Building Towards Common Psychosocial Measures in U.S. Cohort Studies: A Qualitative Assessment of Principal Investigators’ Views regarding the Role of Spirituality in Human Health

CURRENT STATUS: UNDER REVISION

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DOI: 10.21203/rs.3.rs-15662/v1

SUBJECT AREAS
Health Economics & Outcomes Research   Health Policy

KEYWORDS
Religion, Spirituality, Epidemiology, Health Disparities, Cohort Study, Principal Investigator, Interviews
Abstract

**Background.** The goal of this study was to understand prospective cohort Principal Investigators’ (PIs’) attitudes regarding the importance of religion and spirituality (R/S) on disease etiology in order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research.

**Methods.** One-hour, semi-structured qualitative interviews were conducted with 20 PIs representing 24 National Institutes of Health (NIH)-funded prospective cohort studies in the US, collectively capturing health data on 1 in 100 Americans. Sample size was calculated to achieve thematic saturation.

**Results.** The majority of PIs we interviewed saw R/S as a potentially important area to investigate to better understand disease etiology, but some were unsure about the mechanisms through which R/S can impact health and how to translate this knowledge into public health interventions. PIs identified 5 key areas that are lacking in current R/S research that need to be addressed in future research to convince them of collecting more R/S measures in their cohorts: (1) high-quality, prospective studies; (2) examining a plausible biological mechanism; (3) commonly collected, well-validated R/S measures; (4) addressing bias against R/S research; and (5) NIH funding for R/S research.

**Conclusions.** Results of this study provide a roadmap for future R/S research investigating the impact of R/S on disease etiology in the context of U.S. prospective cohort studies. Such research could provide potentially important information concerning how to address existing health disparities in the U.S.

**Background**

To date, genome-wide association studies (GWAS) have identified significant loci implicated in a number of highly prevalent and rare conditions, yet there remain relatively few examples of GWAS informing translational medicine (1). Instead, risk alleles identified in GWAS are now understood to influence disease risk through functional alterations of gene expression levels(2) and complex gene-environment interactions that underlie gene expression (3, 4). The inclusion of the social environment in gene-environment research, however, has been limited by the lack of common measures of these
domains across national prospective cohort studies, even when there is broad agreement on the clinical relevance of the exposure (e.g., stress, quality of sleep, poverty, trauma, early childhood adversity, social support, coping). Complex gene-environment studies also require large numbers of participants for adequate power (5), so it is often necessary to pool data across multiple cohorts. There is thus a critical need to identify the most important social environment measures influencing health and to promote the collection and use of these measures across prospective cohort studies. Over the past few decades, a robust body of research has demonstrated the importance of psychosocial stress (6–8) and resilience (9) in relation to disease etiology. Religion and spirituality (R/S) are important sources of resiliency for many. More than 77% of Americans report that their religion is very or somewhat important to them (10). The figures for African Americans and Hispanics/Latinos are even higher at 91% and 84%, respectively (10). Given that these same communities bear a disproportionate burden of illness, understanding how different dimensions of R/S may support resilience or undermine health may offer new insights in improving population health and reducing health disparities.

The lack of engagement with R/S and health research within the epidemiological research community may be a result of the limited number of robust prospective studies investigating R/S influences on disease etiology (11, 12). There are, however, a growing number of prospective studies on R/S across multiple endpoints. To date, studies on church attendance have produced the most robust evidence, with several prospective studies demonstrating a significant protective effect of church attendance on mortality and depression (13–17). Self-assessed spirituality and religious coping have also been found to have a significant prospective associations with hypertension (18, 19), colon cancer (20), HIV outcomes (21), cognitive functioning and mental health (22–29), change in pulmonary function among adolescents with cystic fibrosis (30, 31), and CD4 levels and viral load among HIV/AIDS patients (32–34).

The lack of robust and consistent R/S measures across cohorts’ data collection efforts has made it difficult to systematically assess the relative importance of various R/S measures across a range of clinical conditions, compare results across cohorts, and replicate findings. Principal Investigators (PIs)
of cohort studies are ultimately responsible for which measures get collected from their study participants. As the final arbiter in deciding which measures get included in each round of data collection, cohort PIs have enormous influence and shape the practice and culture of epidemiological research. This influence is perhaps greatest with respect to research domains at the margins, where opinions regarding the value of collecting such measures are more likely to vary. Such is the case with studying the role of R/S in human health.

It is within this context that we undertook a qualitative study of cohort PIs’ perspectives and attitudes regarding the potential impact of R/S beliefs and practices on human health, the mechanisms or pathways through which they imagine R/S may operate to affect health outcomes, and the kinds of evidence they would need to see before being persuaded to invest cohort resources in collecting new (or additional) R/S measures.

