Clinical Decision Support for Fall Prevention: Defining End-User Needs

Hannah Rice[1] Pamela M. Garabedian[2] Kristen Shear[3] Ragnhildur I. Bjarnadottir[3] Zoe Burns[1] Nancy K. Latham[4] Denise Schentrup[3] Robert J. Lucero[3,5] Patricia C. Dykes[1,6]

[1] Department of General Internal Medicine and Primary Care, Brigham & Women's Hospital, Boston, Massachusetts, United States
[2] Department of Information Systems, Mass General Brigham, Boston, Massachusetts, United States
[3] Department of Family, Community, and Health Systems Science, University of Florida College of Nursing, Gainesville, Florida, United States
[4] Research Program in Men's Health: Aging and Metabolism, Brigham & Women's Hospital, Boston, Massachusetts, United States
[5] School of Nursing, University of California, Los Angeles, Los Angeles, California, United States
[6] Harvard Medical School, Boston, Massachusetts, United States

Address for correspondence Patricia C. Dykes, PhD, RN, FAAN, FACMI, Brigham & Women's Hospital, Boston, MA 02115-6195, United States (e-mail: pdykes@bwh.harvard.edu).

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Abstract

Background and Significance Falls in community-dwelling older adults are common, and there is a lack of clinical decision support (CDS) to provide health care providers with effective, individualized fall prevention recommendations.

Objectives The goal of this research is to identify end-user (primary care staff and patients) needs through a human-centered design process for a tool that will generate CDS to protect older adults from falls and injuries.

Methods Primary care staff (primary care providers, care coordinator nurses, licensed practical nurses, and medical assistants) and community-dwelling patients aged 60 years or older associated with Brigham & Women's Hospital-affiliated primary care clinics and the University of Florida Health Archer Family Health Care primary care clinic were eligible to participate in this study. Through semi-structured and exploratory interviews with participants, our team identified end-user needs through content analysis.

Results User needs for primary care staff ($n = 24$) and patients ($n = 18$) were categorized under the following themes: workload burden; systematic communication; in-person assessment of patient condition; personal support networks; motivational tools; patient understanding of fall risk; individualized resources; and evidence-based safe exercises and expert guidance. While some of these themes are specific to either primary care staff or patients, several address needs expressed by both groups of end-users.

Conclusion Our findings suggest that there are many care gaps in fall prevention management in primary care and that personalized, actionable, and evidence-based CDS has the potential to address some of these gaps.

Keywords
- clinical decision support
- primary care
- human-centered design
- user needs
- falls

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Background and Significance

While most falls are preventable,[1] they present a serious threat of injury and death. Falls are the second leading cause of unintentional injury deaths worldwide, and adults over the age of 60 experience the greatest number of fatal falls. Researchers have demonstrated that engaging patients in the fall prevention process can be effective in reducing falls and injuries in hospital settings.[2,3] Our research team is developing clinical decision support (CDS) to address fall prevention management in urban and rural primary care settings.

CDS is a tool that makes evidence-based knowledge available to health care providers at the point of care.[4] CDS can add value in primary care but providers often resist its implementation due to potential limitations.[5] Health care providers override between 60 and 70% of CDS alerts.[6,7] This repeated, unproductive interaction with CDS contributes to alert fatigue and decreases support for CDS implementation.[8,9] While some electronic CDS has been designed for inpatient settings,[10,11] there is a significant gap in the literature on the development of fall prevention CDS for use in outpatient settings.

Objectives

By utilizing a human-centered design (HCD) approach, our team aims to address the limitations of CDS and enhance usability.[12,13] Because input is gathered from participants during every stage of development, HCD prevents design errors and future usability issues.[14] Design principles include workflow integration, provision of recommendations rather than commands, and presentation of recommendations in a way that cultivates trust with users.[15] Embracing a HCD process will aid researchers in designing interventions that meet the users' unique needs, and therefore enhance adoption.[16] We aimed to involve users in early stages of the development of CDS to support fall prevention management in diverse primary care settings. Our goal is to design an electronic CDS tool to identify patients' individual fall risk factors; provide tailored, actionable recommendations for providers; and help facilitate shared decision-making around fall-prevention planning. This article describes the end-user needs identified through this process.

