. I would do whatever they said because I was fighting for my life. I knew I had to do exactly what the

		doctor told me, or else I wouldn't get a liver. I would do anything the doctor told me to do."
		"The physician's is the final word."
Perceived competence	Patients assume doctors know the benefits/risk	"I let him be in charge. I trust him in what he's doing and saying with the doctors and whatnot."
	Patients believe that only their hepatologists are capable of managing their medications in the context of their liver disease	"Well, yeah, my family doctor, he knows basics, but he doesn't know what's going on with my liver basically."
		"My family doctor, he can deal with the small stuff. I trust him with colds, flu. I'm sure when he prescribed the gabapentin, he had no idea that it would affect my liver."
Material resources	Patients rely on external sources such as the Internet to educate them about their medications	"No, it's just more of a plug it— I put it into Google and see what comes up, and then pick and choose from there."
		"Well, they're always in such a hurry, and I don't always think to ask the questions until I leave. Then I just Google'em instead."
	Using the EMR to contact the care team for medication education	"That's pretty invaluable cuz I can just fire offa question and then continue about my day. Then a couple days later or even.. .just a matter of hours... they'll get back to me about any questions I have."
Deprescribing		
Barriers	Fractured care and	"You ask one doctor this, she says that, you ask another
	communication	doctor this, they say somethin' else"
	Fear symptoms will return or worsen	"Yeah. I was afraid that my anxiety would come back if I stopped klonopin."
		"I'm afraid if there is some kind of regenerative benefit, as
		well as just maintaining, that if I get off the drugs, then I'll

		lose that benefit, if there is one.”
	Belief that there are limited	“It's one of the only ones that's safe enough for my liver-
	alternatives for pain that are	. . . it's proven to be a fact... my numbers have not gone
	safe in cirrhosis	up.”
Facilitators	Patients are willing to deprescribe if their provider recommends it	“I would probably be willing to give it a shot, after we talked
		about it. Give it a shot and see what happens.”
		“Right. But if somebody told me that, “Hey, that gabapentin
		is not making your liver- doing it any favors,” okay, let's
		get rid of it.”
Methods	Patients are willing to take	“Actually, yes, because I see more of them than I do the
	recommendations regarding	doctor. A pharmacy knows what their drugs are all about.
	deprescribing from allied	That's their business. The nurse, yeah, I would trust the
	health professionals other	nurse as well.”
	than their physician	“If they're a health professional. A nurse, they have a lot of
		experience with these drugs, so I definitely value their
		opinion.”
Opioids		
Risks	Patients understand addiction	“You may become addicted to it.”
	as the main risk of long-term opiate use	“Well, just because I did know that they're addictive.”
Risk benefit ratio	Patients feel that the benefits	“If they were to take that pill away at bedtime, I would be
	of opiates outweigh the risks	devastated because I would be in real bad pain.”
Benzo-diazepines		
Risks	Patients understand the risk of addiction	“I know it has potential to be addicting.”

Table 1. Continued.

Code	Theme	Exemplar quote(s)
Risk benefit ratio *PPIs*	Patients feel that the benefits of benzos outweigh the risks	“It was like a miracle drug at that time. It eased the

		withdrawal symptoms that I was having almost completely. I know it has potential to be addicting, but I never was addicted to it. I never had any problems with it." "I thought besides that [addictive potential], I thought they were pretty safe. I couldn't think of any other health issues that might arise from them."
Risk benefit ratio *Gabapentin/pregabalin* Risk benefit ratio	Patients lack an understanding of the benefits of PPIs and express willingness to deprescribe Patients have varying levels of understanding of the risks of gabapentin and pregabalin	"I really didn't see the need for it since I don't think I had acid reflux and I didn't have any varices." "By taking these pills, I can't feel what they're doing for me." "I saw something on TV about gabapentin. It uses are increasing, and it has a potential to be abused." "It was okay for the pain, but it depressed me a little bit. I read up on it, and that was one of the side effects."

PPI: proton-pump inhibitor.

