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Perspectives of Prospective Cohort Pls on the Importance of Psychosocial Stress in Human Health: A Qualitative Study

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COMPETING INTERESTS

The authors declare no conflicts of interest.

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ABSTRACT

Background. Psychosocial stressors are often experienced more frequently by racial/ethnic and socioeconomic minority populations in the U.S., and understanding the mechanisms through which psychosocial stress influences human health may also provide crucial insight into the production of U.S. health disparities. Despite this promise, these factors are infrequently and unsystematically collected in U.S. prospective cohorts studies.

Methods. We sought to understand prospective cohort PIs’ attitudes regarding the importance of psychosocial influences on disease etiology, in order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research. One-hour, semi-structured qualitative interviews were conducted with 20 PIs representing 24 NIH-funded prospective cohort studies in the US, collectively capturing health data on 1 in 100 Americans.

Results. Most cohort PIs see psychosocial stress as an important area to investigate to better understand disease etiology, and agree that this research will be crucial for developing potential public health interventions. Virtually all PIs emphasized that future research will need to elucidate biological and behavioral mechanisms if it is to demonstrate the value of psychosocial research to the epidemiological community more broadly. A lack of pertinent funding mechanisms and a lack of consensus on optimal scales and measures of psychosocial stress were identified as barriers to advancing psychosocial research.

Conclusions. Our interviews emphasized the need for high-quality, longitudinal studies that investigate mechanisms and pathways of psychosocial stress, effort among epidemiological cohorts to broaden and harmonize the measures they use to facilitate replication of results, and the need for targeted NIH funding to study these domains.

KEYWORDS

Qualitative Research; Epidemiology; Public Health; Social Medicine

ARTICLE SUMMARY

Strengths and Limitations of the study

- Psychosocial factors are infrequently and unsystematically collected in prospective cohort studies, with little consistency in measures collected between cohorts.
- We conducted qualitative interviews with 20 cohort study Principal Investigators (PIs) to better understand barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research.
- Interviewing PIs from major cohort studies is a strategic choice that provides insight into the priorities and concerns of those who decide the research priorities for 24 U.S. cohort studies that collectively include roughly 3.2 million Americans.
- Findings from this qualitative study provide a roadmap for how to conduct future, high-impact epidemiological research on psychosocial stress.
- Findings from this qualitative study can also be used as a guide on how to engage leading U.S. cohort studies in future psychosocial research, either through submitting proposals to use existing cohort data or submitting for future funding to collect additional psychosocial factors in cohorts.

function both as a key factor driving disproportionate burdens of disease among underrepresented populations,¹³⁻¹⁵ and also as a key mediator or pathway through which experiences of inequality – such as difficult socioeconomic environments^{16,17} or poor sleep,¹⁸ among others – influence disease or disease-related behaviors.

In order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research, we conducted qualitative interviews with 20 Principal Investigators (PIs) representing 24 different National Institutes of Health (NIH)-funded prospective cohort studies in the U.S. These interviews were used to probe PIs' beliefs and opinions on the impact of psychosocial factors on health and identify the evidence they require to merit adding additional assessments of psychosocial factors in future waves of data collection within their cohorts.

METHODS

Participants and Recruitment

A list of 30 different prospective cohort studies that had received funding from 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. The PI of each study was invited via email to participate in this qualitative study. None of the study investigators had had a previous relationship with the PIs. Telephone calls were scheduled with those interested in learning more, during which PIs were provided with additional information about the study to

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3 168 facilitate informed consent and again invited to be interviewed then or on a future date of their
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6 169 choosing. PIs who agreed to be interviewed were offered a \$100 honorarium. We followed
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8 170 these procedures until we reached our study goal of 20 PI interviews. Only one PI with whom
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11 171 we discussed the study declined to participate. All but two participating PIs refused the
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13 172 honorarium.

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18 174 ***Patient and Public Involvement***

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23 176 As this was a targeted investigation into the perspective of specific cohort study
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25 177 Principal Investigators, no patients or members of the public were involved in the design or
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28 178 recruitment of our study, nor in the dissemination of results. Our semi-structured interview
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30 179 guide was developed by the study team, with input from several investigators participating in
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33 180 the National Consortium on Psychosocial Stress, Spirituality, and Health (COSSH).

