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Research Report

Barriers to Using Legally Authorized Representatives in Clinical Research with Older Adults

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Abstract.
Background: Older adults are at increased risk of cognitive impairments including Alzheimer's disease dementia. Legally authorized representatives (LARs) can provide informed consent when a participant is no longer able to, but little is known about barriers to incorporating them in research.
Objective: Explore reasons for not asking and documenting participant decisions to appoint LARs among researchers conducting clinical intervention trials studying older adults or individuals with cognitive impairments.
Methods: Mixed method design consisting of a survey ($N = 1{,}284$) and qualitative interviews ($N = 40$) regarding barriers to incorporating LARs. Participants were principal investigators and clinical research coordinators.
Results: 37% ($N = 469$) had not asked and documented participant decisions about appointing LARs in the prior year. They had significantly lower confidence in resources available to incorporate LARs and lower positive attitudes compared to their counterparts who had done so. The majority (83%) had no trials studying individuals with cognitive impairments and reported LARs were not applicable. A minority (17%) had at least one trial studying individuals with cognitive impairments and reported being unaware of LARs. Qualitative findings indicate discomfort broaching a sensitive topic especially with individuals who are not yet impaired.
Conclusion: Resources and education to increase awareness and knowledge of LARs are needed. Researchers studying older adults should, at minimum, have the knowledge and resources to incorporate LARs when necessary. Stigma and discomfort discussing LARs will need to be overcome, as early proactive discussions before a participant loses decisional capacity could enhance participant autonomy and facilitate recruitment and retention of older adults to research.

Keywords: Clinical research, cognitive impairments, informed consent, legally authorized representatives, older adults, proxy, research ethics, surrogate

INTRODUCTION

Recruiting older adults into clinical research has become increasingly important in recent years. The NIH "Inclusion Across the Lifespan" policy was implemented in 2019 and mandates that older adults (i.e., individuals over age 65) are included in clin-

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ical research unless there is a scientific or ethical rationale for exclusion [1]. The policy is designed to address the widespread exclusion of two specific populations—older adults and children— from research, and the resulting lack of generalizability of research findings to these populations [2, 3].

The exclusion of older adults from research can be a result of strict eligibility criteria that prohibit participation by individuals with co-morbidities or polypharmacy, which are common in older adults [3, 4]. Another frequent reason older adults have been excluded from research is that they are at increased risk for cognitive impairments [5, 6]. The Centers for Disease Control defines a cognitive impairment as "when a person has trouble remembering, learning new things, concentrating, or making decisions that affect their everyday life" [7].

Older adults are at increased risk of cognitive impairments for multiple reasons. Diseases common with aging, such as diabetes and heart disease, medication side effects, delirium due to serious illness, or depression, are associated with an increased risk of cognitive impairments among older adults [8–11]. Alzheimer's disease (AD) dementia is another leading cause of cognitive impairments among older adults with approximately 6 million Americans living with AD dementia currently [8, 9]. Research on AD and related dementias (collectively referred to as ADRDs) is a national priority given the high burden of disease and lack of meaningful treatments [12]. ADRD research requires recruiting large numbers of older adults—both with ADRDs and those at increased risk of developing ADRDs—and a national effort is aimed at increasing recruitment and retention of older adults to ADRD research [12].

Enrolling individuals with cognitive impairments can create ethical and practical challenges for informed consent [13–20]. As a result, many studies default to excluding all individuals with cognitive impairments, or at increased risk of developing them, from taking part altogether [3]. Notably, individuals with cognitive impairments may still retain decisional capacity, that is the capacity to provide informed consent for a specific study, and cognitive impairments on their own do not necessarily mean an individual cannot provide consent for a specific study [3, 21].

When an individual lacks the capacity to provide informed consent, the Federal Regulations for the Protection of Human Subjects, or Common Rule, requires additional safeguards are in place [22]. Legally authorized representatives (LARs) are one such safeguard. The Common Rule defines an LAR as an individual "authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research" [22]. The role of an LAR is to provide or maintain informed consent throughout the course of a research study when a potential participant is unable—or no longer able—to consent. This latter qualification is essential to understanding the role of LARs: They may be appointed at the start of a study, but they have no decision-making authority unless the participant loses the ability to consent for themselves [23–26]. LARs may also be referred to as surrogates or proxies, but here we use the term LAR unless referring to specific studies or formal guidance that use other terms.

Principal investigators (PIs) and clinical research coordinators (CRCs) will need to be prepared for increased recruitment of older adults in order to meet the requirements of both the NIH Inclusion Across the Lifespan policy and the growing needs of ADRD specific research. We are conducting an implementation science trial (NIA R01AG058254) designed to increase the use of 3 evidence-informed consent practices among researchers working with older adults. Our larger project is focused on implementing the following three best practices: 1) using plain language and formatting consent documents to maximize readability and understanding, 2) using validated assessments of understanding and appreciation of informed consent, and 3) asking participants if they would like to appoint LARs and documenting their preference.