Methods
Defining Religion and Spirituality
There is a lack of consensus in the field regarding how to define R/S. In this study, we define religion as a shared set of beliefs and practices that reflect a particular relationship to the divine (12, 35). Examples include beliefs (such as life after death or that God is forgiving), or practices (such as attending church, praying, or meditating). Such items can be measured in a fairly straightforward way (11). Defining spirituality, on the other hand, is far more challenging. It remains poorly defined in R/S research (36), often intentionally to allow individuals to ascribe their own meanings to the term (37, 38). Spirituality is used broadly to encompass religious practice and beliefs, but also includes diverse self-definitions of the source of meaning in one’s personal “search for the sacred.” (36) While such an open definition of spirituality makes sense from a theological perspective, it hampers the advancement of empirical R/S research, where terms need to be consistently defined to allow clear interpretation and replication of results. For the purposes of this study, we developed a streamlined definition of spirituality that draws on national palliative care guidelines: (38) “That transcendent dimension of human experience through which individuals seek and express ultimate meaning and purpose in their lives and/or relationship to the divine or sacred.”

Participants and Recruitment
A list of 30 different prospective cohort studies that had received funding from the National Institutes of Health (NIH) was developed, with a focus on capturing cohorts that included diverse racial/ethnic communities, a broad range of clinical conditions, and all regions of the country. None of the study investigators had had a previous relationship with the PIs. Contact information for the PI of each study was identified, and each were invited via email to participate in this qualitative study. Telephone calls were scheduled with those interested in learning more, during which time PIs were provided with additional information about the study to facilitate informed consent and again invited to be interviewed then or on a future date of their choosing. PIs who agreed to be interviewed were offered a $100 honorarium as a token of appreciation for their participation. We followed these procedures until we reached our study goal of 20 PI interviews. Only one PI with whom we discussed the study declined to participate in the study. All but two participating PIs refused the honorarium.

Institutional Review Board approval for this study was obtained from the Partners Human Research Committee (PHRC). Verbal consent was given by participants, although this study was deemed to be exempt from continuing IRB review by the PHRC.

Data Collection

One-hour, semi-structured interviews were conducted with each participating cohort PI by the Principal Investigator of our qualitative study (AES) or jointly by two members of the study team (AES and TAB, both female PhD-level research investigators) in 2014-15. A semi-structured interview guide was developed by the study team, with input from several investigators participating in the National Consortium on Psychosocial Stress, Spirituality, and Health (CoSSH). Questions addressed PIs’ experiences with and exposure to research on R/S; reasons why they decided to collect the R/S measures their cohort has collected thus far, or for not collecting any R/S measures; their assessment of the quality of existing R/S research; their assessment of the importance of R/S practices and beliefs in understanding disease etiology; their beliefs regarding the pathways or mechanisms through which R/S might operate to affect human health, if at all; and the kinds of evidence they would need to see before being willing to invest cohort resources in collecting new or additional R/S measures going forward. Based on our team’s previous work (39-44), we anticipated that 20 individual interviews
would be more than sufficient to achieve thematic saturation.

Data Analysis

All interviews were recorded and transcribed. The interviewer later reviewed the transcripts for accuracy. Interviewers’ notes from the interview not only captured initial impressions, but also provided another source of data useful for addressing instances where the audio recording was difficult to decipher. Interview transcripts were analyzed using a grounded theory approach (45, 46). The interviewers and two Master’s-level research assistants (RAs) coded 40% of transcripts and identified key themes. Coding discrepancies were addressed through discussion, comparison of the raw data, and refinement of code definitions. The interviewers then finalized the preliminary coding scheme. The remaining transcripts were coded independently by the RAs, using Atlas-ti software (Version 5.0). Data were analyzed using content analysis to identify major concepts, and axial coding to group and connect related data. (44, 46, 47) Within each topic area, we highlighted statements characteristic of the majority of those interviewed, as well as statements from those with divergent views. The quotes included in this report are illustrative of sentiments expressed by several PIs, unless otherwise noted. No repeat interviews were carried out, and participants were not provided with transcripts or findings to provide comments or feedback.

Many steps were taken to maximize dependability (consistency, reliability) and credibility (the truth of findings, internal validity) of study conclusions (48). We incorporated triangulation at two levels: (1) involving a multidisciplinary research team in coding and analysis (investigator triangulation); and (2) including PI participants from diverse communities and disciplines whose cohort studies include participants from diverse racial/ethnic communities and geographical regions of the country (data triangulation). The Kappa score for assessing congruence of coding between coders was 0.95.

Results

The final study sample of 20 PIs represented 24 different cohorts, and included men and women from several different racial/ethnic communities (approximately one-quarter were from minority communities). They represented a wide range of ages, although few were younger than 55 years old. Epidemiology was the academic discipline of the vast majority of those interviewed, although a few
were trained in medicine or other disciplines, or had training in more than one discipline. The public health research infrastructure overseen by this relatively small group of PIs is enormous. Collectively, the 20 PIs interviewed for this study represent longitudinal health data on nearly 3.2M individuals, or roughly one out of every 100 people in the U.S. This includes data on approximately 400,000 African Americans and 120,000 Latinos, as well as many other ethnic communities (Figure 1). Below we report on key findings with respect to key questions asked of PIs. Supplementary tables 1-4 summarize key themes identified and a representative quote for each theme.