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37 182 ***Data Collection***

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42 184 One-hour, semi-structured interviews were conducted with each participating PI by the
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45 185 Principal Investigator of our qualitative study (AES) or jointly by two members of the study
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48 186 team (AES and TAB, both female PhD-level research investigators) in 2015. Questions addressed
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50 187 PIs’ experiences with and exposure to research on psychosocial stress; reasons why their cohort
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52 188 has collect psychosocial stress measures in the past; assessment of the quality and value of
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55 189 existing psychosocial stress research; assessment of the importance of psychosocial stress in

understanding disease etiology; beliefs regarding the pathways or mechanisms through which they imagine psychosocial stress might operate to affect human health, if at all; and the evidence they would need to see before being willing to invest additional cohort resources in collecting new psychosocial stress measures. Based on our team's previous work,¹⁹⁻²⁴ we anticipated that 20 individual interviews would be more than sufficient to achieve thematic saturation.

Data Analysis

All interviews were recorded and transcribed. Transcripts were analyzed using a grounded theory approach.^{25,26} 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.^{24,26,27} 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.

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211 Many steps were taken to maximize dependability (consistency, reliability) and
212 credibility (the truth of findings, internal validity) of study conclusions.²⁸ We incorporated
213 triangulation at two levels: (1) involving a multidisciplinary research team in coding and analysis
214 (investigator triangulation); and (2) including PI participants from diverse communities and
215 disciplines whose cohort studies include participants from diverse racial/ethnic communities
216 and geographical regions of the country (data triangulation). The Kappa score for assessing
217 congruence of coding between coders was 0.95.

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219 **Ethics Approval**

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221 Institutional Review Board approval for this study was obtained from the Partners Human
222 Research Committee (Protocol # 2015P000014/MGH).

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224 **RESULTS**

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226 The final study sample of 20 PIs included men and women from several different
227 racial/ethnic communities, although the vast majority were white. PIs represented a wide range
228 of ages, although few were younger than 55 years old. Most PIs had led only one prospective
229 cohort study in their career, although some had served as PI for more than one study.
230 Collectively, the 20 PIs interviewed for this study represent longitudinal health data on nearly
231 3.2M individuals across 24 cohorts, or roughly one out of every 100 people in the U.S. This

includes data on approximately 400,000 African Americans and 120,000 Hispanics/Latinos, as well as many other ethnic communities (**Figure 1**).

Importance of the Psychosocial Domain

First, we sought to understand PIs' views about the importance of psychosocial stress influences on health. When asked about the importance of psychosocial measures more broadly, for example, one PI responded this way:

I mean, I think it is very, very important. We've tried to pay a lot of attention to it in our own cohort...I think it's very important to pay a lot of attention to this, because I feel that many psychosocial variables are definitely modifying factors for disease risk, and can also be causally associated.

PIs with clinical experience often cited their observations of the influence of psychosocial experience on their patients' outcomes: "I think it's based on my clinical experience...if you don't address the psychosocial factors, you'll never be able to help improve that person's treatment, and their care for diabetes." Those with clinical experience also seemed to appreciate the complex ways in which psychosocial factors interact with other "traditional" risk factors:

Certainly my feeling is that there's probably some complex interplay between psychosocial factors and, for lack of a better word, more traditional factors -- say, for instance, a blood level of cholesterol or blood pressure...In my clinic, I can certainly see that some of these psychosocial factors have enormous impact on the other potent, traditional risk factors.

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Others viewed psychosocial measures in general as “soft” measures that would never be as informative as “hard” biological measures, but even these PIs believed that to ignore psychosocial influences would be a mistake:

This [psychosocial influences] is not a solid measure of exposure. But I do think that to ignore it, when you’re talking about symptoms and presentation of disease, is a mistake, because it’s all together...I think it all goes together to create this person’s sense of well-being, and you can’t ignore it.

Others noted tensions within the field of epidemiology regarding the importance of psychosocial factors in disease etiology, particularly regarding the extent to which psychosocial factors were captured in other measures of behavior or social support already collected. As one PI explained:

I think there’s two camps...The skeptics feel it’s not an independent risk factor, and you can account for it with all the other factors and behaviors like smoking, alcohol use, etc. But there’s a very strong camp that believe that these are upstream of the lifestyle behaviors, and if you don’t measure them correctly, you may be artificially saying that they are all explained by behaviors, and that they may actually be independently related to disease outcomes.