Our implementation science trial is guided by the Consolidated Framework for Implementation Research (CFIR), a framework for understanding barriers, facilitators, and attitudes toward implementing a particular evidence-informed practice [27]. In implementation science, barriers refer to factors that impede the process of implementing evidence-based interventions, and facilitators refer to factors that enable the process of implementing evidence-based interventions [28]. Attitudes are an individuals' favorable or unfavorable evaluation of an evidence-based intervention [29, 30]. Our study, and the CFIR framework, is premised on the notion that in order to increase use of evidence-informed practices we must first discover and address barriers to use, and provide tools and resources to overcome barriers and facilitate implementing best practices. The study will evaluate whether regularly sending a toolkit containing educational materials and practical resources designed to help researchers implement each of the

three evidence-informed consent practices increases adoption.

Our randomized implementation trial has recruited over 1,200 PIs and CRCs who work on interventional clinical trials studying older adults or individuals with cognitive impairments including those caused by AD dementia. Prior to randomizing participants to our toolkit intervention, we surveyed them to understand attitudes, current use, and the barriers reported to using these three practices. We have separately reported our survey findings regarding participants' current use of, and barriers to using the other two practices [31, 32]. In this paper we report our survey findings regarding LARs with a focus on understanding the barriers to discussing and documenting participant decisions for appointing LARs.

When and why to incorporate LARS

Appointing LARs involves pre-existing trusting and close relationships [33]. As such, most LARs are spouses, adult children, or close friends, who know the participant well [34–37]. Evidence indicates that the majority of older adults and adults with mild to moderate AD dementia support the idea of letting an LAR, especially if they are a family member or loved one, make research decisions on their behalf across a range of study risk levels [34, 35, 38–40].

Studies have also shown that even when individuals lose the capacity to consent to a complex research study, they often retain the ability to appoint an LAR because this is a simpler cognitive task than understanding a complex clinical trial [33]. While consenting to research involves learning new and unfamiliar information, as previously noted deciding who to appoint as an LAR often involves pre-existing trusted relationships [33]. This data supports asking participants about their decisions for who they would appoint as an LAR even if they are unable to consent to a particular study [13, 34, 39, 41–43]. This could potentially increase recruitment and retention of older adults who are often excluded [34], although there is no direct evidence that appointing LARs positively impacts recruitment and retention [34, 35, 38–40].

Importantly, LARs only make decisions on behalf of the participant if, and when, the participant has lost the capacity to consent. In such cases, the participant often still retains the ability to express their assent or dissent about participating in the research, even if they do not have decisional capacity [23–26, 44]. This can help the LAR make decisions that align with participant preferences.

For longitudinal research, the NIH recommends asking participants to appoint an LAR at the outset of the study even if participants are able to provide informed consent to ensure "a designated representative would be ready to step in" if the need arises [45]. Preparing for the possibility of needing an LAR among currently unimpaired individuals, and designating a person who would be the LAR should the need arise, could facilitate continued participation in longitudinal research even if an individual loses decisional capacity after enrolling. Of note, unless a study partner is appointed as an LAR, they lack the legal authority to provide ongoing consent for study participation. This may be especially pertinent for ADRD research which frequently relies on longitudinal studies of individuals who are at increased risk of developing ADRDs.

Proactively discussing and helping a participant designate or document their decisions regarding an LAR actually enhances participant autonomy by enabling participants to have a say in who makes research participation decisions on their behalf, so long as this occurs before individuals are too impaired to make this decision and their preferred LAR is willing and able to serve if needed [3]. Proactively documenting individual decisions should they become incapacitated in future is analogous to asking a participant to appoint a durable power of attorney or healthcare proxy for healthcare decisions should capacity diminish in future [46]. Importantly, when an unimpaired participant proactively designates an LAR for future needs, the LAR does not step in until the individual's capacity is actually diminished, similar to how proxies operate in healthcare settings. In contrast, once an individual is incapacitated and can no longer express a choice regarding their LAR, researchers may be forced to rely on State or IRB hierarchies of who can serve as the LAR, which may not be consistent with who the participant would have chosen (see below).

Challenges of incorporating LARs

At the same time, there are multiple challenges to enrolling participants who may require LARs. Very few U.S. states have laws that specifically address or provide criteria for who can be an LAR in research, leaving a vacuum in legal guidance [47]. The U.S. Office for Human Research Protections (OHRP) has provided guidance that anyone who can serve as a proxy or surrogate decision maker for healthcare decisions could serve as an LAR

for research participation decisions about the procedure(s) involved in research, absent local laws to the contrary [45]. Among the few states with statutes addressing appointing LARs for research, they provide a hierarchy of who can serve as an LAR if the participant is no longer capable of appointing someone. However, in the majority of states, there are no statutes specifically defining criteria for LARs and institutional IRBs are left to make determinations about who can be appointed as an LAR and in what contexts. As a result there is wide variability in guidance and policy by institution, leaving no national or coordinated guidance for researchers to rely upon [34]. A survey of 30 AD research sites found that many researchers (40%) were not familiar with, or had an inaccurate understanding of, their state laws [48]. Sites also had divergent practices about who could be a proxy in research settings, and researchers varied considerably in their understanding of who could provide informed consent on behalf of a participant in research [48].