Patients felt there was insufficient time during their clinic visits to discuss medication concerns saying, for example, "they're always in such a hurry, and I don't always think to ask the questions until I leave." Often they feel the need to research medications online, "I just Google 'em instead." Many patients feel empowered by electronic health records enabling after-visit messaging, "That's pretty invaluable cuz I can just fire off a question and then continue about my day. Then a couple days later... they'll get back to me." Patients report that they would welcome any trusted member of their healthcare team to proactively approach them to initiate deprescribing, "A [pharmacist] knows what their drugs are all about... The nurse, yeah, I would trust the nurse as well." However, patients with cirrhosis would prefer that this was initiated by their hepatologist's office, "My family doctor, he knows basics, but he doesn't know what's going on with my liver." Patients felt they would do as instructed by their hepatologist, "If I'm uncompliant, it takes me off the [transplant] list."

Patients are unaware of the potential risk of HE associated with psychoactive medications and PPIs, "I thought besides that [addictive potential], I thought they were pretty safe. I couldn't think of any other health issues that might arise from them." Patient understanding of risk appears to be couched in terms of laboratory patterns (e.g. model for end-stage liver disease (MELD) scores, liver enzymes), "I ask all the time, 'Well, is there something else I could take... that's not an opioid'... it's proven to be a fact... my numbers have not gone up."

Patients who see strong benefits from a medications are hesitant regarding deprescribing.

My anxiety was in the morning... I liked it [benzodiazepine]... It was like a miracle drug.

If they were to take that pill away at bedtime, I would be devastated because I would be in real bad pain.

Overarching physician-reported themes

In Table 2 we characterize the major codes and themes that emerged from transcripts of physician interviews. We found that patients with cirrhosis are co-managed by multiple clinicians, none of whom feel comfortable deprescribing. One hepatologist mentioned "I generally defer that to primary care physician (PCP)," while another acknowledged "decompensated cirrhosis is often so complicated and scary to many other doctors who don't deal with it a lot that you do wind up being their primary-care physician." Ownership is also deferred due to the perceived difficulty of the deprescribing conversation regarding medications with addictive potential, "Patients that have tried them are absolutely convinced they're the only things that work, period." Providers think it may be easier to deprescribe PPIs, "For benzos and narcotics, I think there will probably be more patient-attitude barriers or patients desiring to stay on these medications than for PPIs."

Providers are less comfortable deprescribing for fear of unintended consequences, "I didn't know that you

Table 2. Quotes from providers about barriers, facilitators, and methods of deprescribing.

Iode	Theme	Exemplar quote
Organizational culture and climate	Providers require training and knowledge about how to appropriately deprescribe	"Even some providers I've seen that have mental- health backgrounds will tell people it's okay to stop benzos, and it's not. Just that knowledge piece of it, that's a big barrier."
	The established clinic workflow causes providers to overlook medications on patients' medication lists	"I think in some respects, there's a clinic-efficiency thing that we've done that I think, also, takes it out of my brain. Our medical assistants are the ones that review the medications with the patient, right?"
		"I don't know if there's anyone focusing on that to follow up of when you should follow up with a patient and say, "Hey, it's been four months since you tried. Maybe we should stop or titrate down the PPI."
		"I think we overlook it. I know I overlook it all the time. When I don't overlook it is when there's a symptom, right? When a symptom comes up like they're more confused or they feel sleepier, then you start really looking at their med list, and