Despite a general acceptance of the importance of psychosocial stressors in health expressed by the majority of PIs, some were more positive about certain psychosocial domains over others. While PIs were often quick to accept the importance of measuring stressors such as social support, abuse, and discrimination, many were far less certain about the contribution of religion and spirituality (R/S), for example, since it has been less extensively studied in cohort studies. Among our PI informants, three believed that R/S were not important to study in research on human health, eight were open to the possibility that R/S may be important to

health but believed that the “jury is still out,” and nine felt that R/S likely had an important impact on health.

The need for studies on psychosocial stress and clinically relevant biomarkers

The vast majority of PIs suggested that for future psychosocial research to gain greater currency among epidemiologists, it will need to explore clinically relevant biomarkers in relationship to stress. As one PI put it, “I think the emphasis today in epidemiological sciences is to delineate a clear biological mechanism.” Some offered ideas about creative avenues for exploring these relationships: “I would love to see studies on the effect of psychosocial stress on the microbiome, because of stress’s influence on the immune system.”

When asked where they see the field of psychosocial research going, one PI responded, “I think it is moving into trying to be more anchored in actual biologic changes...to identify people who are actually more likely to have a biologic response in relation to some external stressor.” One PI noted that recent studies investigating psychosocial stress in relationship to biological variables are changing epidemiologists’ opinions on the importance of psychosocial stress to health:

Studying psychosocial factors and stressors is relatively new, and [was] met with a lot of skepticism until fairly recently... But I think what’s changed [is] the view somewhat is the fact that...there’s now biological evidence that stressors may affect various biomarkers.

Another PI detailed how psychosocial research should ideally be framed in terms of a biological pathway:

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3 309 I wouldn't require that you would have the whole pathway -- that is, exposure to
4 310 intermediates to health outcome -- because that's probably the kind of link
5 311 we're looking for in studies. But having something between the intermediate
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7 313 something along that initial pathway, I think would be very helpful to justify
8 314 doing measures in a cohort study.

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13 316 Although all PIs discussed the value and contribution of conducting future research to
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16 317 elucidate the biological mechanisms through which psychosocial stress operates, several also
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18 318 had concerns about potential directions this kind of research could take, particularly concerning
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21 319 genomics research. As one PI articulated, it's "a little frightening to think about genes and
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23 320 behavior, or genes and things in the psychological realm. You know, some sinister images can
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26 321 pop up...it frightens some people that, you know, you can look at a genome, characterize
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28 322 somebody, and discriminate against them." Others worried that genomics research with a focus
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31 323 on psychosocial stressors and biological mechanisms of disease might be used in the future to
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33 324 discriminate against minority groups studied in their cohorts, and that results might provide
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35 325 further biological justifications for racism in the hands of someone who doesn't understand the
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43 328 ***Psychosocial stress as an important domain for potential interventions***

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48 330 Roughly half of the PIs interviewed also discussed psychosocial research as potentially
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50 331 helpful in developing public health interventions. One PI articulated this particularly well:
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53 332 We've had half a century of risk-factor epidemiology that tends to focus on the
54 333 individual as the driver of behavior change. I think this field of stress and

psychosocial stress is one that can help us look at the social context and other environments in which people live, and help us think about interventions.

A third PI echoed this enthusiasm, but also expressed concerns about how to actually operationalize insights about psychosocial stress research for public benefit. As he explained, “So to the extent that observing that racial discrimination increases stress and can impact high blood pressure...that’s a useful, almost intuitive observation. But then what?...How do we then break that influence on health?”

PIs’ abilities to envision how psychosocial research would translate into improved public health interventions varied by the type of psychosocial domain discussed. Some PIs, for example, had difficulty seeing how R/S research could be used to develop interventions to improve health. As one PI explained:

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.

Challenges in the field

Despite expressing uniform appreciation for the potential of psychosocial stress as a factor influencing disease onset or survival, many PIs described a number of circumstances that they see as inhibiting their own cohorts, and the larger epidemiological community, from engaging in robust assessments of psychosocial stress.