**Importance of Religion and Spirituality to Understanding Human Health**

We began our interviews by asking PIs how important they believed R/S were to understanding human health and risk of disease. We provided the working definitions of R/S noted above. Of the 20 PIs interviewed, nine felt that R/S were important psychosocial influences that likely had a significant positive impact on health. Another eight PIs were open to the possibility that R/S influences could be important, but believed “the jury is still out.” Only three PIs believed that R/S were not important constructs to study in understanding human health.

*Positive views about the importance of R/S in understanding human health*

Five sub-themes emerged regarding PIs’ positive views on R/S and health. These included: (1) R/S as a critical locus for resilience and personal identity; (2) R/S as an important source of communal support; (3) R/S promoting healthy behaviors; (4) R/S being especially important in minority communities; and (5) barriers to R/S research.

PIs most often connected R/S as important resources for resilience with stress, but also alluded to a powerful, transcendent dimension of life and identity that is difficult to measure. This reflection on spirituality by one epidemiologist is illustrative of the PIs who held this view:

As an epidemiologist, I think of it [spirituality] primarily as a modulator of stress, but it’s more than that. There are positive social networks, and support, and healing connected with [spirituality], and sort of self-affirmation about who I am, what I’m doing, that almost for sure have physiological effects. So I look at [spirituality] as part of complex physiological networks dealing with pathways that are almost for sure related to cardiovascular disease.
PIs also focused on R/S as integrally linked to community and social support. As one PI said, “My personal sense is that [spirituality] is an integral part of life, which might also link into social support, because it’s hard to separate the two.” This PI described spirituality and social support as “two key sorts of primordial factors associated with disease outcomes.” Others viewed religious communities as providing critical social support based on their own experience within religious communities, regardless of their own religious beliefs. As one self-described agnostic Jew described in explaining why she believes R/S “definitely affect health”:

The social support people get from church is tremendous. My own personal experience [as someone who is agnostic] makes it hard for me to judge what the added coping and support and well-being people get from their religious beliefs is, as opposed to the social framework. But for me, you know personally, going to a synagogue when I was [experiencing a personally difficult time] was a tremendous social boon... And so I do believe that the support that comes from that allows people to cope better with challenges, to be less overwrought, to help them get things done, to reinforce messages about healthy lifestyle. So you know, from that perspective, I think it’s a no-brainer [that R/S affects health].

A third group of PIs viewed R/S as influencing health primarily through promoting healthy behaviors, such as diet and exercise, and curb unhealthy behaviors, such as smoking and alcohol use:

Seventh Day Adventists have a whole pattern of behavior based on their religion that influences their risk of disease, as do people of Eastern sects, in Hindus and other groups, have very specific sorts of prescribed behavior patterns based on religion. So it can be very powerful.

A fourth important sub-theme was PIs’ belief that the impact of R/S on health likely differs across racial/ethnic communities. Several PIs believed that R/S influences might be especially important to study in African-American or Hispanic/Latino communities, where religion plays a central cultural role. Regardless of their own personal R/S beliefs or practices, PIs whose cohorts had large numbers of minorities were especially likely to believe that R/S are important influences on health. One PI whose cohort included large numbers of African Americans explained:

I think it [religion and spirituality] would be more important to study in minority groups, who are
under other stressors... We’re putting more emphasis on that [religion and spirituality] as factors that moderate stressors or factors that could turn things around, and thus improving the quality of life or life expectancy, or even prevent the recurrence of certain diseases... So for African Americans, religious activities are really, really important.

Lastly, nearly all of the nine PIs who reported believing that R/S likely had important influences on health noted dissatisfaction with the quality of existing R/S research, while also noting barriers to pursuing high-quality epidemiological research on R/S and health. Some had even engaged in R/S research, but had experienced a bias against R/S research among their colleagues. One PI described sharing some interesting preliminary results from a pilot study on R/S, but found her colleagues decidedly unenthusiastic about pursuing this area of research: “So though the question of spirituality might seem reasonable to us, spirituality is something that many members of my team might go, ‘Blah!’”

Nearly all PIs who believed R/S were important influences on health discussed the limitations of existing R/S measures, seeing them as “all over the place,” lacking rigorous validation, or being insufficient to capture such a complex phenomenon. Despite their criticisms, PIs were very engaged in thinking about what they saw lacking in existing measures, often offering recommendations for how to improve them. For example, one PI suggested a shift in focus of R/S measures:

I think the types of questions where you get at how R/S affects people, like strength and comfort questions – where you get at the resulting feelings from your religious participation – I think those are probably more important than your habit of going or not going to church, which can just mean a lot of different things.

PIs also noted the lack of consistent measures across cohorts, making replication of results in other cohorts impossible.

