UCSF

UC San Francisco Previously Published Works

Title

Caught in a Loop with Advance Care Planning and Advance Directives: How to Move Forward?

Permalink

https://escholarship.org/uc/item/6cn6p8tb

Journal

Journal of Palliative Medicine, 25(3)

ISSN

1096-6218

Authors

Periyakoil, Vyjeyanthi S von Gunten, Charles F Arnold, Robert et al.

Publication Date

2022-03-01

DOI

10.1089/jpm.2022.0016

Peer reviewed

JOURNAL OF PALLIATIVE MEDICINE Volume 25, Number 3, 2022 © Mary Ann Liebert, Inc.

DOI: 10.1089/jpm.2022.0016

25th Anniversary Roundtable

Open camera or QR reader and scan code to access this article and other resources online.



Caught in a Loop with Advance Care Planning and Advance Directives: How to Move Forward?

Moderators: Vyjeyanthi S. Periyakoil, MD^{1,2} and Charles F. von Gunten, MD, PhD³ *Participants:* Robert Arnold, MD,⁴ Susan Hickman, PhD,⁵ Sean Morrison, MD,^{6,i} and Rebecca Sudore, MD^{7,8}

Abstract

Completion of an advance care planning (ACP) process and/or an advance directive should result in patients receiving the care they desire at the end of life. However, three decades of research have shown that is just not the case. ACP has been a front runner in developing the science within palliative care. Some positive outcomes such as lowering levels of surrogate grief may be associated with ACP. Yet, it does not appear that further ACP research will ensure that seriously ill patients will get goal-concordant care. An unfortunate consequence of palliative care research and advocacy so far is the misguided notion of many hospital systems trying to solve their palliative care problems by only implementing an ACP initiative. At best, ACP is but one tool in the collective palliative care toolbox. New tools are needed. Given that we have finite resources, future research should focus more on tools to improve symptom management, better models of care, and systems that will ensure goal-concordant care that meet the needs of the population that the health care system is designed to meet.

Keywords: advance care planning; advance directives; clinician/patient communication; models of care; palliative care

DR. VON GUNTEN: This is the second part of a series celebrating the 25th anniversary of *Journal of Palliative Medicine*. The purpose is to discuss topics that are important to the palliative care field right now. I am looking for a sense of us sitting around in the doctor's lounge sharing ideas and bouncing them off each other. What is on your mind these days about advance care planning (ACP) and advance directives?

DR. SUDORE: The biggest thing on my mind is how we define ACP. What goes into that bucket? Does it include

advance directives and check box forms as well as other things such as preparing people and surrogate decision makers for communication and decision making? Are all of these things ACP? Should we be calling preparation for communication and medical decision making something other than ACP? I think defining what we mean when we say ACP is top of mind and when we say "it doesn't work," what are we talking about?

Second, of the outcomes that we thought were the most important things to measure, can ACP really do those things, such as affect end-of-life outcomes? ACP has been shown to

¹Department of Medicine, Stanford University, Palo Alto, California, USA.

²Extended Care and Palliative Medicine Service, Veterans Affairs Palo Alto Health Care System, Palo Alto, California, USA.

³Journal of Palliative Medicine, Empire, Colorado, USA.

Section of Palliative Care and Medical Ethics, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

⁵Indiana University Center for Aging Research, Regenstrief Institute, Indianapolis, Indiana, USA.

⁶Brookdale Department of Geriatrics and Palliative Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA ⁷Division of Geriatrics, University of California, San Francisco, San Francisco, California, USA.

⁸San Francisco Veterans Affairs Medical Center, San Francisco, California, USA.

ⁱORCID ID (https://orcid.org/0000-0003-0830-5100).

Accepted January 15, 2022.

affect other things that are as meaningful to patients, such as decreased surrogate grief and burden. So, the outcomes may be different from what we had hoped or thought that ACP might affect. Third is thinking about systems and holistic approaches for how we can help people when they have serious illness and at the end of life, including preparation for medical decision making, and how that dovetails into supporting people during "in the moment" decision making.

DR. MORRISON: My things are very similar to Rebecca's, to be honest with you. What is really on my mind is the disconnect between what patients are receiving in the setting of serious illness versus what they are actually getting. Too often, our patients are getting traditional medical care and not goal-concurrent palliative care.