Challenging funding landscapes

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Several PIs mentioned that despite their own interest or the interest of their colleagues, a lack of relevant funding mechanisms, or even a lack of certainty about future NIH cohort funding in general, has prevented efforts to investigate psychosocial stress. Several made off-hand comments similar to this one: “Oh, we’re always open to new projects. So we’d be happy to ask questions if there was funding available.” Many PIs also described that their funding organizations had specific scientific priorities and expectations for the parameters of their cohort’s questionnaires, which would limit their ability to add in survey questions on psychosocial stress. Several cohort PIs also noted that they do not currently have funding from NIH lined up for another wave of data collection.

Reproducibility and consensus surrounding measures of psychosocial stress

Several PIs noted that for researchers to be able to reproduce robust research on psychosocial stress and health, it will be a priority that multiple cohorts collect the same measures. Describing the field of psychosocial research at large, one PI recounted, “My sense is that...it’s still very broad. And different people are doing different types of psychosocial stressors...I’m hoping that the field might narrow a little bit if we’re able to do this kind of linkage [between cohort studies].”

PIs often articulated that this would necessitate pooled analyses across cohort and racial/ethnic groups: “I think the kind of data that I would like to see are large, multicentric, multiethnic cohorts, with reasonable duration of power -- of follow-up, with adequate

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3 380 statistical power, with appropriate characterization of the exposure with validated instruments,
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6 381 appropriate adjustment for multiple layers of confounding.” As another PI described, however,
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8 382 the downside is that “we always go back to the least common denominator when we pool. And
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10 383 to do gene environment interactions, you almost have to pool cohorts...You’re going to lose
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16 17 18 386 **DISCUSSION** 19 20 387

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23 388 The PIs we interviewed almost unanimously agreed that future research on psychosocial
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25 389 stress is likely important, but emphasized the need to elucidate the biological and behavioral
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31 392 stress. To conduct rigorous future research on psychosocial stress, investigators will need to
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33 393 have access to both robust and clinically relevant biological data as well as comprehensive
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37 395 Data are also needed at both the individual and neighborhood levels to properly assess a
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49 399 Our interviews also showed that many cohort PIs see psychosocial stress as an
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developing disease. For instance, one review outlined reasonably strong evidence that physical activity can blunt the cardiovascular response to psychosocial stress.²⁹ Despite this enthusiasm exhibited by PIs, our interviews also highlighted challenges to the feasibility of this research, in particular the lack of adequate funding and the lack of consensus on key measures to be collected and/or harmonized across studies.

Our study had several limitations worth noting. While the 20 PIs interviewed represented diverse ethnicities, ages, and clinical domains of interest, they may not fully capture the diversity in PIs' attitudes towards psychosocial research. According to NIH institute websites, there are 70 cohorts studies currently funded by NCI and NHLBI, and thus our results reflect roughly a quarter of all NIH-funded cohorts. 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 psychosocial stress on disease etiology, and identifies challenges for the field from the perspective of these thought leaders in epidemiology. Results of this study provide a roadmap for future psychosocial research to be conducted within epidemiological settings.

CONCLUSION

Looking forward, our interviews with cohort PIs emphasized that: (1) future research will need to investigate biological and behavioral pathways through which psychosocial stress influences disease; (2) funding bodies need to create funding mechanisms and requests for proposals that specifically support these types of analyses as a scientific priority; and (3)

psychosocial research will need to be carried out with a focus on building consensus within the greater epidemiological community regarding optimal scales and measures of psychosocial stress, in order to encourage reproducibility and improve power. By understanding the mechanisms through which psychosocial factors—including both stress and resources for resiliency—operate to affect vulnerability to disease across diverse populations, researchers will not only be able to better understand the etiology of many chronic diseases, but will also hopefully be better able to the production of health disparities in the U.S., and develop innovative strategies to reduce these disparities.