Equivocal views regarding the role of R/S in health

Eight of 20 PIs interviewed believed that R/S influences may significantly affect health, but felt “the jury is still out.” Sub-themes within this larger theme included: (1) insufficient evidence to determine if R/S influence health, and (2) the lack of a sufficiently nuanced conceptual framework that addresses
the complex ways in which R/S may affect important health outcomes. They emphasized the lack of high-quality (i.e., prospective) studies demonstrating that R/S does indeed have a strong direct or modifying effect on disease etiology. Of particular concern were the lack of longitudinal studies that included the full range of expected covariates in the analysis, and the lack of replicated results. PIs in this group were not dismissive of R/S research, but simply felt that the field of R/S research had not yet produced the quality of evidence that the epidemiological community would find compelling: I think the findings on spirituality measures have been sort of mixed in relation to disease outcomes. Well, that's the nature of our field, isn't it? [laughs] A lot of factors, when you look at the data, are mixed. And it's only after a crucial body of evidence has emerged that you're able to look at the totality of studies... So right now, the field is not mature. You don't have a lot of studies in this area, and findings are mixed. Many PIs also believed that the field had not yet presented a robust and cohesive conceptual framework for research on R/S and health, pointing to a failure to study R/S influences in conjunction with the biological, environmental, and other psychosocial factors already established as affecting the etiology of a particular disease. They emphasized the need for R/S research to both include biological variables in analytic models and conceptualize R/S influences within the context of known biological pathways or mechanisms at play in the studied disease. One PI explained this challenge, using the example of cardiovascular disease:

As you know, CVD is a lifecourse disease, and it's a lifestyle disease...we understand all this is a constellation of biological phenomena that translate into an event on a particular day, in a particular time, in a particular moment in a person's life. But, you know, it follows if you look back - there's a cascade of events, which begins with the genetics that you are born with, and a series of environmental factors that you're exposed to, including the built environment, and including your socioeconomic position over the lifecourse. And on top of that, a number of bio-behavioral risk factors. So religiosity is one of a gamut of [influences] on a complex risk factor. So I think one of the challenges is going to be to build a framework, a thesis, or a scientific model that places religiosity in the context of a lot of other pathways that eventually condenses into a biological model.
Beliefs that R/S are not importance influences on human health

Only a handful of PIs (3/20) believed that R/S influences were simply not important domains to study in health research. Subthemes included: (1) a lack of compelling research demonstrating importance of R/S in understanding health; (2) beliefs that R/S measures are merely proxies for other, more critical factors influencing health; (3) an inability to identify plausible mechanisms through which R/S might influence health; and (4) an inability to imagine how R/S research could generate new knowledge that could lend itself to interventions.

While this small group of PIs similarly criticized the quality of R/S research to date, these PIs tended to express a general discomfort with the domain of R/S in general, often because they were not spiritual persons themselves. As one PI explained, “As somebody who has a hard time picturing what it means to be praying, it’s hard to know what those many hours are doing...I just don’t know what it’s a measure of.”

To the extent that R/S influences were shown to be significant, such as church attendance, they believed that any potential influence of R/S could be better captured by other measures that focused on the downstream effects of individuals’ spirituality, such as social support or stress reduction. As one PI explained:

I don’t feel like, personally, that these [R/S] variables are very important variables to be looking at – if anything, they are proxies of something else that I would prefer to get at. So if they’re proxies of social support, I’d prefer to get a measure of social support. If they’re proxies for stress mitigation, I’d like to get at more of a proxy of stress.

This group of three PIs had difficulty envisioning a potential biological pathway or mechanism through which spirituality might affect disease etiology, and thus they viewed R/S as biologically irrelevant. A PI whose work focuses on cancer captures this sentiment: “This exposure couldn’t possibly cause or protect one from cancer, therefore we don’t see this [the role of R/S in health] as a reasonable scientific question.”

Like other groups, these PIs had difficulty imagining how R/S research could be translated into public health interventions, but were consequently pessimistic about R/S research. One PI, for example,
despite acknowledging the robust studies on church attendance and mortality, stated, “I mean, what are you going to do? Prescribe that people start going to church??” The inability to envision how knowledge about R/S and health could be translated into appropriate interventions greatly reduced the value of R/S research among this small group of PIs.

**Rationale for Collecting Extant Measures of Religion or Spirituality**

Although there are relatively few R/S measures collected by U.S. prospective studies to date, 17/24 cohorts represented by this group of PIs had collected measures of religious denomination or religious service attendance in the past, but few had collected any additional measures. We explored with PIs their rationale for collecting the R/S measures they had collected to date, or reasons why their cohort has not collected any R/S measures.

*Reasons why PIs collected the R/S measures they did*

Among those whose cohorts had collected previous R/S measures, three subthemes emerged: (1) study teams were persuaded by recent literature; (2) measures collected reflected interest of a particular team member; and (3) R/S were known to be important to the particular ethnic communities represented in their study.

PIs who were persuaded by literature universally cited studies demonstrating a significant inverse association between church attendance and mortality (13, 15). Some also emphasized hypotheses that R/S influence healthy lifestyle behaviors, which leads to better health outcomes:

You know, the other concept that we had, which I think is still valid, is that religion could be considered in one sense to be the parent, or if you like, to be behind behaviors. In other words, religion is driving the dietary behaviors in the path, which in turn results in some differences in chronic disease.