		you're like, 'Oh, okay. This is what's going on. You're really on some meds that you need to be dose reducing'."
Describing		
Barriers	Time is a significant barriers to deprescribing	"We don't have enough time to sit there and go in and talk to the patient about the reason why we're not prescribing opioids or why I'm trying to get them off of opioids, and that's what it comes down to, I think."
	Fractured care makes effective deprescribing challenging	"No, I usually send my discharge summaries to their specialists... but I don't reach out to them directly."
		"I forward the discharge summary, which has medication changes and things like that to their hepatologist. Whether the hepatologist reads all that because they're so busy, I don't know."
	Patients are hesitant to deprescribe because they fear that their symptoms will return or worsen	"They're having pain. They're having symptoms that it helps them with. I think they're having real symptoms, and they need something."
		"They have psychiatric angst. I think a lot of these patients rely on these medications for at least some relief."
	Limited alternatives to pain medication(s) are a large barrier	"Pain is probably the most difficult thing to treat because we don't have great options and you're tryin' to do what's best for the patient;
		what's the lowest risk to the patient."
		"Also, you have to have an alternative for the patient. You can't just deprescribe and expect the patient to be fine."
	Tools for preventing medication overuse exist are burdensome	"I think some of the tools people are using try to minimize overuse, are more just plain creating burdens that don't add very much."
	Inadequate reimbursement for nonpharmacological alternatives	"We pay for the pill. We pay for the surgery. We pay for the

	deprioritizes deprescribing	procedure. We don't pay nearly as well for behavioral management. That's almost a policy-level issue.”

Code	Theme	Exemplar quote
Facilitators	Clinic and discharge follow-up procedures car ried out by pharmacists could be used to facilitate deprescribing	“It could also be a note to the PCP for the two- week follow up after discharge about why they have it. If it's for a GI bleed, how long it's indicated, and should they follow up with them for stopping it”
		“Having the pharmacist able to do that right away afterward or the nursing right away after they get out to make sure that they know what they're doing with their medication... I think it is really helpful.”
	Providers' rapport with their patients effects the success of deprescribing	“It depends on the rapport I have with a patient
		If I've a good rapport with them, I think that they would listen.”
		“I think a lot of patients are actually very open to coming off of these drugs if we as their trustee physicians tell them it's okay”
Provider role	Primary care providers feel that they are expected to be the main node for medication management, but do not feel comfortable managing medications of patients with cirrhosis	“I'm like, 'Well, I don't know why you're on this.'
		don't feel comfortable saying, 'You should stop this if you did have a high-risk ulcer bleed, and
		I just don't know about it,' and that type of thing.”
		“I think all of it tends to fall on the primary care physician for looking at the whole picture and stopping medications.”
	Hepatologists feel that they take on the role of PCP for advanced liver disease patients, as other providers do not feel comfortable managing patients' medication in the context of advanced liver disease	“Patients will ask me to refill things that I didn't prescribe, and I won't because I didn't precribe that.”

		"Cirrhosis, particularly decompensated cirrhosis is often so complicated and scary to many other doctors who don't deal with it a lot that you do wind up being their primary-care physician."

PPI: proton-pump inhibitor.

shouldn't pull people off benzos until I talked to our psychiatrist." Additionally, providers have concerns about how to address symptoms that may return after medication discontinuation, "Pain is probably the most difficult thing to treat because we don't have great options." Providers do not believe effective alternative therapeutics exist, "Lotta patients can't take NSAIDs [non-steroidal anti-inflammatory drugs] because for cirrhotics, bleeding risks, and kidney function... so the option is taking a narcotic ... or give them gabapentin."

Physicians are generally aware of the risk of HE associated with medications. If an adverse event was attributed to a medication, providers feel comfortable stopping it. In contrast, pre-emptive deprescribing is felt to be a low priority.

> I know I overlook it all the time. When I don't overlook it is when there's a symptom, right? When a symptom comes up like they're more confused or they feel sleepier, then you start really looking at their med list.

Providers unanimously support the introduction of more healthcare resources to facilitate deprescribing. They do not believe that electronic decision supports will be helpful, "You click past those." In contrast, providers welcome assistance from pharmacists and nurses for deprescribing.