Methods

Study Design

This was a qualitative user research study based on principles of HCD. As defined by ISO 9241–110, a main principle of HCD is that "design is based upon an explicit understanding of users, tasks, and environments."[17] In accordance with this principle, our team designed this study to further understand user needs with the ultimate goal of identifying specific user requirements for our CDS tool. The principles of HCD define user requirements as the features and functions that the user requires to accomplish their goals.[18] Previous studies have demonstrated the importance of analyzing user needs while designing CDS and other electronic tools.[19,20]

Study Setting and Context

Primary care team staff (primary care providers, care coordinator nurses, licensed practical nurses, and medical assistants) and adults aged 60 or older associated with Brigham & Women's Hospital (BWH)-affiliated primary care clinics and University of Florida Health Archer Family Health Care (UF) clinic were eligible to participate in this study. Primary care staff participants at both sites received an emailed or physical copy of a recruitment letter that described the purpose of the study and participation details. Primary care staff referred their patients 60 years of age and older, interested in participating in the study, to the study team. A research team member contacted these patients by email or in-person and provided them with the patient-facing recruitment letter. Due to coronavirus disease 2019 (COVID-19) restrictions, recruitment largely took place virtually. All participants consented to participate in the study and received reimbursement in the form of a gift card.

Data Collection

Based on the literature and previous experience, our team of registered nurses, physical therapists, and usability experts designed a guide for semi-structured and exploratory interviews with primary care staff and patients. Since both primary care staff and patients will engage with the CDS tool and its supported recommendations, our team interviewed both groups of end-users to better understand their goals and needs. The semi-structured interview guide for primary care staff included questions to elicit perspectives on what staff need for effective fall prevention and the development and use of personalized fall prevention plans, and current state practices for addressing preidentified fall injury risk factors (see ►Supplementary Appendix A [available in the online version]). Our goal was to gain a detailed understanding of current-state fall prevention practices in clinics so that we may identify the gaps and needs in those processes and address them in our CDS design. Based on a review of the literature and previous experience, clinical members of the project team identified three fall injury risk factors (mobility limitations, fall risk increasing drugs, and osteoporosis) to be addressed in the CDS tool.[21] Team members examined each risk factor individually to determine which were identifiable through data extracted from the electronic health record (EHR), with the goal of creating an electronic tool that could automatically identify individual fall risk factors and provide personalized recommendations (i.e., discuss starting bisphosphonates medication for patients with osteoporosis). Our team designed the semi-structured interview questions to help us understand what direct users, or staff who engage with the decision support, would require from the tool when addressing these risk factors. The semi-structured interview guide for patient participants comprised questions to elicit insights from their personal experiences with falls and fall prevention (see ►Supplementary Appendix B [available in the online version]). Our team designed these questions to help us understand what indirect users, or the recipients

of recommendations supported by the CDS, would require from the tool.

Our team designed the exploratory interview guide for primary care staff to facilitate a virtual workflow observation where the provider would demonstrate the activities, steps, and thought processes involved in fall risk assessment and prevention planning using their EHR during a patient encounter (see ►Supplementary Appendix C [available in the online version]).

Recruitment continued until we reached thematic saturation. Staff participants completed a demographic form that included years of experience and self-report of how well they currently engage in fall prevention. Older adult participants completed a similar form that included questions about fall history and fear of falling. Participant completion of the full demographic form was optional.