Second, PIs reported that the decision to collect particular R/S measures was due to the advocacy of a particular team member, or even a doctoral student, who wanted to study R/S influences on health and had succeeded in making the case to add R/S measures to their survey. One PI explained:

In every case, you have advocates. You have folks who say, here’s our rationale. Here’s why we think it’s important...And, you know, just thinking about quality of life, thinking about social support,
thinking about the importance of spirituality in a global sense, of how it would contribute to us really understanding not only the sort of overarching factors associated with things like cardiovascular disease, but also recognizing that we have a very diverse cohort in which spirituality may mediate or may be protective differentially in one of our racial/ethnic groups. So that’s the overall rationale for inclusion of spirituality [measures].

Lastly, PIs explained that they had collected measures of R/S previously because of the importance of R/S to particular communities included in their cohorts, especially in cases where cohorts included a sizable proportion of African Americans and/or Hispanics/Latinos. One PI whose cohort included large numbers of African Americans explained that including measures of spirituality “was pretty important to do for any study that was thinking about getting a thorough assessment of African Americans’ health and disease.” She continued:

I think again, you can’t speak for all African Americans, but in general, particularly in the South, you are speaking about a society that sees religion and spirituality as a central aspect of life. And that, I think, has been true for generations, and is impressively true today. I think if you were to ask 100 African Americans in the South whether they attend church regularly, I would say that 85 of them would say yes...And I think most feel that... one of the great methods of dealing with stress is to turn to turn to God, to turn to a higher power...These are very, very important ideas and ways of life, really. And [African Americans] do see them [R/S] as ways of coping, but they see, beyond that, that this is fundamental to how life should be lived.

Other PIs whose cohort include racially diverse participants echoed this sentiment. One explained:

We have...African-Americans on our advisory board who have expertise in various areas. And we also have some Black investigators, and some Black staff, and even if we hadn’t, we would have been well aware of the fact that in this country anyway, African-Americans tend to be religious, or to take part in religion. That’s a big part of their lives. And we’re aware that there’s a body of literature suggesting that religiosity or spirituality may be protective against the occurrence of certain diseases, or if not against the occurrence, it might be good for prolonging survival. So for all those reasons, we were interested in having some questions on spirituality or religious practices in [our cohort study].
Reasons for not collecting R/S measures to date

In exploring why certain cohorts had not collected any R/S measures thus far, 4 sub-themes emerged: (1) R/S measures did not “meet the bar” for inclusion in epidemiological research; (2) study team’s lack of knowledge about, or self-proclaimed bias against, R/S research; (3) difficulty imagining how research demonstrating an effect of R/S could be translated to interventions; and (4) lack of NIH funding in this arena.

PIs whose cohorts had not collected any R/S measures to date viewed R/S research as adding little explanatory power beyond that provided by social support measures, as captured in this comment: “You’d expect social support to have an impact on a number of domains. But, from my vantage point, I’ve not seen evidence that [R/S] is at least as strong at this point in time.” The robustness of R/S measures in the field were not seen as “meeting the bar” for inclusion in cohorts’ national surveys. As one PI explained:

I work in the large population arena. That doesn’t mean that everybody has to. And there’s certainly insights that can come from small populations, but to be able to be translated into large population research, the [R/S] field has to evolve to the point where we can actually capture what the experts in the field feel are the true measures of those domains in a rigorous way, and yet, in a way that’s really convenient.

Again, several PIs talked about their own bias or the bias of others against R/S research. They described being uninterested in R/S research because they could not imagine how results showing a protective effect of R/S on health outcomes could be applied to improving population health, and thus concluded that the domains of religion and spirituality were “outside the scope of public health.” As one PI described:

With [R/S research on church attendance], I just wonder what the message is...is the message that people should find God? Or go to church more often? From a personal background, I would feel uncomfortable with public health messages that had to do with religious matters.
Lastly, PIs whose cohorts had not yet collected any R/S measures addressed the lack of interest in R/S among funders, particularly NIH. They described how Requests for Applications (RFAs) influence the kinds of research conducted, particularly in times when funding is tight, explaining that if R/S research was not a priority for NIH, researchers would not study it. As one PI put it, “We had no funding for them (R/S measures); nobody was writing a specific grant related to those hypotheses.”

**Likely Pathways or Mechanisms through which Religion and/or Spirituality Operate to Affect Health**

Among 17 PIs who believed R/S were potentially important constructs in understanding disease etiology, we explored the various biological mechanisms or pathways through which they believed R/S might influence health. By far, the most common mechanism discussed was R/S as a vehicle for garnering social support and coping with stressful life situations. As one PI said, “I think we are talking about things that are generally incorporated into the stress pathway, and so I would think of the autonomic nervous system. I would think of the HPA axis right off the bat.” Another PI elaborated on this perspective, rooted in his cohort study’s own findings:

Probably the most immediate and obvious is related to the stress pathways. And they are related to physiology all over the body – immune function, endocrine function – that would potentially interface with pathways related to cancer, but not as directly as to cardio-metabolic outcomes, one would think. So cortisol, epinephrine, those pathways would be presumably the most immediately directly affected it [R/S], whether through hypothesized immune markers, which do seem to be related, secondarily at least, but perhaps primarily to the stress pathway.