A systematic review of empirical literature on the accuracy of LARs decisions reported that LARs make decisions that are inconsistent with the decisions the participant would have made if they had the capacity [49]. As a result researchers may be concerned about whether the LARs' decision represents what the participant would have wanted before impairment.

Another challenge of including individuals who may require LARs is the difficulty in determining when an individual truly lacks capacity to provide informed consent, which can wax and wane from day to day [16, 19, 43]. Thus, it may be challenging to decide when an LAR should assume responsibility for providing informed consent.

There is also tremendous stigma surrounding the loss of decision-making capacity associated with cognitive impairments, including AD dementia, and many individuals are fearful of losing their decision-making capacity, which is fundamental to autonomy [50–52]. As a result, researchers may be reticent to raise the topic of who the participant might want to appoint as an LAR given the sensitive nature of the subject. Participants may become embarrassed, angry, or frustrated by the implication that they need an LAR, or could need one in future, leaving researchers uncomfortable raising the issue altogether [53–58]. The stigma associated with losing decisional capacity combined with researcher variability in determining when an individual lacks capacity may contribute to discomfort with discussing participant decisions for appointing LARs altogether.

The current study

To better understand the barriers to involving LARs in clinical trials, in this paper we explore the reasons reported for not asking and documenting participant decisions to appoint LARs among our survey of $N = 1{,}284$ PIs and CRCs. As discussed, there are a number of challenges to incorporating LARs in research, but no large empirical studies explore barriers as a whole, and we seek to identify the barriers PIs and CRCs perceive and experience. Empirically identifying barriers is a crucial first step given the purpose of our overall implementation trial is to increase use of evidence informed practices, and there is no empirical literature regarding facilitators to appointing LARs in research. We also examine qualitative findings from interviews with 40 PIs and CRCs, which provide additional insight to the barriers encountered by researchers.

METHODS

We used a mixed method approach, gathering qualitative and quantitative data, to understand the barriers and facilitators to adopting evidence informed practices [59]. The research was approved by the Washington University in St. Louis IRB (#201807033 and #201909154). The study samples consisted of PIs and CRCs. We included PIs because they have overall responsibility for trial conduct and the ability to make changes to the consent process, even though they may not obtain informed consent. We included CRCs because they most often obtain informed consent from research participants and prepare IRB protocols.

Qualitative procedures

Qualitative interviews recruitment and procedure

We conducted telephone interviews with PIs and CRCs prior to administering the quantitative survey ($N = 40$). Qualitative interviews informed survey development and also provided a richer understanding of barriers [59]. Interview participants were purposively sampled to ensure we had representation from researchers conducting ADRD research; but all interviewees conducted clinical interventional research with older adults.

All groups were recruited via email and provided informed consent before completing an online demographic survey. Participants then completed a semi-structured telephone interview. Participants received a $40 Amazon eGift card. All interviews were audio recorded, and professionally transcribed.

Qualitative interview materials

Semi-structured interview guides were developed to follow the CFIR framework and explore barriers and facilitators to implementing the three consent practices being promoted in our trial. Our qualitative findings regarding the remaining two practices are reported elsewhere [31, 32]. Qualitative interviewees were provided with a definition of an LAR and their role before being asked about their attitudes and current practices. Our interview guide also included detailed instructions for interviewers to help in cases where participants were confused or described what they thought was an LAR but where they actually described a different role (like a caregiver or study partner).

Qualitative interview participants

Participants were PIs ($N = 20$) and CRCs ($N = 20$). Participants from each group were identified using publicly available information and snowball recruitment. PIs and CRCs were identified via ClinicalTrials.gov using advanced search criteria to ensure they all conducted interventional trials with older adults [60].

Qualitative interviews data analysis

Qualitative interview transcripts were uploaded to Dedoose, a qualitative data analysis software program. Data were coded using inductive and deductive coding, guided by the CFIR framework [61]. Two coders were assigned to each dataset. Coders obtained a Cohen's kappa score of 0.80 in the Dedoose Training Center before coding the data, and kappa was re-calculated half way through coding to ensure there was no drift. Our kappa remained at 0.80 so coding continued without further changes to the codebook. Coders met weekly to discuss and resolve any coding discrepancies.

Quantitative survey measures

Survey development

The survey was designed by PhD level experts in research ethics, clinical trials, and survey design. Cognitive interviews with 8 clinical research professionals were conducted to ensure item clarity.

Measures

The survey included items on current use, perceived barriers, attitudes, and confidence in resources needed to use LARs, as well as demographics. We asked respondents if they had asked "participants if they would like to appoint a legally authorized representative and document their decision." We provided participants with a definition of LARs before all the LAR survey items.

Reasons for not incorporating LARs

Only participants who reported not asking participants if they would like to appoint an LAR and documenting their decisions in the prior year were given a list of reasons regarding why they did not do this (e.g., "*I did not think this practice was important,*" "*I was unaware of this practice,*" "*I'm not sure how to do this,*" *etc.)*. Two of the answer options indicated that participants were being asked to appoint LARs and their decisions were being documented by someone else ("*the sponsor already required it*" and "*my research team, group, or lab already uses this practice*"). Individuals who endorsed either of these options were not included among the group categorized as not having asked participants if they would like to appoint an LAR and documenting their decision.