What I also worry about, and this is what prompted some of the writing that I and others have done, is when you ask the general public, "what is ACP?" 99 out of a 100 will say, "Oh, I have a living will," or, "I've talked to my doctor about what I would want when I'm seriously ill." And occasionally somebody will say, "I have a healthcare proxy." They do not think of ACP as the complex process that Rebecca identified. What also worries me is that our patients believe that if they go through the ACP process and complete an advance directive, then they will receive the treatments that they desire at the end of life.

We are making false promises. Over 30 years of research has shown that is just not the case. No matter how hard we study ACP or how hard we tweak the process, no matter what innovations and interventions we have made over that time, we still cannot assure people that when they sit down and talk with their doctor about a future medical decision, then they are going to get the treatments that they specify. Rather than focusing on the hypothetical, what I would really like to do is help people and their surrogates make decisions in the moment when those decisions need to be made and not try and predict what people would want if x, y, or z happened. We should not be focusing on the decisions *per se*, but how we help people make these decisions.

DR. HICKMAN: I am fascinated by the complexity of implementation. A lot of the ACP research that is been done to date has focused on discreet components without looking at a holistic picture of the broader system. I think we have a lot to learn from implementation science and from human factors engineering about how we structure and set up systems that consider this greater complexity. The existing literature largely does not address this complexity and this is in part a reason the state of the science is uninspiring. When you look at the studies that are included and reviewed, for example, in the Jimenez 2018 systematic review of systematic reviews, there are many poor-quality studies.

ACP has been a front runner in developing the science within palliative care. There is a lot of interest in ACP, but there is typically a lack of appreciation of the complexity about how you make an ACP intervention work. If you look at ACP within the CFIR contextual framework for implementation research model, for example, it pushes you to think about the characteristics of the outer and inner setting that includes individuals involved. Is there leadership buy in and engagement? Are there resources provided? All the way down to are the clinicians involved in the conversa-

tions actually receiving training and having that training be reviewed? When you start digging into it, it is an incredibly complex endeavor.

I love a slogan on an elementary school signboard that I drive past on a daily basis; it says "we can do hard things." I think that applies here. We can do hard things because it is so fundamental to patient-centered care and patient-centered or person-centered decision making. If we do not provide patients and family members with the opportunity to engage in reflection and education outside of that "in the moment" decision making, I think we do people a disservice.

DR. ARNOLD: We only have a certain amount of attention. You learn what you put your mind to when you focus. For the past 25 years, we focused on ACP. It is unclear to me that it has fulfilled its promise. We should move our focus to something that has a higher yield because we only have a certain number of investigators. There is only a certain amount of research that we are going to do. There is only a certain amount that we can ask government to do. Where do we put our focus to have the biggest bang?

Like most things in the United States, we like to believe one-on-one conversations are going to fix system problems. Yet, regardless of what patients want, they do not get it because our health system is not built to give it to them. Most people want to stay at home and not be in nursing homes, but we do not give social supports to help people stay at home. Most people would rather not go in to see their doctor and spend three hours. Yet, compared with Canada, we put all our palliative care clinicians in hospitals rather than put them in the community. It seems to me that, if we really want to build systems that work for our patients, we should stop our focus on individual autonomy and build a system that would deliver for everyone. It distracts us to continually focus on conversations about what we are not going to do when you get sicker in a hypothetical situation.

I am also thinking about the degree to which we agree. We all agree that conversations with sick patients who are facing complicated decisions are really important. We agree we need to do better at it. We agree we need to teach people to do better at it. As a health care system we need to be more honest about what we can do and what we cannot do. I worry that these [research] articles [about ACP] will distract us from what we agree on and what we need to do to take really good care of patients.

DR. PERIYAKOIL: The real question here is not whether we are for or against advance directives. If you look back in the past 20 years at the toolkit of palliative care, into the old doctor's bag, ACP is just one tool. Under what circumstances and for whom is this the right tool? What are the other empirically validated tools that are missing from the collective palliative care toolbox? Yes, the ACP tool has value, but we should also focus our energy on building some other tools so that we can deliver on the full promise of palliative care, which is providing the best possible care for all seriously ill patients.

We still have not solved the pain problem, though we have created an opioid problem. Why aren't we like cardiology? Why don't we have all these acronym-named studies on the most effective management of burdensome issues such as dyspnea, nausea, vomiting, and other nonpain symptoms bothering seriously ill patients?