Another PI put it this way: “I think it [spirituality] might be a modifying factor or a mediator. Like social support, for example, mediates certain biological relationships, or even genetic relationships.”

Some PIs were convinced that R/S has an effect on coping with stress through their own experience with chronic disease patients. One PI who had participated in several different studies with diabetes patients offered this observation:

My personal view is that [religion and spirituality] do reduce the stress tied to [illness] when you are, - -when you surrender to the notion that there is a plan. No matter what happens, there is a plan that
you may not fully comprehend, but you put your trust in a higher power that things will be OK.

The second most-cited mechanism or pathway PIs envisioned was that R/S may affect health-related behaviors, such as motivating individuals to refrain from smoking or drinking, or encouraging healthy behaviors, such as exercise or healthy diets. They viewed this behavioral mechanism in two ways:
either a “proscriptive function of R/S” – delineating acceptable behavior – or an “affirmative function of R/S,” helping people believe that they are worth taking care of as shown in religious teachings (e.g., they are “children of God,” or their body is the “temple of God”). One PI describes the proscriptive function this way:
The jury is still out [regarding how R/S affects health], but I think that one can pretty reasonably postulate that some of these [R/S beliefs or traditions] might be driving dietary behavior and so may not be confounders in that sense, but rather the dietary behavior might mediate, in part, the effect of religious variables.

Another PI articulated what we call the “affirmatory function of R/S,” encouraging a sense of self-worth and appreciation for life:
I think it’s well accepted that behavior is critical, and behavior is rooted in something. And if people are spiritual and feel that, one, that their personal existence is important to them, and two, [their personal existence] is important to others, that they’ll often feel more of a responsibility to take care of what they’ve been given...that they see life as a gift, then they are more likely to respect that gift.

Several PIs felt that R/S were definitely important psychosocial constructs, but had more questions than answers regarding potential mechanisms or pathways through which R/S might affect health:
What actually is it that’s helping them? Is it the fact that they have a spiritual leaders who can help them with their problems? Is it that they have people that they’re seeing, and it’s simply this group kind of support that’s helping them?...Or is it actual belief in God actually changes something in the brain, or wherever?...Well, [stress] is certainly one pathway. But I don’t know enough about the biology to express an opinion about what other pathways may be involved. But there probably are other pathways. I mean, there always do seem to be multiple pathways.

**What Would PIs Need to See to be Persuaded to Collect New or Additional R/S Measures?**
We concluded the interviews with a discussion of the kinds of evidence that PIs would find persuasive in demonstrating that R/S significantly affect health, and thus would encourage them to collect new R/S measures in the future. While PIs’ attitudes towards R/S research varied, all PIs interviewed articulated a strikingly similar set of criteria that R/S researchers would need to meet before prospective cohort PIs would be persuaded to incorporate R/S measures into ongoing data collection efforts. Five themes emerged: (1) the need for high-quality, prospective studies that include all appropriate covariates, replicated in at least one other cohort; (2) the need to posit a plausible biological mechanism through which R/S operate to affect health outcomes; (3) the need for well-validated R/S measures, collected in common across multiple cohorts; (4) the need to address bias against R/S research within the epidemiology research community; and (5) the need for NIH funding for R/S research.

*High-quality, prospective studies replicated in at least one other cohort*

The most foundational requirement cited was that more high-quality, prospective studies of R/S be conducted that demonstrate a significant influence of R/S on important health outcomes. PIs also emphasized that these analyses needed to include the full range of covariates expected in high-quality studies of a given condition. Few PIs were aware of any prospective R/S studies meeting their bar for high quality beyond those associating church attendance with reduced mortality, and characterized existing R/S research as being dominated by cross-sectional studies with variable findings. As one PI put it, “Any more association studies will just add to the confusion.”

*Posit a plausible biological pathway or mechanisms through which R/S affect health*

Virtually all PIs emphasized the need for R/S studies with significant results to at least posit, and eventually demonstrate, a plausible pathway or biological mechanism through which R/S operate to affect health. As one PI plainly stated: “We need studies that have some kind of biologically relevant hypothesis.” One PI who studies cancer captures this emphasis:

What would be very persuasive to me would be some well-designed research that showed biological changes, or some physiologic effects, that were associated with people’s religion or spirituality, on pathways that were meaningful for cancer – cancer pathways.

PIs noted the increasing importance of biomarkers in understanding disease etiology, as biomarkers
were often seen as the critical link between the social constructs measured and the biological mechanism hypothesized to be at play. Incorporating biomarkers into R/S research would also demand a significant investment of resources. One PI explained that “what is needed are multiple questionnaires over time [that include R/S measures], with multiple blood samples that parallel it [to support biomarkers]."