Barriers. All participants were asked if anyone might prevent them from implementing LARs in their research. Only participants who responded "yes" were presented with a list of options as to who might prevent them from implementing LARs (*i.e.,* "*IRB,*" "*sponsor,*" "*participants,*" "*research team members,*" and "*other*").

Positive attitudes

We measured attitudes by asking two questions: whether participants thought LARs were useful, and if they were interested in improving their use of LARs using a 5-point Likert scale. We created a positive attitude score by adding together the interestedness and usefulness responses.

Confidence in resources

Participants used a 5-point Likert scale to rate "*How confident are you that you have the resources you need to use these practices well?*".

Demographics

We collected data on participant's gender, age, race, education, and information about trials they worked on.

Quantitative survey recruitment and procedure

We used non-probability, criterion-based sampling to ensure we targeted CRCs and PIs conducting research with individuals with cognitive impairments or older adults because they are at higher risk for developing cognitive impairments. We targeted US researchers only since regulatory requirements vary by country. We used publicly available information from the clinicaltrials.gov database [60] to contact researchers working in the US on interventional clinical trials either focused on AD ($N = 527$) or involving participants age 65 or older ($N = 20{,}086$). These potential participants were emailed a link to our Qualtrics survey. We also recruited individuals through the Association of Clinical Research Professionals listserv and social media platforms, which included 9,774 clinical research professionals including CRCs and PIs working in the US.

Informed consent was obtained online prior to completing the survey. Participants were screened to verify they were a CRC or PI working in the US with at least one new clinical intervention trial that would open in the next 18 months to ensure they were eligible. Participants received a $20 Amazon eGift card for completing the survey.

Quantitative survey participants

After cleaning and removal of ineligible or incomplete responses, there were 1,284 participants in total.

Quantitative survey data analysis

We conducted data analysis using SPSS version 26 and Stata 16.

Qualitative interview findings

Demographic characteristics of the qualitative sample are reported in Table 1. Qualitative findings are reported in Table 2.

Statements of support and concern

The majority of PIs and CRCs expressed a combination of supportive statements (16/20 PIs, 16/20 CRCs) and concerns (15/20 PIs and 12/20 CRCs) about LARs. Participants indicated that LARs help respect individual autonomy, enable recruitment and retention of individuals, comfort, reassure and communicate with participants especially since LARs tend to know the participant well. Interviewees' statements about LARs providing comfort and reassurance suggest some confusion between the role of study partners, caregivers, and LAR (see Discussion). However, participants also expressed multiple concerns regarding LARs such as the potential for discordant wishes between the LAR and participant, uncertainty regarding when an LAR is needed, concerns that asking the participant to appoint an LAR if they were not truly needed could violate individual autonomy, and the LAR could become impaired and no longer be able to make decisions for the participant. Participants also expressed discomfort raising a sensitive topic among participants, especially with those who are still healthy and may be unwilling to consider the possibility of diminished autonomy in future, or with those who are in denial about having any impairments.

Barriers to using LARs

PIs and CRCs reported numerous barriers to using LARs in research, which we categorized in two broad themes: 1) adding burden and 2) challenges identifying who can serve as an LAR. PIs (11/20) and CRCs (12/20) reported that using LARs could add complexity or burden to existing study processes and hinder recruitment. The extra burden could be due to a lack of resources, skills or training, adding too much time to already lengthy consent processes, or that using LARs is unnecessary because individuals who require LARs are already excluded from taking part in studies or participants are currently cognitively normal. PIs (12/20) and CRCs (13/20) also reported challenges with identifying, and asking the participant to appoint LARs, due to state laws, lack of clarity about who can be an LAR, or LARs being difficult to contact or unavailable, and that some participants have no one readily available to serve as an LAR due to social isolation or no living relatives or friends (also referred to as "unbefriended") [62].

Quantitative survey findings

Among our survey of PIs and CRCs ($N = 1{,}284$), 37% ($N = 469$) reported not asking participants if they would like to appoint an LAR and documenting their decision about who they would appoint as an LAR in any of their study protocols in the prior year. They also reported that no one else, such as a study sponsor or research team member, was already asking par-

Table 1
Demographic characteristics of quantitative survey and qualitative interview samples

	Quantitative Survey		Qualitative Interviews	
	Full Sample	LARs Not Incorporated	PI	CRC
Variable	%	%	%	%
Gender*				
Female	77	83	65	85
Male	22	17	35	15
Other	<1	<1	0	0
Prefer not to answer	1	1	0	0
Age*				
Below 30	17	16	0	35
30–39	33	31	25	45
40–49	26	25	30	10
50 or older	24	27	45	10
Race/ethnicity[a]				
American Indian/Alaska Native	1	2	0	0
Asian	9	8	20	5
Black/African American	5	3	0	5
Hispanic or Latino	9	7	5	5
Native Hawaiian/Pacific Islander	<1	<1	0	0
White*	83	86	75	90
More than one race*	3	1	0	0
Prefer not to answer	2	2	15	5
Education*				
High School Diploma or GED	3	3	0	0
Associate's Degree	6	6	0	0
Bachelor's Degree	38	36	0	35
Master's Degree	31	28	0	50
Doctoral Degree	20	24	95	10
Other	2	3	5	0
Trial types[a]				
Drug*	76	72	45	65
Device	48	49	5	20
Behavioral*	31	35	60	70
Biologics*	25	21	10	20
Surgical	24	24	0	15
Funding sources[a]				
Federal agencies*	65	70	80	80
Private foundations*	36	32	50	35
Industry	75	74	65	50
Other*	9	13	5	10