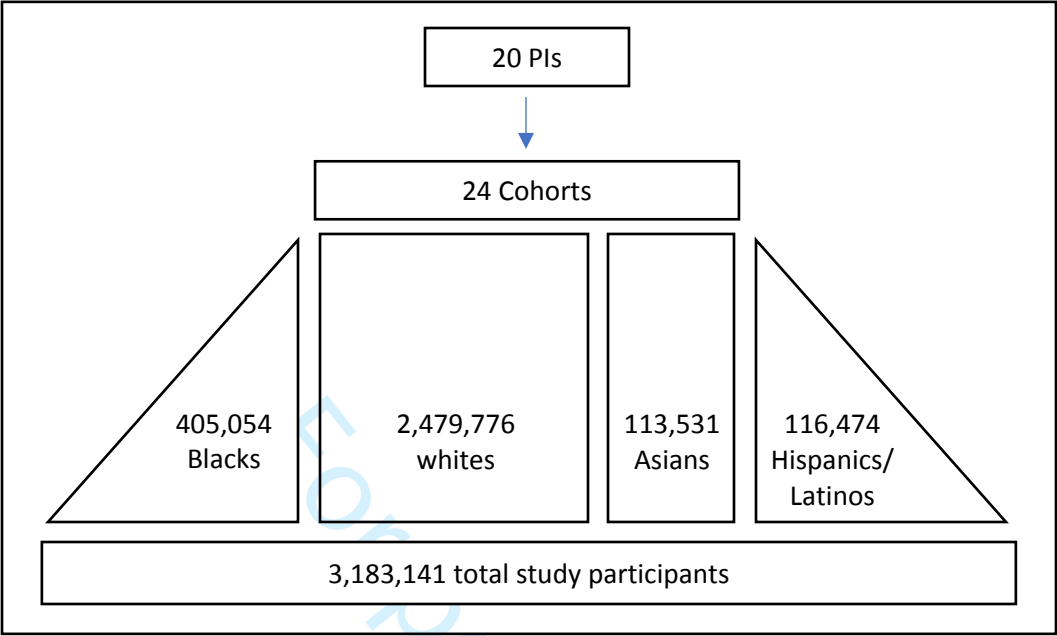


Figure 1. Total number of study participants represented by participating PIs’ cohorts, including breakdown by race/ethnicity.

AUTHORS’ CONTRIBUTIONS

AES and TB completed interviews and interview data analysis. MAA indexed qualitative transcripts, wrote initial drafts of the manuscript, and created figures. All authors read and approved the final manuscript.

DATA SHARING

Interview transcripts are available, upon reasonable request, by emailing the corresponding author directly.

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COREQ (Consolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
<i>Personal characteristics</i>			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	
Occupation	3	What was their occupation at the time of the study?	
Gender	4	Was the researcher male or female?	
Experience and training	5	What experience or training did the researcher have?	
<i>Relationship with participants</i>			
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
<i>Theoretical framework</i>			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
<i>Participant selection</i>			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	
Sample size	12	How many participants were in the study?	
Non-participation	13	How many people refused to participate or dropped out? Reasons?	
<i>Setting</i>			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	
<i>Data collection</i>			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	
Field notes	20	Were field notes made during and/or after the interview or focus group?	
Duration	21	What was the duration of the interviews or focus group?	
Data saturation	22	Was data saturation discussed?	
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	
Software	27	What software, if applicable, was used to manage the data?	
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	
Clarity of major themes	31	Were major themes clearly presented in the findings?	
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

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A Roadmap for Conducting Psychosocial Research in Epidemiological Studies: Perspectives of Prospective Cohort Study Principal Investigators

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COMPETING INTERESTS

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ABSTRACT

Background. Psychosocial adversity disproportionately affects racial/ethnic and socioeconomic minorities in the U.S., and therefore understanding the mechanisms through which psychosocial stress and resilience influence human health can provide meaningful insights into addressing U.S. health disparities. Despite this promise, psychosocial factors are infrequently and unsystematically collected in U.S. prospective cohort studies.

Methods. We sought to understand prospective cohort Principal Investigators' (PIs') attitudes regarding the importance of psychosocial influences on disease etiology, in order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research. One-hour, semi-structured qualitative interviews were conducted with 20 PIs representing 24 U.S. prospective cohort studies funded by the National Institutes of Health (NIH), collectively capturing health data on 1.25 of every 100 American adults. A hypothesis-free, grounded theory approach was used to analyze and interpret interview data.