At BWH, a user experience expert (P.M.G.) conducted all interviews on virtual video calls. At the UF site, a registered nurse with user experience training (K.S.) collaborated with the site principal investigator (R.J.L.) (i.e., subject matter expert) to conduct in-person semi-structured interviews and virtual exploratory interviews. Additional research team members took notes while observing the interviews. At the conclusion of each interview, other research staff who were present had the opportunity to ask questions to clarify any statements or observations. The 30-minute semi-structured interviews were audio-recorded. The 45-minute to 1-hour exploratory interviews were video- and audio-recorded. The de-identified audio from each interview was transcribed. While the reliance on remote technologies to conduct this study produced some barriers to participant recruitment, it did allow patients to participate in interviews without needing to travel. Additionally, it allowed our team to review recorded interviews and make increasingly detailed notes and observations.

Data Analysis

Previous studies have shown content analysis to be an effective method for classifying and deriving meaning from qualitative data.[22–24] Our team conducted a content analysis to identify user needs for CDS to prevent falls among urban and rural community-dwelling older adults (►Fig. 1). At BWH, the first author independently reviewed transcripts to identify key ideas and develop a preliminary coding system for user needs. The first author and our team's user experience expert (P.M.G.) met regularly to iteratively review, modify, and validate the codes and emerging themes. Once they reached a consensus, the first author grouped and sorted common responses into major themes according to similarity. Throughout this process, the first author presented their findings to the broader research team at weekly meetings, where they reviewed, validated, and finalized the codes and their themes. This process also occurred at the UF site, and their team members validated and added supporting data to the end-user needs identified at their site.

Results

In total, we completed interviews with 24 primary care staff and 18 patients. We completed 20 semi-structured interviews with primary care staff, including 12 primary care providers, 3 care coordinator nurses, 2 licensed practical nurses, and 3 medical assistants across both sites (►Table 1). We completed 8 exploratory interviews with primary care staff, including 7 primary care providers and 1 nurse. 3 primary care providers and 1 nurse participated in both a semi-structured interview and an exploratory interview. We interviewed a total of 18 patients 60 years and older from both sites combined (►Table 2). As a result of content analysis, our team categorized user needs for primary care staff and patients into 8 themes (►Table 3).

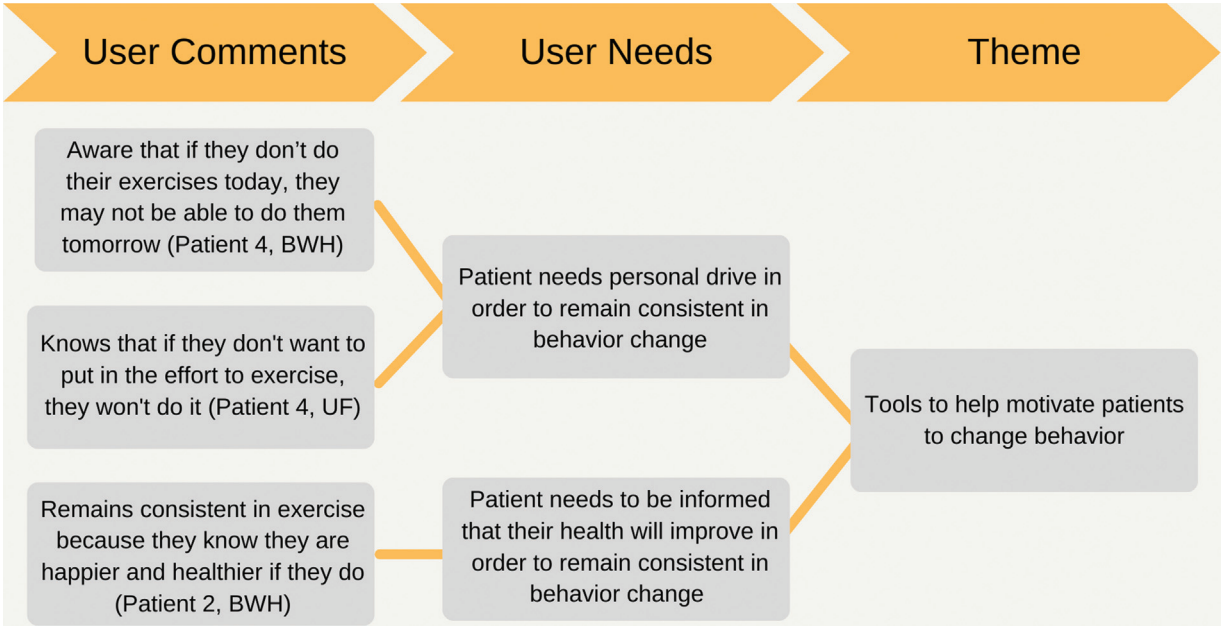


Fig. 1 Using content analysis to uncover user needs and generate themes.