Discussion

HE is a debilitating complication of cirrhosis with serious implications on hospitalizations, mortality, and quality of life.[3] It is known that episodes of HE are linked to opioids, benzodiazepines, gabapentin/ pregabalin, and PPIs,[13,14] all of which are commonly, and increasingly, prescribed.[15,16] Deprescribing interventions can safely reduce polypharmacy for atrisk populations.[17] None, however, have been trialed in patients with cirrhosis. Additional data was needed to inform the needs of both patients and providers. We conducted the first qualitative assessment of provider and patient-level barriers and facilitators to deprescribing potentially harmful medications in cirrhosis. As summarized in Figure 1, we found that the barriers to deprescribing started with the delegation of responsibility and were further exacerbated by knowledge gaps and time constraints. In general, providers endorsed a reactive approach to medication risk management - removing a medication known to trigger HE in a given patient - rather than a proactive approach - stopping a medication with the potential to trigger HE. In Figure 2, we summarize some potentially successful deprescribing interventions that were identified to address these barriers.

Who owns medication risk management?

One of the most important barriers to deprescribing is determining the responsible party. Although some patients preferred the deprescribing process be led by their hepatologist, most welcomed involvement of all care-team members, including nurses and pharmacists. Consistent with prior studies, most felt the initial prescriber should manage or discontinue the medications in question.[18] In contrast, both patients and providers deferred deprescribing discussions in cirrhosis care to hepatologists owing to the complexity of cirrhosis.

However, hepatologists and transplant surgeons felt ill-equipped for this responsibility. Conversations are often avoided due to perceived time constraints, fears of upsetting the patient, opinions that other topics are of higher priority, and discomfort around discussing sensitive or stigmatized medications.[19] The latter is further exacerbated in cirrhosis due to the high rates of comorbid substance abuse and psychiatric disorders. Our results, however, show that both patients and physicians value open communication in regard to medication safety and use. Time remains a major barrier. For these reasons, deprescribing efforts require either actively assuming responsibility for medication management (as in the case of a recent pharmacist-led trial)[17] or a behavioral intervention to encourage and support responsibility amongst hepatologists.

Knowledge gaps

Physicians are unsure how to safely discontinue medications and they fear unintended consequences. Sudden discontinuation of opiates can lead to unpleasant symptoms. An inappropriate tapering of benzodiazepines can be fatal. Patient knowledge gaps compound this problem. Patients remain unaware of the increased risk of incident HE that our queried medications carry. Patients report being informed by commercials and websites. However, these sources do not speak to the cirrhosis-specific risks. Furthermore, websites may contain incomplete or inaccurate information. Multiple methods are available to address the knowledge gaps preventing deprescribing. Targeted education will raise awareness of risks.[20] Shared decision-making aids may facilitate a tough discussion by adding structure to the discussion while clarifying risks. Even simply offering to discontinue a medication is sufficient. Three- quarters of residents of a nursing facility taking benzodiazepines agreed to attempt medication discontinuation when simply presented with this option by their provider.[21] By addressing the needs for both education and dedicated time, pharmacist-led initiatives may be the most promising.[17,22]

Figure 1. Conceptual model of barriers to deprescribing from patient and provider perspectives.

The diversity and overlap of the themes derived from patient and provider perspectives on deprescribing.

Figure 2. Conceptual model of solutions to overcome barriers to deprescribing.
Effective deprescribing initiatives must be responsive to the human factors and systemic barriers present in current clinical practice. This figure summarizes the solutions identified from a qualitative study of patients with cirrhosis and their providers.

Limited alternatives

Compounding the problem of knowledge barriers are patient and provider concerns about a recurrence of symptoms after describing, as well as uncertainty about the availability and efficacy of alternative interventions. This extends to the use of non- pharmacological interventions, such as mindfulness, support groups, and physical therapy, which have shown benefits in decreasing anxiety, reducing sleep disturbances, and alleviating chronic pain.[23] Patient engagement in the deprescribing process is diminished when there is limited information provided about the process of deprescribing and how recurrent symptoms will be managed. However, willingness to attempt deprescribing can be improved when patients have confidence in the tapering regimen, knowledge of the available alternatives, and reassurance that resumption of the original medication can be considered should alternatives

fail.[21] Patients reported both a willingness to follow recommendations and hesitancy regarding worsening of symptoms. To assuage patient concerns, deprescription must be paired with a deliberate alternative approach to symptom control.