DR. VON GUNTEN: When ACP was proposed, there was a "fix-it" quality to the argument. All problems will be solved if we simply have the documents and the conversations. Then, the complexity of all of it emerged. Specialist palliative care teams got involved in the challenges of decision making in the hospital where there is high emotion and family systems at work. Then, it turns out that the physicians and everybody in health care have their own needs that affect decision making. Calling it implementation science is an understated way of saying we need to find a way to make better decisions in the middle of this mess. Looking back, the contrast with, "Oh, fill out this document" or "Have this conversation that Medicare will pay for," is stark.

Yet, in community medicine, I see hospitals thinking they will solve their palliative care problems by pushing an ACP initiative. They say, "We need no new employees. We need no new training. All we need is a quality improvement project to improve completion of advance directives to reach the target of 80% by the third quarter of the year. Sean, you used a quotation in your editorial to the effect that "for every problem there's a simple solution that's wrong." Is that what we have got here? It looked simple back in the 70s and now that we have waded into it, it is way more complicated.

DR. MORRISON: Somebody pointed out to me how antisemitic [Menken] was, and also his antisemitic writings, so I have stopped using that quote. Susan put it really well. We are facing a complex problem or a complex set of issues, which, as Bob said, are fundamentally system-level issues. I have enough gray hair to remember when the Patient Self-Determination Act was passed and doing the early ACP studies that moved into the conversation studies. I do think having a conversation about your values and goals is important, do not get me wrong. But I do not think that a series of ongoing conversations is going to meaningfully impact the care that you receive when you are seriously ill given all of the other external pressures.

As V.J. pointed out, we have really focused ACP as our only tool. Moving forward, we need other tools. Does ACP help around the margins? May be. Do we need better studies? May be. But at least if we look at the studies that have been published since Rebecca's really nice review, all of which have been well designed randomized clinical trials (RCTs), they just do not even give us a hint that we are getting the results that we want.

There is another piece that makes me think we are going in the wrong direction. Diane Meier, in a Kaiser Health News article today, noted that despite all of our efforts over so many years, only a third of the people in the United States have completed an advance directive. Although advance directives are not ACP, it is not a bad surrogate measure. We have never been able to push that higher. I think this is not something the public is engaging in nor truly wants despite our hard work.

If we are really going to change care for the seriously ill, I would come back to what Susan and V.J. said, it is going to be a toolbox. It is going to require recognizing the complexity of health care and it is got to be about system level change. The thought that we are going to fix it in the individual doctor's office by having a conversation is wrong. It is a very simple solution, it is a very complex problem, and it is not a good match.

DR. VON GUNTEN: I searched with Google to find that testamentary wills have been advocated since the time of the ancient Greeks. Now, after thousands of years of experience, only 25% of the American public have executed a will before they die. I think it is striking that the proportions are about the same as for advance directives. Only a small number of people are "planners" as opposed to those who prefer to react in the moment or avoid planning. It is extraordinary to observe that the number of different personality styles, the family systems, and what will make the doctors and the nurses feel better are the drivers of decision making, particularly if it is in the hospital.

DR. SUDORE: I notice we keep saying "it." ACP is "it." I would say that we still, as a field, have not decided what "it" is. For the field, it is not new to say that a sole focus on advance directives does not work. We agree that ACP should focus on preparing surrogate decision makers, preparing people so that they can make medical decisions. And then some say that "it" doesnot work. There is an article that Darren Heyland published in *Healthcare* in 2020 where he advocated for calling preparation for communication and decision making something other than ACP and instead calling it Advance Serious Illness Preparations and Planning (ASIPP).

The thing we do know, when we look at the research, is ACP, however it is defined, is getting us something that is meaningful, but maybe not what we expected. The patients (people), caregivers, and the clinicians who have had to make serious medical decisions for themselves or for other people are the very people who report that they think ACP is important and meaningful. And, when we looked at outcomes in high-quality RCTs from the past decade in our recent scoping review in *Journal of the American Geriatric Society* (JAGS) in 2020, we found evidence of positive outcomes including decreased surrogate grief, post traumatic stress disorder (PTSD), and burden. All of these outcomes were positive.

We have talked a little bit about the challenges of measuring goal-concordant care. The veterans administration (VA) is doing a really great job looking at the bereaved family survey to assess this. They survey family members three months after somebody dies in a VA facility. There was a beautiful study published by Cary Levi and Mary Ersek in *Journal of Pain and Symptom Management* (JPSM) in 2021 looking at home-based primary care patients who have the VA life sustaining treatment note in the chart.