Quantitative full survey sample $N = 1,284$ (232 PIs and 1,052 CRCs). Quantitative non-user sample $N = 469$ (86 PIs and 383 CRCs. Qualitative interview sample $N = 40$ (20 PIs, 20 CRCs). [a]Participants could select more than one response. * Indicates there was a statistically significant difference between participants who incorporated LARS and those that did not incorporate LARs on that variable (the latter group's data is shown in the table). Specifically, participants who did not incorporate LARs were significantly *more* likely to report being female, older, White, higher educated, conducting behavioral studies, having federal funding, and having "other" funding. They were also significantly *less* likely to report being more than one race, conducting drug studies, conducting biologics studies, and having private funding. While these differences were statistically significant, the differences were small and either do not seem meaningful or there is no underlying theoretical basis to explain them. In addition, many are non-modifiable and our study is focused on modifiable factors that can be targeted by an intervention.

ticipants if they would like to appoint an LAR and documenting their decision. Table 3 provides descriptive statistics of the overall sample as well as those who report not asking and documenting participant decisions to appoint LARs. All of these individuals had at least one trial open to older adults, with 17.5% having at least one trial studying individuals with cognitive impairments.

Table 2
Attitudes towards and barriers to asking about and documenting discussions about appointing LARs among qualitative interview participants

Representative Quotes		PI ($n = 20$)	CRC ($n = 20$)
	Supportive Statements	16 PIs	16 CRCs
Respects Autonomy	"If an individual said, "I'd like my daughter or spouse to help me with these decisions," I want to, again, respect their wishes. This would allow me to do that." (PI15, Male, Age 30–39, Asian) "I think, again, it's necessary to make sure that, along the way, as somebody does progress through an illness, that they have someone there that's vouching for them that they do wanna participate. Yeah. I think it's a very important thing to have with working this patient population." (CRC19, Female, Age 20–29, Asian)		
Comfort and reassure participants	"They're there not only to explain, perhaps, things the patient can't understand, but they're there to provide support and reassurance." (PI5, Female, Age 40–49, White, Hispanic or Latino) "They feel more comfortable asking questions, obviously, to their loved one than they do to a stranger sitting in front of them talking about a bunch of things, a lot of information at once. It just makes the participant more comfortable, just to have someone in the room with them that they're familiar with. . . and someone who has, of course, their best interest at heart." (CRC4, Female, Age 20–29, White)		
Enable recruitment and retention	"I think it will only positively impact because one it will help with enrollment of a difficult population, which is not otherwise enrolled frequently in many studies because of this issue, but having the proxy be able to do the consent and everything would definitely help." (PI18, Male, Age 30–39, Asian)		
	Statements of Concern	15 PIs	12 CRCs
Sensitive topic	"For a small number of participants, actually they don't like it for a number of reasons, especially for people who have mild cognitive impairment. Maybe they have not told anyone their cognitive problems, so they don't want to identify that surrogate because they basically don't want to talk about it." (PI8, Female, Age 60 or older, White) "I think one of the challenges is if somebody is newly diagnosed, and is still working, and is still relatively healthy, sometimes, family members can be in denial about that, or they don't wanna come in and sign things, or the patient sometimes can get angry and say, "Why does this other person need to be signing for me? I can sign for myself." (CRC19, Female, Age 20–29, Asian) "I think, sometimes, it can cause them frustration, though, too, because they feel like they can't understand all the information on their own or may feel insulted by that." (CRC1, Female, Age 20–29, White)		
Uncertainty about when to use	"I can vividly remember times when it's still hard to figure out whether a person is capable or not. . ..There's a lot of fuzziness, and you don't know for a fact. . . . If you made the decision to have somebody sign and—on behalf of somebody else, and the patient could have done it, you've made a mistake. You've taken away somebody's autonomy a little bit. . . so I do worry about making the wrong choice." (PI11, Age 60 or older, White)		
LAR becomes impaired	"Then the other thing is, what if the surrogates are getting dementia? I don't think anyone's prepared for that. If you are enrolling someone in a study and their partner is their surrogate, that's a real possibility. That's another thing that's—we talk about it, but I don't think we have good protocols for addressing that." (PI12, Female, Age 40–49, White)		
Different wishes for LAR and Participant	". . . There could be huge secondary gain issues and all kinds of issues that doctors really aren't equipped to handle. I don't feel like I'm equipped to handle figuring out if the daughter has the best interest of her mom at heart. . . . You can see the egregious ones where they don't, but I don't know—and if the patient doesn't speak much, that might just be their Alzheimer's, or it might be that they're not happy with their daughter. There's so much to that." (PI12, Female, Age 40–49, White)		