**High-quality, well-validated measures collected in unison across cohorts**

One of the greatest challenges in advancing research on the role of R/S in health, voiced by the majority of PIs, was the difficulty of adequately defining the complex dimensions of R/S. They expressed a need for well-validated measures of R/S that are easy to collect across cohorts in order to facilitate replication of results. Here one PI discusses the challenge of measuring R/S influences compared to other more easily quantified influences on health, and the relationship between how easy a measure is to collect and how much it is studied:

For example, coffee is a habitual activity that a large number of people partake in. Very, very easy to measure, and thus we’ve got dozens or hundreds of studies on coffee! – almost every epidemiologist looking for something that’s either protective or is caused by coffee, though there’s no findings there...It’s easy to ask somebody what their coffee habit is. But it’s very hard to get at these kinds of things [R/S influences]...This [R/S research] is so ripe for epidemiological discovery if you can figure out how to measure it.

All PIs interviewed had been engaged in consortia that conduct pooled analyses across multiple cohorts, and experienced the problems of having different measures of the same construct across individual cohorts. Often, constructs not available across cohorts get dropped from the analyses altogether. If there are some measures across cohorts, but with varying levels of nuance, the measure is often reduced to the lowest common denominator of measurement. As this PI warns:

You’re going to lose quality if people don’t ask the question in a manner that you can pool across studies. We’re seeing that in everything we do right now, you know? And sometimes we get down to just yes/no when we think about exposure to carcinogens, or hormones, or even diet, whatever. We get down to yes/no and we don’t get anything about dose, dose intensity. Because everybody asks it
Several PIs also pointed out that the need for sufficiently robust body of high-quality research before it makes sense to move towards consensus regarding which measures are important to collect. Timing is important. As one PI explained:

Well, you know, there are reasons to move towards consensus, because it makes it a lot easier to harmonize the data. And so, that’s the pro. The con is, if you don’t choose the right set of questions, then there really isn’t a fit. So I think it’s a bit early to be moving towards a consensus [on R/S measures]. But I think that first we need to have some more actual studies that provide results.

**Address bias against R/S research among epidemiologist**

Several PIs also noted that even if a body of high-quality R/S research evidence from prospective studies “met the bar” of world-class epidemiological research, there would still be bias against R/S research within the epidemiological community. PIs offered various explanations for such bias: “For one thing, because most of the investigators are biologically inclined – you know, to look for more biological or genetic explanations of things.” This PI further believed that this focus on biological causes of human disease was likely due to the lack of religiosity among PIs themselves: “My anecdotal impression...is that they [PIs] are not religious. Probably there’s a bigger percentage of naysayers [about the importance of R/S to health] among scientist investigators than maybe other groups of people.” Others noted a tendency among many epidemiologists to view R/S research, along with other psychosocial research, as “soft science” unlikely to have a significant clinical impact. Some PIs believed the lack of R/S research was “just not on our colleagues’ radar,” even when studying populations known to have high levels of religiosity:

I mean, there is a group of people – the behaviorists – who are particularly interested in [R/S]. But it’s not very high on the radar, which I have to say is actually surprising, considering that, in the Hispanic community, for example, two-thirds [of the community] consider their religion either very or extremely important. It indicates that in terms of the population we’re studying, it is important. But the -- the researchers don’t give it the commensurate weight in looking at it research-wise.

**Increase the availability of NIH funding for R/S research**

Finally, PIs emphasized the central importance of NIH funding to support R/S research. Without
sufficient interest and commitment of NIH Institutes to advance research in this area, it is unlikely that PIs will use the limited space on their survey instruments to collect R/S measures. Prospective cohort studies are extremely expensive and mostly NIH-funded, and thus very driven by the research agenda advanced by NIH through various topical RFAs. Nearly all PIs interviewed were operating their research groups almost entirely on grant funding. With a difficult funding environment for researchers whose salaries are completely grant-funded, it is a practical concern to take their cue from NIH and invest in areas of research where future NIH funding is likely going to be awarded. As one PI explained:

I’m not sure if people would fund it (research on R/S and health). And when I say, ‘fund it,’ I mean at NIH. I’ve never applied for funding anywhere except through NIH. So I think it’s hard to come by... I think many of us would be interested in doing it [R/S research] if we could, but the resources are hard to come by.”

Discussion

Within the broad domain of psychosocial influences on health, research addressing the impact of R/S on health has received relatively little attention in epidemiological research, despite recent calls for R/S to be recognized as important domains in public health research (49). The public health “cost” of not appropriately assessing psychosocial influences on health, specifically R/S influences, is likely to differentially affect those in low-income and minority communities – groups with higher levels of religiosity. The relatively small number of prospective R/S studies to date is largely due to the lack of R/S measures collected within national prospective cohort studies. Cohort study PIs have enormous influence in shaping epidemiological research, yet little is known about their perspectives on R/S research. In this first national study of PIs’ attitudes regarding the role of R/S in health, we interviewed 20 PIs of NIH-funded cohort studies to analyze what kinds of evidence they would find persuasive in establishing a causal link between various R/S dimensions and important health conditions.