Table 1 Primary care staff participant demographics

	Primary care staff participants
Gender	
Male	5 (20.8%)
Female	19 (79.2%)
Race	
American Indian/Alaska Native	
Asian	6 (25.0%)
Native Hawaiian or Pacific Islander	
Black or African American	2 (8.3%)
White	16 (66.7%)
More than one race	
Not reporting	
Provider type	
Nurse	5 (20.8%)
Nurse Practitioner	3 (12.5%)
Physician	9 (37.5%)
Physician's Assistant	3 (12.5%)
Medical Assistant	3 (12.5%)
Self-report: Compared with your peers, how do you rate yourself for helping patients prevent falling?	
Above average	4 (16.7%)
Average	17 (70.8%)
Below average	3 (12.5%)

Table 2 Patient participant demographics

	Patient participants
Gender	
Male	5 (27.8%)
Female	13 (72.2%)
Race	
American Indian/Alaska Native	
Asian	
Native Hawaiian or Pacific Islander	
Black or African American	4 (22.2%)
White	14 (77.8%)
More than one race	
Not reporting	
Age	
60–70	6 (33.3%)
70–80	7 (38.9%)
80+	5 (27.8%)
Self-report: Are you afraid of falling?	
Yes	6 (33.3%)
No	12 (66.7%)
Self-report: Have you fallen 2 or more times in the past year?	
Yes	4 (22.8%)
No	14 (77.8%)
Self-report: Were you injured from a fall in the past year?	
Yes	5 (27.8%)
No	13 (72.8%)

Table 3 User needs and sample quotes from participants

Theme	User type	Sample quote
No increase to workflow burden	Primary care staff	"Not that I shouldn't [address fall prevention], but the visit is only 35 minutes, there are probably 5 prescriptions that came up to be refilled, and 2 other questions. It gets buried among a lot of other stuff." – Provider 1, BWH
Systematic communication between staff, patients, and family	Primary care staff	"Most of [fall prevention] has been communication, talking with families, and getting other services involved to help with that." – iCMP Nurse 1, BWH
In-person assessment of patient condition and diagnoses	Primary care staff	"Usually, when [nurses] walk the patients in that's when they look [for signs]. Then I always document if they're using any kind of assistive device. If they're in a wheelchair, if they have a cane then I'll always put that in my notes." – Staff 5, UF
Patient support network to encourage adherence to fall prevention plans	Patient	"Well, right now, my partner, he is very involved in doing things and would definitely help me, as I would him for any type of exercises or things that are needed to do for improved balance." – Patient 3, UF
Tools to help patients change behavior	Patient	"I do exercise every day, but I know me, and I wouldn't do anything that takes longer than 15 minutes…I know that if I were supposed to do 20 minutes, I probably wouldn't do it." – Patient 6, BWH

Table 3 (*Continued*)