	"If I just get in my gut feeling like I feel like the caregiver wants them to do it, but then that person doesn't. Sometimes what I do is I reflect it back on the caregiver and I says, "Well, we need to respect the patient here, or the participant. We need to respect what they want. If they really don't wanna do it, then we should respect that." That actually happened the other day." (CRC20, Female, Age 30–39, White)		
	Challenges of Identifying LAR	12 PIs	13 CRCs
Inability to locate	"I think the biggest barrier is one, identifying who that authorized representative would be and then actually getting in contact with them . . . a lot of the times especially with this new change in the law as well it could be that the adult daughter is the one that does all of the medical decision making for the mom, but with the hierarchy now, you still have to get the consent from the patient's husband. Then one tracking down who that is, getting them on the phone since a lot of this is done by phone that makes it a little bit just more challenging. There's a lot of phone tag that's involved." (CRC11, Male, Age 20–29, White)		
No one to serve as LAR	"If we required that they designate someone, they may not have anyone in mind that they may wanna be in the study, and right now, they may be competent. If we made it a requirement to be in the study, it's possible to lose participants, because they can't figure out anyone right now. Or . . . they may want to face that they're getting worse. They may not know anyone, or they may not have the funds to pay an attorney to be it . . . " (PI6, Male, Age 50–59, White)		
	"Often a challenge we face in recruitment was that people don't have the—say, the surrogates available to even move forward with research, even though they'd otherwise be a candidate." (CR6C, Female, Age 20–29, White)		
	Burden	11 PIs	12 CRCs
Adds complexity and burden	"—the real barrier is the training, the capabilities of that surrogate and how you recruit people to become surrogates. It would make the process just so much more difficult and we want people to do research with people with dementia. . . . " (PI2, Female, Age 60 or older, White)		
	"I think as long as it wasn't a separate 20-page consent document, I think that it would not be additional burden. I don't think there'd be any barriers. The only barrier would be like if it were another 20-page consent document that we then had to go over for an hour. That would be a barrier. People would get irritated by that, I think." (CRC12, Female, Age 50–59, White)		
Not needed for my type of study	"I don't feel like we need to because most of our patients are not—none of them have dementia that's diagnosed or identified. We do not expect anyone to have that happen." (PI4, Female, Age 40–49, Asian)		
	"For the participants that we recruit, I would say no because . . . then we would have to—basically they would have to be removed from the trial." (PI14, Male, Age 50–59, White)		

Table 3
Means and standard deviations of quantitative survey sample

z	Incorporated LARs ($n = 648$)			Not Incorporated LARs ($n = 469$)			
Variable	*M*	*SD*	Range	*M*	*SD*	Range	*t*-test
New trials submitted to the IRB in past year	6.1	7.3	1–70	4.8	5.4	1–67	–3.3*
Number of trials that study individuals with or AD	1.8	4.2	0–45	0.5	1.7	0–26	–6.5*
Number of trials open to older adults	8.9	10.5	0–100	8.0	9.4	0–75	–1.5
Confidence in resources	3.7	1.0	1–5	2.9	1.2	1–5	–12.6*
Positive attitudes	7.6	1.8	2–10	6.7	2.0	2–10	–7.2*

t-tests are comparing those incorporating LARs to those not incorporating LARs. *$p < 0.001$.

Comparing individuals who asked participants to appoint LARs and documented their decision to those who had not done so

We were interested to understand differences between those who reported not asking and documenting participant decisions to appoint LARs in any study protocols in the prior year ($N = 469$) from those who reported doing so in at least 1 study ($N = 648$) across variables of interest (Table 3). Our comparative analyses focused on modifiable factors such as attitudes and resources as these could be targeted for change by our intervention, as opposed to funding sources or job title. (In Table 3, we present comparisons between groups on all variables; but differences were few, generally small, and not based on any theoretical model.)

Those who had not asked participants to appoint LARs and documented their decision reported significantly lower confidence that they had the resources necessary to help do this in their studies, and had lower positive attitudes about LARs compared to those who were using them. In addition, those not asking and documenting participant decisions to appoint LARs had significantly fewer trials studying individuals with cognitive impairments and submitted fewer protocols in the prior year compared to those who had used LARs in the prior year.

Reasons reported for not asking participants to appoint LARs and documenting their decisions

Only those individuals who reported not asking and documenting participant decisions to appoint LARs in the prior year were asked to indicate the reasons why ($N = 469$). The most commonly endorsed reasons for not doing this among those with at least 1 trial studying individuals with cognitive impairments were being unaware of the practice (36.6%), LARs not being applicable (20.7%), or being unsure how to ask participants if they would like to appoint an LAR and documenting their decision (12.2%). Among those with trials focused on older adults but not those with cognitive impairments, the top reasons for not asking and documenting participant decisions to appoint LARs were that LARs were not applicable (40.3%), being unaware of the practice (24.5%), and not thinking this was important (11.6%) (Table 4). The primary reasons LARs were deemed not applicable were that individuals who require LARs are formally excluded due to Sponsor, IRB, or protocol requirements. Participants also stated that LARs were not applicable because none of their participants currently had cognitive impairments.