Contextual factors

Our data must be interpreted within the context of the study design. First, our single-center study may limit generalizability. Second, deprescribing patterns and behaviors were reported by physicians themselves and may have introduced attribution bias. It is plausible that other explanatory reasons for deprescribing behaviors were withheld due to concerns of how they would be perceived. Similarly, while most patients endorsed significant willingness to discuss the deprescribing of high-risk medications, this may not reflect their actual behaviors during real-time clinic discussions. Third, many risky medications may predate the diagnosis of cirrhosis. While PPIs are generally prescribed because *of* cirrhosis (even if inappropriately), opioids or benzodiazepines are not. Cirrhotic complications make long-standing medications riskier, but duration of use is a dimension that may have implicitly influenced discussions.

Conclusion

Despite mounting evidence of the increased risk of HE with the use of opioids, benzodiazepines, gabapentin/ pregabalin, and PPIs, these medications remain commonly found on medication lists. Patients and providers mutually view deprescribing as an important clinical goal, but the process is hindered by deferred prescriber responsibility, uncertainty about the deprescribing process, and time constraints. Deprescribing interventions must account for these concerns.

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Declaration of conflicting interests

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Ethics approval

This study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. This study was approved by the University of Michigan Ethical Review Board on 5/2/2019 (HUM00161296).

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Informed consent

Written, informed consent was obtained from each patient in this study.

Supplemental material

Supplemental material for this article is available online.

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Table 1. Continued.

Code	Theme	Exemplar quote(s)
	Patients feel that the benefits of benzos outweigh the risks	"It was like a miracle drug at that time. It eased the withdrawal symptoms that I was having almost completely. I know it has potential to be addicting, but I never was addicted to it. I never had any problems with it." "I thought besides that [addictive potential], I thought they were pretty safe. I couldn't think of any other health issues that might arise from them."
PPIs		
Risk benefit ratio	Patients lack an understanding of the benefits of PPIs and express willingness to deprescribe	"I really didn't see the need for it since I don't think I had acid reflux and I didn't have any varices." "By taking these pills, I can't feel what they're doing for me."
Gabapentin/pregabalin		
Risk benefit ratio	Patients have varying levels of understanding of the risks of gabapentin and pregabalin	"I saw something on TV about gabapentin. It uses are increasing, and it has a potential to be abused." "It was okay for the pain, but it depressed me a little bit. I read up on it, and that was one of the side effects."

PPI: proton-pump inhibitor.

Table 2. Continued.

Code	Theme	Exemplar quote
	Clinic and discharge follow-up procedures carried out by pharmacists could be used to facilitate deprescribing	"It could also be a note to the PCP for the two-week follow up after discharge about why they have it. If it's for a GI bleed, how long it's indicated, and should they follow up with them for stopping it"
		"Having the pharmacist able to do that right away afterward or the nursing right away after they get out to make sure that they know what they're doing with their medication. . . I think it is really helpful."
	Providers' rapport with their patients effects the success of deprescribing	"It depends on the rapport I have with a patient. If I've a good rapport with them, I think that they would listen."
		"I think a lot of patients are actually very open to coming off of these drugs if we as their trusted physicians tell them it's okay"
Provider role	Primary care providers feel that they are expected to be the main node for medication management, but do not feel comfortable managing medications of patients with cirrhosis	"I'm like, 'Well, I don't know why you're on this.' I don't feel comfortable saying, 'You should stop this if you did have a high-risk ulcer bleed, and I just don't know about it,' and that type of thing."
		"I think all of it tends to fall on the primary care physician for looking at the whole picture and stopping medications."
	Hepatologists feel that they take on the role of PCP for advanced liver disease patients, as other providers do not feel comfortable managing patients' medication in the context of advanced liver disease	"Patients will ask me to refill things that I didn't prescribe, and I won't because I didn't prescribe that."
		"Cirrhosis, particularly decompensated cirrhosis is often so complicated and scary to many other doctors who don't deal with it a lot that you do wind up being their primary-care physician."

PPI: proton-pump inhibitor.