Theme	User type	Sample quote
Patient understanding of personal fall risk	Both	"I find it's very difficult, because in the population that I see, which is primarily older, people are very resistant to accepting that they have a risk for falls." – Provider 5, BWH "I'm probably a big denier when it comes to physical stuff because I think I'm pretty strong and very active. How could somebody really assess the truth for me…it's self-realization of [fall-risk] and how do you get someone to really realize that?" – Patient 3, BWH
Awareness of individualized fall prevention resources that fit patient characteristics and strategies	Both	"Like I said, keeping in mind that some seniors aren't able to because we're individuals, and everybody is individual—they may have similar ailments, but emotionally and mentally, we're all a little different." – Patient 1, BWH "Well, it depends on the patient. Mobility; there's quite a variety of what a patient will consider to be reasonable mobility for themselves. If patients aren't driving, or if they're having difficulty maneuvering just to their mailbox—so it's really gonna range, I guess. I don't know if I can give you a standardized answer, because it just is very patient-specific." – Staff 5, UF
Evidence-based, safe exercises and expert guidance to inspire trust and confidence in fall prevention recommendations	Both	"I really don't want [patients] trying to do [exercise prescriptions] on their own because I'm concerned they're going to hurt themselves." – PA 2, BWH "Because for that kind of advice, which I get from my physical therapist, I'm totally compliant. I do the exercises that I do religiously. I'm careful about walking, but I just follow her directions. I don't think the primary care doctor has the knowledge to do that or the time that I told you of." – Patient 7, BWH

User Needs for Primary Care Staff and Patients

Workload Burden

Workload burden in primary care is a well-documented challenge for staff.[25–27] Multiple primary care staff participants reported that fall prevention CDS should not add burden to their patient care workflows. Semi-structured and exploratory interviews revealed the typical workflow patterns at both primary care study sites (►Fig. 2). While most primary care staff agreed that fall prevention is an important topic to cover during an office visit, they are constrained by packed schedules and short patient visits. Staff also noted that it is helpful to share tasks with other care staff to reduce individual workload burden.

Systematic Communication

Because the target population of this study is adults aged 60 years or older, staff participants reported that many conversations around fall prevention are most productive when care partners are present. Staff participants noted that because fall prevention planning often involves behavioral or environmental changes, having family member support can improve adherence to prevention plans. When family members participate, it is easier to create fall prevention plans tailored to the patient's individual needs, barriers, and environmental conditions. Staff reported that systematic communication between staff and patient care partners would ensure that patients understand their fall prevention plans, remain well-monitored, and receive quality care.

In-Person Assessment of Patient Condition

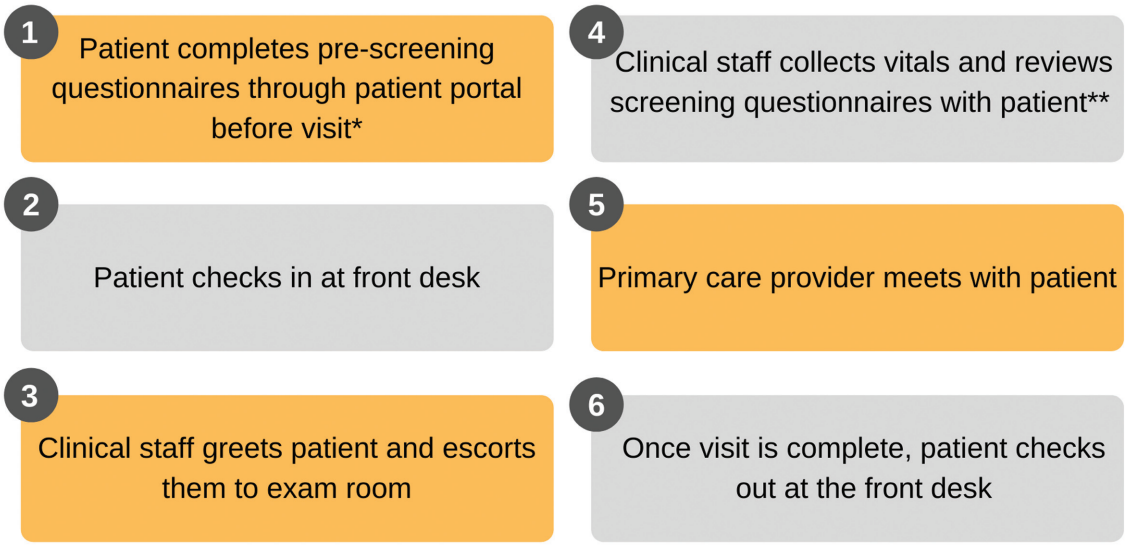
Staff noted that they observe a variety of signs to identify patients at risk for falls. For instance, providers watch patients walk to assess their gait and balance during a visit. If abnormal, this observation prompts a fall prevention discussion. During the COVID-19 pandemic, in-person visits became less common and therefore have made observation more difficult. Many staff members rely on this in-person observation to signal concern about falls. Without observing these signs, staff are unlikely to cover fall prevention or act on fall prevention CDS during a visit.