DISCUSSION

Among our survey of PIs and CRCs ($N = 1{,}284$), 37% ($N = 469$) reported not having discussed and documented participant decisions regarding LARs in the prior year, even though they all worked on interventional clinical trials open to older adults, including some specifically studying individuals with cognitive impairments. Our analyses focused on understanding the reasons for not asking and documenting participant decisions to appoint LARs among this group, as identifying barriers is an important first step given our overall implementation trials' goal to increase use of the practice. Our goal is consistent with NIH guidance that when recruiting people who are at risk of cognitive impairments (whether due to age or disorders) to multi-visit studies, appointing LARs at the outset of the study can ensure "a designated representative would be ready to step in" if the need arises [45].

Compared to individuals who had asked participants to appoint LARs and documented their decisions in at least one of their studies ($N = 648$), those who had not done so ($N = 469$) had significantly fewer trials studying individuals with cognitive impairments and also submitted fewer protocols in the prior year compared to those who had asked and

Table 4
Reasons LARs were not incorporated among quantitative survey sample

Survey question	Not Incorporated, trials studying cognitive impairments ($n = 82$)		Not Incorporated, no trials studying cognitive impairments ($n = 387$)		χ^2
	N	%	N	%	
Reasons for not incorporating					
I was unaware of this practice	30	36.6	95	24.5	5.0*
LARs are not applicable to my study[a]	17	20.7	156	40.3	11.1**
I'm not sure how to do this	10	12.2	36	9.3	0.6
I did not think appointing an LAR was important	7	8.5	45	11.6	0.7
I do not believe the IRB would allow this	5	6.1	19	4.9	n/a[b]
I do not have time to make optional edits to study protocols	3	3.7	8	2.1	n/a[b]
I did not want to risk a delay in IRB review time	3	3.7	8	2.1	n/a[b]
Other	9	11.0	42	10.9	<0.1
Do you think anyone might try to prevent you from using this practice?	19	23.2	94	24.3	0.05

For reasons for not incorporating LARs, participants could select all response options that applied. For whether anyone might try to prevent them from using this practice, numbers in the table reflect participants responding "yes." When asked who might try to prevent them from using this practice, the most common responses were the IRB, sponsors, and research team members. *$p < 0.05$. **$p < 0.001$. [a]The response "LARs are not applicable to my study" was not a response option, rather, it was the largest write-in response for those that responded "Other". [b]Chi Square test has one cell with an expected value less than 5, which violates an assumption of the test.

documented participant decisions regarding LARs. Notably, they also had significantly lower confidence that they had the resources available to help them appoint an LAR, and lower positive attitudes about LARs compared to those who had asked participants about appointing LARs and documented participant decisions in some of their studies. It is possible that participants who had asked about appointing and documented participants decisions regarding LARs also faced barriers but these were overcome, potentially leading to more positive attitudes and confidence in resources. Although we did not assess barriers among those who reported asking and documenting participant decisions to appoint LARs, they did have significantly more trials studying individuals with cognitive impairments and submitted more trials in the prior year so they may have had more opportunities to incorporate this practice and overcome barriers encountered. We do not know if they asked participants to appoint LARs and documented their decisions for all trials where it would be appropriate; we only know that they sometimes use the practice.

Among those who reported not asking and documenting participant decisions to appoint LARs into any protocol in the prior year, 17% had at least 1 trial studying individuals with cognitive impairments yet 36.6% report being unaware of LARs altogether with another 12.2% reporting not knowing how to ask participants to appoint LARs and document their decision. Further education and resources are needed so that all researchers who work with individuals with cognitive impairments are at a minimum aware of LARs and know where to find resources on how to ask participants to appoint LARs and document their decision should the need arise. This includes education reinforcing that LARs make decisions on the participant's behalf only if the participant loses the capacity to make decisions, and that participants can often still provide their assent or dissent to participate [23–26, 44].

We found that some clinical investigators did not use LARs because their exclusion criteria prohibit individuals with cognitive impairments from being enrolled. As noted in the NIH Inclusion Across the Lifespan Policy, such exclusionary practices can threaten the generalizability and applicability of research to older adults unless there is an explicit rationale for excluding them (for instance a study of cognition that requires participants to have no impairments). Further, by involving LARs in the consent process, participation by individuals with cognitive impairments is consistent with legal precedent in most jurisdictions and is consistent with principles of research ethics articulated by the NIH and common rule.

Other participants in the study who had not asked and documented participant decisions about appointing an LAR—all of whom conduct research with older adults—asserted that LARs were unnecessary because none of their participants have cognitive impairments. This too is noteworthy because it appears to assume that so long as one works with older adults without any known or identified cognitive impairments, then it is safe to assume that no

one has them. However, many older adults are at higher risk of cognitive impairments, for instance due to co-morbidities such as diabetes or hypertension [10–11, 63–65], that may go unrecognized given the wide variability in individual researchers' judgment of capacity to provide consent [16, 19, 43]. Validated assessments of consent are one solution for helping researchers determine capacity to consent in such situations [32].

Asking individuals their decisions regarding LARs while they still have the capacity to make this choice enhances participant autonomy by enabling these participants to have a say in who will make research decisions on their behalf before they have lost this capacity. If we wait until an individual is already impaired and unable to express a choice about their LAR, then the individual will be dropped from study or the choice of an LAR will be determined by institutional rules or State laws [66]. Moreover, raising the issue of LARs routinely can actually help reduce stigma as it avoids labeling particular groups of people or people with particular diseases as necessarily requiring additional safeguards [67]. However, our qualitative data suggest there are barriers to such early discussions.