Those who do were found to have better bereaved family survey scores. So something is happening that is meaningful, even if ACP is affecting outcomes that will not fix our broken health system. ACP, by itself without systems changes, is not likely going to be able to ensure that everybody gets the care that they want. As Sean was saying, maybe we just need to be upfront about that. But it still does seem to be doing something meaningful.

Also, from working during the pandemic and with underrepresented and disenfranchised populations, many many people do not see clinicians or the health system as trustworthy and reliable. There is a ton of experiential racism and people do not all look to us, even if you are a palliative medicine physician with amazing training with the most wonderful communication skill, as a trustworthy safe space.

I think many people will not come to the hospital until they are in a crisis. I think it really is important that we do give

them some tools to help with preparation outside of the medical context. Everybody should have the chance to do some preparation and to prepare themselves and their family members before they are in that crisis. Because I can tell you, my own family members have not had access to good palliative care or clinicians who can help walk them through that process in the moment and they had to rely on their own prior preparation.

DR. PERIYAKOIL: Being in California, I think of this a little bit like earthquake preparedness. You have your little checklist: secure the refrigerator and water heater, have a robust supply of food and water, etc. And then there are people who go really hardcore on this, where they have huge kits outside their house in the event that the house collapses. And then there are others who say, "Well, if it happens, I'll die, I'm not going to worry about it." So then the question is, what is the value to doing this? For whom? To what extent? Going back to what Bob and Sean were saying, just having a little earthquake kit or having a checklist or some flashlights and extra batteries is not going to do it. You still need to have the entire system prepared.

At the end of the day, if we had endless dollars, we could do endless things. But given that we have finite resources, not only financially, but also human capital, with a large portion of the physician workforce retiring (it takes like two decades to grow doctors), where is the bang for the buck? If we think about financial planning for the entire field of palliative care, what would that look like? How does one deliberately make decisions for the future in terms of devoting X% of research dollars to ACP, Y% to pain and nonpain symptoms, and Z% in implementing and evaluating various systems of care for seriously ill patients.

The number one request from my palliative care clinic patients is for home help—home health aide services and homemaker services. So going back to what Sean was saying, if we listen to the customer, they want to live the lives that they want in the place that they love, which often is their home. And they want the best care possible if they get to the hospital. And that goes back to Rebecca's point that not everyone gets to the hospital, nor do they want to, nor do people trust hospitals either.

DR. VON GUNTEN: I have been working in a community health system where everything you have described in a U.S. fee for service market is revenue destroying. There is no enthusiasm for helping that because the hospital is where all the revenue is generated. I see those same patterns in the centrally planned systems. There are still reasons to want to drive people toward hospitals and doctors and complexity rather than the workforce initiatives for care at home. I do not know what you do for that, but I do think we have to look at the economics since it is such an important driver of human behavior.

DR. ARNOLD: We only have a certain amount of attention. If you look at James Tulsky's study in the early '80s where he looked at how people talk to seriously ill patients about code status. And Wendy Anderson doing a study 20 years later showing its not palliative care, because remember it's not

about us, because we are not going to provide most of the care for seriously ill patients. If I wanted people to focus, I would want them to focus on good conversations just in the moment. I would love there to be better health care publicity and information about what it is like to have serious illness and what serious illnesses look like and prognosis looks like so that people are better prepared.

And I agree with Rebecca, maybe we just have not looked at the right outcome. And yet, if we are going to focus on communication skills, it seems to me there is so much we can do about talking honestly about prognosis, just where people really are in their disease. And I worry that the incentives that the federal government has pushed about ACP make things worse rather than better.

DR. MORRISON: I struggle with this. When we look at ACP efforts in this country and the industry behind that, it is really not teaching people to do what both Susan and Rebecca say is important for us to be doing with our patients and their families. I think what pushed the writing that I did last year was what I saw of ACP during the COVID-19 surge in New York City. When COVID-19 hit, we spent an exorbitant amount of effort as a health system to get everybody to do ACP, because we were terrified of what was going to happen. What that translated into was getting people to fill out electronic medical-orders-for-life-sustaining-treatment, getting proxies designated, and making sure wishes for care were documented. We were very successful at that.