Despite diverse attitudes and beliefs regarding the importance of R/S as domains to study in health research, PIs were in almost complete unison in articulating the kinds of evidence they would find
persuasive in judging R/S research to be important and being willing to collect more R/S measures in their cohorts. Specifically, PIs called for more high-quality, prospective studies that include the full range of covariates that experts in a clinical area would expect to see, are replicated in additional cohorts, and posits a plausible biological mechanism or pathway through which R/S affects health. The limited number of R/S measures currently available within our nation’s prospective cohort studies makes it difficult to meet PIs’ foundational bar of conducting prospective R/S studies and replicating results in additional cohorts. In a recent analysis we undertook of R/S measures in 20 U.S. prospective cohorts, for example, while 13/20 and 10/20 cohorts collected church attendance and religious denomination, respectively, fewer than 5 of 20 cohorts collected more diverse and functional measures of R/S, such as participation in church social groups (4/20), finding strength or comfort in R/S beliefs (4/20), or using R/S to cope with stressful life situations (2/20). Beyond these, no other R/S measures have been collected by more than 2 out of the 20 cohorts (https://atlas.mgh.harvard.edu). While other national surveys collect R/S measures from large national samples over several years, these datasets often do not include biomarker data or the full range of covariates needed to conduct an epidemiological assessment of risk of diabetes, CVD, mental illness, cancer, or other high-priority chronic conditions.

There are further challenges in demonstrating a plausible biological pathway or mechanism through which R/S operates to affect health outcomes. Such analyses typically require biomarkers that reflect activity within specific biological pathways, which are expensive to collect (e.g., $400/sample for the Illumina 850K array or $700/sample for the SOMAscan proteomic assay). Without using cohort study data where biomarkers have already been collected or obtaining NIH funding, it will be extremely difficult for researchers to conduct such sophisticated analyses on the role of R/S in human health. One striking finding from our study is the extent to which the selection of measures to be collected by cohorts is a nonlinear process determined by the interests and biases of particular research teams. The field of research on the role of R/S in disease etiology is in a nascent stage, and thus needs champions within established epidemiological cohorts to convince colleagues to commit resources to collecting the R/S measures needed to test R/S hypotheses.
Our study has several limitations that should be mentioned. First, as with all qualitative studies, this is not a systematic empirical assessment of PIs’ attitudes towards R/S research that can be generalized to the community of PIs of cohort studies nationally. Rather, our goal was to deeply explore the attitudes, beliefs, and perspectives of the 20 PIs interviewed, who are national leaders in the field of epidemiology, and to better understand what gives rise to these attitudes and beliefs. Second, while the 20 PIs interviewed represented diverse ethnicities, ages, and clinical domains of interest, they may not fully capture cultural and sex differences in PIs’ attitudes towards R/S research. According to NIH institute websites, 61 cohorts studies are currently funded by NCI and 9 are funded by NHLBI. Our results reflect roughly a quarter of all NIH-funded cohorts, but future research could survey PIs nationally to quantitatively assess a broader array of perspectives.

Despite these limitations, this study provides the first assessment of cohort PIs’ attitudes and beliefs regarding the influence of R/S on disease etiology, and identifies challenges for the field of R/S and health research from the perspective of these thought leaders in epidemiology. Results of this study provide a roadmap for future R/S research investigating the impact of R/S on disease etiology in the context of U.S. prospective cohort studies.

Conclusion
Given the high levels of religiosity among low-income and minority communities in the U.S., and the concomitant high prevalence of chronic illness among these groups, better understanding R/S as resources for resiliency may provide new insights into the reduction of health disparities within these populations. As more studies demonstrate clinically significant effects of R/S on important health outcomes, including biomarkers to demonstrate a mechanism of effect, PIs may become invested in collecting a limited set of R/S measures in unison across cohort studies. Such a development could usher in a new generation of research demonstrating the complex ways in which individuals’ R/S beliefs and practices intersect with their biology, but only if the NIH begins funding R/S research at the level of other important psychosocial influences affecting human health.

Declarations
**Ethics approval and consent to participate**
Institutional Review Board approval for this study was obtained from the Partners Human Research Committee (Protocol # 2015P000014/MGH). Verbal consent was given by participants, although this study was deemed to be exempt from continuing IRB review by the Partners Human Research Committee.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was funded by a grant (#48424) from the John Templeton Foundation (AES). The funder had no role in the design of the study; the collection, analysis, and interpretation of data; nor in the writing of the manuscript.

Authors' contributions

AES and TB completed interviews and interview data analysis. AES wrote initial drafts of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors wish to thank Bobak Seddighzadeh, Alexandra Nichipor, and M. Austin Argentieri for their superb research assistance. We also wish to thank Sylvia Smoller and Martha Daviglus for valuable comments on an earlier draft of this manuscript.

Abbreviations

PI: Principal Investigator; R/S: Religion and/or spirituality; NIH: National Institutes of Health; GWAS: genome-wide association study; CoSSH: National Consortium on Psychosocial Stress; PHRC: Partners Human Research Committee.

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Figures

Figure 1

Total number of study participants represented by participating PIs’ cohorts, including breakdown by race/ethnicity.

Supplementary Files

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