Our qualitative findings reinforce our quantitative findings that institutional or state policies that proscribe who can serve as a LAR and lack of knowledge, skills, training, and resources among researchers are barriers to asking participants to appoint LARs. They also provide additional insight into the more subtle and complex barriers to asking participants to appoint LARs than captured in our survey. Qualitative interviewees conveyed concerns regarding raising a sensitive topic that could be upsetting for individuals to think about, or that individuals might be in denial, or become frustrated and angry at any suggestion of future impairment. Participants expressed concerns about the LAR and participant having different wishes, and there is evidence that suggests there may in fact be a lack of concordance between LARs and research participants in decisions about whether to take part in research [49]. Interviewees also expressed difficulties determining when capacity is impaired, and the potential to make an incorrect judgement about an individual's capacity, which may deter researchers from using LARs altogether. These last two concerns provide further support for why early and proactive discussions, while participants can still convey their preferences, could overcome some of researcher concerns about respecting the participants' wishes.

Some qualitative interviewees indicated that the role of an LAR was to comfort, support, and reassure participants, which suggests there is confusion between the role of LARs, caregivers, and study partners. Study partners are often required in ADRD-specific research to serve as a collateral source of information about the participant, assist with transportation to appointments and other study related procedures, and reassure participants [37, 68]. Although the role of a study partner may overlap with an LAR, they are not the same. The role of an LAR is specifically for the purpose of providing or maintaining informed consent in research. In many cases, a study partner can also be an LAR, but only if appointed as such [35]. Having early discussions with participants and their study partners at the outset of a study about who the participant would want to be the LAR should capacity diminish in future could ensure that a study partner is able to become an LAR should the need arise and enable researchers to retain these participants [33].

Asking participants to appoint LARs and documenting their decision is arguably the most challenging of the three practices our overall implementation study is promoting, with a weaker evidence base relative to the other two practices (i.e., using plain language and formatting consent documents to maximize readability and understanding; using validated assessments of understanding and appreciation of informed consent). While using plain language and formatting to maximize understanding in consent documents, and administering validated assessments of understanding of consent have been demonstrated to increase participant understanding, the practice of asking participants to appoint an LAR does not, by itself, increase participant understanding since the LAR provides consent [69–71]. Similarly, while LARs theoretically could increase recruitment of older adults with cognitive impairments, there is no evidence to indicate this is the case. In fact, for those individuals who do not have anyone available to serve as an LAR, they could actually be hindered from taking part in research if protocols required, rather than merely requested, an LAR.

Intervention to help overcome barriers

Knowledge, resources, and attitudes are all potentially modifiable, and our online toolkit (ConsentTools.org) contains resources to address barriers identified in our study [72]. For example, we provide education on regulatory definitions and

guidance regarding LARs, available empirical data, sample forms to document participant wishes, a tool to assess LARs' understanding of consent information, and template language to use with IRBs when justifying the decision to involve LARs. These practical tools and resources are specifically designed to facilitate conversations with participants about appointing LARs and ensuring this is documented in the research record. Overcoming the discomfort and stigma associated with discussing cognitive impairments and addressing the need for an LAR in future should the need arise, will likely be more challenging to overcome. To begin to address this, our toolkit includes talking points for broaching the topic of LARs, both with individuals who are unimpaired currently and may need one in future, and those who are currently impaired. The toolkit will be disseminated broadly to the research community when our implementation study is complete.

Limitations

Our survey respondents included individuals who worked with older adults without cognitive impairments, and those who worked with individuals with cognitive impairments including those caused by ADRD. We did not ask how many of participants' studies were longitudinal, which may affect whether asking about, and documenting, participant decisions about appointing LARs is indicated or required by a particular institution, sponsor, or IRB. Our participants also include CRCs and PIs, who may have different power to effect change (although individuals were able to indicate if a practice was implemented by someone else on the team). Our survey relied on self-reporting on the use of LARs because it is not possible to access institutional records such as protocols, consent forms, or IRB decisions. We only included US-based researchers given that informed consent regulations will vary by country.

CONCLUSION

Recruitment and retention of older adults is essential not only to meet the needs of ADRD specific research, but also in light of the NIH Inclusion Across the Lifespan Policy. The default exclusion of individuals who require an LAR will not be feasible going forward. Proactively discussing participant decisions about LARs before they are too impaired to state their decisions, and documenting this discussion, is a way to enhance participant autonomy by ensuring that if a participant is no longer able to make research decisions, researchers are aware of who they would have wanted to make these decisions on their behalf. This will also benefit researchers who may otherwise be concerned that they are not respecting participant autonomy when LARs are appointed after an individual no longer has capacity to make this choice. This will require changing attitudes, overcoming stigma and discomfort, and providing resources and education about LARs. Our toolkit provides resources for those who wish to implement LAR protocols. Further education and awareness will be needed to overcome the stigma of cognitive impairments and the involvement of LARs in research.

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CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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