Personal Support Networks

Both primary care staff and patient participants agreed that patients need a support network to successfully adhere to fall prevention strategies. This could consist of family members, care partners, neighbors, peers, or others who are regularly present in the patient's life. Patient participants agreed that they could more easily maintain behavior changes, such as regular exercise, when others are there to encourage them or do the exercises together which would hold them accountable. A patient support network can also be crucial to initiating conversations about fall prevention with primary care staff. Staff noted that family members or care partners who are present at a visit, and have observed concerning signs or fall risk factors, often prompt fall prevention discussions themselves.

Motivational Tools

In addition to a personal support network, patients require sources of motivation to help them to adhere to fall



* Only available at urban sites. Not all patients choose to complete the pre-screening questionnaires through their patient portal.
** If a patient did not complete the pre-screening questionnaires before the visit, this is when the Medical Assistant would complete them with the patient.

Fig. 2 Fall prevention management workflow at BWH and UF study sites. BWH, Brigham & Women's Hospital; UF, University of Florida Health Archer Family Health Care.

prevention practices. While these forms of motivation varied across participants, several spoke of their independence as both an extrinsic and an intrinsic motivator. Some patients were intrinsically motivated knowing that fall prevention planning could allow them to remain physically strong and independent. Staff used independence as a motivator in fall prevention conversations with their patients. Patients acknowledged that external motivators, such as exercise prescriptions that are quick and easy to complete, were necessary to encourage engagement in fall prevention practices. Several noted that knowing that an exercise would be quick, less than 15 minutes, for example, would be enough to push them to integrate it into their routines.

Patient Understanding of Fall Risk

Another barrier to successful implementation of fall prevention plans was patients recognizing their own risk for falling. Staff need patients to acknowledge their own risk to have productive conversations about fall prevention. Staff found it difficult to encourage patients to acknowledge their symptoms or diagnoses as risk factors for falls. For example, if patients believe they are physically strong enough to be safe from falls, it is difficult for staff to help them understand otherwise.

Patient participants also acknowledged that they would first need to accept that they are at risk for falls before being willing to engage in a fall prevention discussion. Many patients reported the fear that admission of fall risk could threaten their independence. Others noted that because they feel healthy and strong for their age, they do not believe they are at risk. Several participants mentioned that even though they feel safe, they know that their fall risk will increase with age and hope to engage in preventive care so they can remain independent.

Individualized Fall Prevention Resources

Although staff participants generally agreed that it is important to address fall prevention, several felt ill-equipped to do so. Primary care staff reported a need for personalized resources to help them provide evidence-based fall prevention advice and design prevention plans that fit patient characteristics and preferences. Staff acknowledged that their approach to fall prevention is unique to each patient. Prevention discussions and plans are based on personal risk factors and barriers, thus requiring an individualized set of resources. For example, staff participants noted that they must consider a patient's age, activity levels, cognitive ability, environmental and social barriers, and other risk factors to provide recommendations that are likely to be well-suited to the individual patient.

Patient participants confirmed that personalized resources are necessary to address the variety of individual risk factors. Most patients were quick to note that their needs are different than those of their partners, neighbors, or friends, making it difficult to know what any one person would require to adhere to fall prevention recommendations. Several patients cited individual access to technology as a potential barrier to designing fall prevention plans. For example, if a patient is less likely to or unable to access resources electronically, they would need to be printed and shared with the patient during a visit to fit the patient's preference.