Then, when I was walking through emergency departments that were completely overwhelmed, what I saw really worried me. Exhausted physicians were taking these written documents at face value, acting on them, and not engaging patients and families in real-time nuanced discussions.

The majority of ACP is not focusing on the people who most need those conversations, which is people who have real serious illness right now. We should not be talking to people like me about what I would want when I develop Alzheimer's disease in 10 or 20 years. That is not a meaningful conversation for me right now. But that is what the majority of ACP interventions are doing. I would really like to focus on how we talk to people about prognosis and about real-time decision making because we know we do not do a good job at that.

DR. HICKMAN: There is this question about what the field of palliative care should do about ACP. I think that is an interesting framing because I think it presumes an ownership over ACP that is not broadly shared. I have been deeply involved in efforts around our State of Indiana over the past decade and nationally through Physician's Order for Life Sustaining Treatment (POLST) for the past two decades. Although we might see ACP as something that palliative care gets to "decide about," it is really much bigger than that. It involves a much broader range of areas of health care as well as the faith community and, of course, the legal community, who is heavily invested. So I think we need to be aware that this is not just something that we "own" in palliative care. It is much bigger than that and the roots and the demand for it are much broader.

Sean has a couple of times referenced the general U.S. population's understanding of ACP as an indication that we need to discard the name "ACP." I think that is interesting, given that palliative care suffers the same kind of branding issue. There has been a lot of conversation about

"palliative care," and whether it should be "supportive care," or "comfort care?" Or "supportive oncology." How should we label this? I am not sure "understanding" is the indicator I would use to decide about how we move forward. I think we have responsibility to educate and that is part of the bigger picture rather than relying on the existing knowledge based on what are often really brief conversations in an attorney's office, for example. Instead, we need to think more comprehensively.

DR. ARNOLD: I think that not only don't we own it, 99.9% of conversations with seriously ill patients are not going to be done by palliative care. One of the things that worries me is that very well-done studies may not have made the differences that we wanted at the beginning. They may have caused some of Rebecca's other outcomes. I worry about what happens when it is done broadly in the community for incentives, as Charles points out, that are being driven by money.

DR. VON GUNTEN: "So, what should the next 25 years look like?" It does not have to be within the palliative medicine community or palliative care, but broadly, where does the research need to go? If you could direct the funding or if you could direct the junior people who are just now trying to wrestle with what you have been saying and now want to move us forward, what would your prescription be? What would you like to see?

DR. ARNOLD: I want the field of palliative care to focus on what systems we need to build that support the most common glide paths for our patients. If you go to a restaurant and they give you a 23-page menu, it is a bad restaurant. Yet, we have treated conversations as if you can have any option; we need to stop doing that. You cannot have any option. We have a difficult enough time in our health system choosing three glide paths and doing an excellent job with them. I want to see implementation science help us choose a couple of the most important, from patients' point of view, glide paths, and figure out how to implement them. It is not really about specialty palliative care. We can serve as the helping hand, most of the care is not going to be done by us.

DR. HICKMAN: I think Bob said it perfectly, although the phrase "glide path" makes me a little bit nervous as I think about the Liverpool Pathway. We do need to be thinking more comprehensively about implementation and more broadly about what is important to patients, caregivers, and community members and use that to inform our work moving forward. I think so much of the work has been done without the perspectives of diverse including community members from diverse backgrounds. I would really love to see us move forward in that direction and use that feedback and input to think about what is important, what matters most to people.

DR. SUDORE: Even if the work that many of our colleagues are doing is not "ACP," but rather trying to help prepare surrogate decision makers, when things get published that say ACP does not work, that means all the work that might be about trying to prepare people is thought of in a negative light as well. I have been asked by our primary care col-

leagues whether we should stop asking people if they have a surrogate decision maker. I have been asked by my surgical colleagues whether we should not be helping patients do preparatory guidance for their surgery, because that might be ACP and they read "it" does not work.

In other words, in a sound bite, it is hard to have all those nuances about ACP and preparation for decision making. I do not think any of us would say we should not be helping patients and surrogate prepare for medical decision making, but I think we just have to be careful ourselves when we say "it" does not work, what we mean by "it." Should we very quickly come up with a new name or adopt Daren Heyland's proposed name of ASIPP? Should we adopt that and very quickly pivot and write something about it to help educate the public?