Evidence-Based Safe Exercises and Expert Guidance

While primary care staff participants expressed interest in recommending exercise to patients, several were concerned about sharing exercises that are not evidence-based or unsafe for frail patients or patients with poor balance.

Exercises to prevent falls often involve strength, gait, and balance training,[28] which primary care staff worried may be unsafe for patients to complete while unsupported or unsupervised. Participants agreed that knowing exercise prescriptions are evidence-based would alleviate these concerns.

In line with staff needs, older adult participants also expressed a desire for evidence-based exercise recommendations. When asked about their willingness to engage in regular exercises prescribed by their primary care provider, patients expressed a need for a trusted clinical expert to instruct them. Trust and an existing relationship were both reported as important factors to older adults' willingness to engage in fall prevention interventions. However, some patients reported skepticism in their primary care providers' knowledge of exercise and were more likely to adhere to recommendations from a physical therapist.

Discussion

Using a HCD process, our team defined end-user needs to inform the design of a CDS tool for fall prevention management in urban and rural primary care sites. The main findings gleaned from our interviews highlight that primary care staff and patient needs can be categorized into the following themes: workload burden; systematic communication; in-person assessment of patient condition; personal support networks; motivational tools; patient understanding of fall risk; individualized resources; and evidence-based safe exercises and expert guidance. There were no substantive differences between these findings at urban and rural settings.

Currently, there is a significant gap in the literature on defining end-users' goals and the requirements necessary for the successful use of fall prevention CDS in primary care. Our study contributes to the existing literature by identifying user needs for successful use and adherence to CDS recommendations. Interviews revealed that motivational tools that inspired behavior change were necessary to encourage patient adherence to fall prevention practices. While overcoming barriers to staff use of CDS is part of the solution, another is to ensure that patients follow through with their health care provider's recommendations. This demonstrates the importance of designing tools centered around both direct and indirect users. In this case, the primary care staff who engage with the decision support are the direct users, and the patients who are recipients of the supported recommendations are the indirect users. In the case of this study, we discovered that there is a significant overlap between user needs for primary care staff and patients, thus highlighting the importance of addressing the needs of both sets of end-users. These results will inform design decisions for a CDS tool considered useful by all users.

In addition, our study supports previous findings examining primary care staff perspectives and barriers toward implementing fall prevention practices. Several studies confirm that resolving patients' ambivalence about fall risk is a requirement for implementing fall prevention practices.[29,30] A systematic review completed by McConville and Hooven found that commonly reported barriers to fall risk management in primary care are a lack of available resources and coordination between staff members.[31] This finding validates our finding that standardized resources and systematic communication constitute user needs for fall prevention CDS. Following the implementation of the Centers for Disease Control and Prevention's STEADI tool, an electronic tool for fall prevention in primary care, Casey et al confirmed the importance of building interventions into pre-existing workflows.[32] Their team also emphasized that gathering user feedback at each stage of the development process allowed for important improvements in the tool, highlighting the importance of HCD principles.[32] End-users expressing a need for individualized fall prevention resources also confirms previous evidence demonstrating that individualized programs can prevent falls and related injuries.[1,33,34]

Since identifying these user needs, our team has designed a CDS tool to identify patients' individual fall risk factors; create tailored, actionable recommendations; and help facilitate a shared decision-making process between patients and providers. Throughout the design process, we met regularly with stakeholders to continue to gather feedback and ensure our design met practice and workflow needs. While we were not able to address all user needs due to constraints of EHR integration, several influenced the design of the CDS end-product. For example, we learned that our CDS tool needed to integrate into pre-existing workflows so as not to increase provider workload burden. In recognition of this need, our tool preselects risk factors detected in the patient's medical record and automatically generates tailored recommendations. To address both staff and patient needs, preidentifying risk factors also allows providers to facilitate a personalized conversation about fall risk and help patients understand what makes them at-risk. Identified risk factors are shared alongside talking points that providers can use to engage the patient in discussion and help them further understand their risk. In response to staff and patient needs for evidence-based safe exercises and expert guidance, we included resources throughout the tool that cite the evidence supporting exercise-based recommendations. Patient exercise handouts include a link to a video tutorial led by the research team member with physical therapy background who designed each exercise. We continued to follow a HDC process through the development cycle to test and iterate on these design decisions.