In terms of where the field needs to go, I agree with what everyone is saying. We need the customer's voice. We have been very medical centric, we need to hear from the community about what they want. We need a systems approach to figure out how are we going to do this. I do not think it is *either/or*, it is *and*. How are we going to do all these things together in a way that, at the end of the day, helps patients and families?

DR. ARNOLD: It is always hard when colleagues misinterpret articles. It is very hard to provide the nuances Rebecca asks for when one is writing articles—particularly short articles. We did use the words that the meta-analysis and research used. Maybe the point is that we need a different name for different conversations as Rebecca points out.

I am convinced that what I said 30 years ago, where I wrote about having ACP with everybody >65 years, was wrong. I do not think it is a problem that I was wrong, it shows that I can learn something, which is a good thing. The question is, how can we take what we have learned and move in a new direction. We do not have enough time, we do not have enough resources to continue to do what the research has shown does not work.

DR. MORRISON: I come back to two questions that you asked, Charles. The first at the very top of the hour, which is, "What is on your mind?" And the second is, "Where should the research be going?" What is on my mind is that in eight years, all the baby boomers will have turned 65 years. The number of people over the age of 65 years will eclipse the number of people under the age of 18 years for the first time in all of human history.

If our health care spending continues along the line that it is, it will be 30% of our gross domestic product (GDP). We know that every single one of those people over the age of 65 years is going to, at some point, if they do not get hit by a bus on Madison Avenue, develop one or more chronic illnesses, which they are going to live with for a very long time. We have a health system that is completely mismatched to care for that population. That conclusion is not only based upon the education we are providing, but also the research and our models of care delivery.

It is too late. It is too late to train up palliative care specialists. It is too late to train up geriatricians. It is too late to tweak. And so, I think the research really needs to focus on what models of care and systems are the match for the population that our health care system is going to be caring for and not the health care system of 1965 when Medicare was started. To reduce my anxiety, we need to invest in that type

of research and focus our money on the health services research that is going to create care models that take care of our population. Otherwise, as Bob has said, we are not going to have money to do anything else. And I literally mean anything else, not just health care, but also anything else, unless we fix that and fix it quickly.

DR. HICKMAN: I appreciate the circle back to systems and looking at models of care. I think that is a shared consensus of the group here today. However, Bob, I did not hear anyone today talking about little changes. I think there are big changes that need to be made. I agree with Sean's statement that we need to be thinking about models of care, we need to be thinking about systems. I do not think that precludes thinking about ACP or ASIPP, if we want to adopt Darren Highland's new proposed terminology. I think ultimately, we need to look at the bigger picture and implement these models of care in ways that are rigorous. That applies not just to ACP, but also to any interventions we are going to develop within palliative care. I think there are many areas where the science could be improved.

DR. PERIYAKOIL: It makes me nervous when I hear us say that ACP is not fully owned by palliative care. It also makes me nervous when I hear Bob say that most of the care of most seriously ill patients is going to be done by nonpalliative care people. Both statements are true. But are we signing off on our field's responsibility toward seriously ill patients by saying, "Well, it ain't our problem. After all, palliative subspecialists are going to care for only a small fraction of seriously ill patients. So let the chips fall where they may." Isn't it our responsibility as subspecialty experts to create the empiric research knowledge that guides care of all seriously ill patients?

We should have a deliberate strategy for allocating research dollars to study a variety of key issues. What are the under-watered plants in the palliative care research garden? Where do we need to water and how much is required? What percentage of the research dollars should be allocated to research on better symptom management, effective communication, and on building comprehensive systems of care? We should convene a group of experts to build a strategic plan for our field for the next 25 years and use it to guide our collective fellows, postdocs, and junior faculty.

DR. VON GUNTEN: Well, we are at the top of the hour. It is a thorny thicket of issues. I learned a lot. I am grateful to each of you for being willing to engage and not shy away from the difficult parts in this, because I cannot think of anything more difficult right now.

Acknowledgments

Dr. Periyakoil's time is funded by the following grants: P30 AG059307/AG/NIA NIH HHS/United States; R01 AG062239/AG/NIA NIH HHS/United States; U54 MD010724/MD/NIMHD NIH HHS/United States.

Address correspondence to: Vyjeyanthi S. Periyakoil, MD Department of Medicine Stanford University 3801 Miranda Avenue, 100-4B Palo Alto, CA 94304 USA

E-mail: periyakoil@stanford.edu