The results of this study are limited and may not apply in all primary care settings. We did not explore additional sociotechnical and contextual factors related to fall prevention management beyond what was reported by our participants, which may vary across urban and rural primary care settings. While testing at both BWH and UF sites did reveal user needs at urban and rural primary care clinics, their generalizability may vary outside of these sites. Although we acknowledge the limitations of interviewing majority female-identifying patients, we were able to reach acceptable saturation in our findings and believe that, despite the gender imbalance, our study population is representative of those most afflicted by falls.[35] Formal inter-observer reliability testing was not completed as a part of this study,

though the research team members responsible for conducting interviews at the UF site were present at all BWH interviews for the purpose of observing and reproducing similar methods with UF participants. The testing process for this study was also limited by the COVID-19 pandemic, which made it necessary to conduct interviews virtually.

Conclusion

Our study defines the primary care team and patient user needs for a CDS tool designed for fall prevention management in primary care. Our processes highlight the benefits of following HCD principles in understanding end-user goals while designing CDS tools. These needs informed the iterative design and formative usability testing of a prototype CDS tool that aligns with primary care staff and patient needs. Next steps include a sociotechnical analysis of how primary care staff and older adults are managing fall risk, integration of a live prototype, and summative testing and evaluation based on the RE-AIM framework.

Clinical Relevance Statement

There is a lack of CDS to support primary care providers in effective fall prevention management with their older patients. By following a HCD process, our research team identified end-user needs important to consider in striving for successful use and adherence to CDS recommendations. Our findings highlight the importance of identifying the needs of direct and indirect users and informed the design of a prototype CDS tool.

Multiple Choice Questions

1. Which of the following was a user need identified in this study?
   a. Virtual assessment of patient diagnoses and symptoms.
   b. Organizational support from local health centers.
   c. Access to mobility devices (i.e., cane or walker).
   d. Evidence-based, safe exercise recommendations.

   Correct Answer: The correct answer is option d. A user need identified in this study was "in-person assessment of patient condition" making answer choice a similar, but incorrect. While one could argue that organizational support from other local health centers could benefit primary care clinics, it is not a need specific to fall prevention or one identified in this study, making answer choice b incorrect. Mobility devices are proven to prevent falls but answer choice c was not a user need identified in this study. Many study participants, both primary care staff and patients, noted their need for evidence-based, safe exercise recommendations to trust and feel confident in fall prevention recommendations. This makes answer choice d correct.

2. Which of the following was a method used in this study?
   a. Focus groups.
   b. Blind interviews.
   c. Semi-structured interviews.
   d. Optional surveys.

   Correct Answer: The correct answer is option c. While answer choices a, b, and d are methods that can be used to collect qualitative data and user comments, answer choice c is one of the methods that was chosen for this study. The semi-structured interview guide for primary care staff included questions to elicit perspectives on what staff need for effective fall prevention and the development and use of personalized fall prevention plans, and current state practices for addressing preidentified fall injury risk factors. Our team designed these questions to help us understand what direct and indirect users would require from the tool.

Protection of Human and Animal Subjects

This study was approved by Partners HealthCare Humans Research Committee under protocol number 2020P002075. The committee granted implied consent by voluntary participation in the study.

Author Contributions

P.M.G., R.I.B., N.K.L., R.J.L., D.S., and P.C.D. were involved in the design of the study. H.R., P.M.G., and K.S. were involved in the coding of the data. All authors were involved in the analysis of the data. H.R. and P.M.G wrote the manuscript. All authors read and approved the final manuscript.

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Conflict of Interest

None declared.

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