Results. Most cohort PIs view psychosocial factors as an important research area to further our understanding of disease etiology, and agree that this research will be crucial for future public health innovations. Virtually all PIs emphasized that future psychosocial research will need to elucidate biological and behavioral mechanisms in order to be taken seriously by the epidemiological community more broadly. A lack of pertinent funding mechanisms and a lack of consensus on optimal scales and measures of psychosocial factors were identified as additional barriers to advancing psychosocial research.

Conclusions. Our interviews emphasized the need for: (1) high-quality, longitudinal studies that investigate biological mechanisms and pathways through which psychosocial factors influence health; (2) effort among epidemiological cohorts to broaden and harmonize the measures they use across cohorts, to facilitate replication of results; (3) and the need for targeted funding opportunities from NIH and other grant-making institutions to study these domains.

KEYWORDS

Qualitative Research; Epidemiology; Public Health; Social Medicine

ARTICLE SUMMARY

Strengths and Limitations of the study

- We conducted qualitative interviews with 20 prospective cohort study Principal Investigators (PIs) to better understand barriers and opportunities for greater inclusion of psychosocial factors in high-quality epidemiological research.
- Interviews and data analysis were performed by a multi-disciplinary team with training and expertise in both qualitative methodology and epidemiology.
- Interviewing PIs from major cohort studies is a strategic choice that provides insight into the priorities and concerns of those who decide the research priorities for 24 U.S. cohort studies that collectively include roughly 3.2 million American adults.
- Findings from this qualitative study provide a roadmap for how to conduct future, high-impact epidemiological research on psychosocial factors.
- Findings from this qualitative study can also be used as a guide on how to engage leading U.S. cohort studies in future psychosocial research.

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124 INTRODUCTION

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126 Psychosocial factors encompass a broad set of experiences, including childhood
127 adversity, isolation and loneliness, job-related stress, discrimination, trauma, religious and
128 spiritual experiences, social support, healthy neighborhoods, and many other dimensions of
129 life. While acute stressors normally elicit a healthy and adaptive stress response, severe or
130 prolonged psychosocial stress can lead to long-term dysregulation of the stress reactivity
131 system and disease.^{1,2} In particular, psychosocial stress has been implicated as a factor
132 contributing to cardiovascular disease,^{3,4} hypertension,⁵ type 2 diabetes (T2D),⁶ obesity,⁷ and
133 cancer,⁸ among other conditions. Likewise, positive psychosocial factors are also important
134 sources of resilience, support, and engagement that can have positive impacts on mitigating
135 stress and improving health.⁹⁻¹¹

136 Despite the important role that psychosocial factors may play in disease etiology, they
137 are not often assessed comprehensively in epidemiological research, particularly within
138 prospective cohort studies. Furthermore, a lack of precise and operational definitions and
139 clinical cut-off points for many psychosocial exposures has kept them from being incorporated
140 more routinely into clinical guidelines and practice.^{12,13} The influence of psychosocial factors on
141 disease etiology potentially encompasses both acute and chronic experiences, occurring
142 throughout the lifecourse in both childhood and adulthood, that may associate with human
143 disease through many different biological pathways.^{6,14} It is therefore important that
144 epidemiological research can investigate these domains more systematically.

Given that psychosocial adversity and stress are often experienced more frequently by racial/ethnic and socioeconomic minority populations in the U.S.,¹⁵ understanding the mechanisms through which psychosocial stress influences human health may also provide crucial insight into the production of health disparities in the U.S. Psychosocial stress may function both as a key factor driving disproportionate burdens of disease among underrepresented populations,¹⁶⁻¹⁸ and also serve as a key mediator or pathway through which experiences of inequality – such as difficult socioeconomic environments^{19,20} or poor sleep,²¹ among others – influence disease or disease-related behaviors. Likewise, fostering tools for psychosocial resilience and community building among underrepresented populations may also have a positive impact on health inequality.¹¹

In order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research, we conducted qualitative interviews with 20 Principal Investigators (PIs) representing 24 different U.S. prospective cohort studies funded by the National Institutes of Health (NIH). These interviews were used to probe PIs' beliefs and opinions on the impact of psychosocial factors on health, and were also used to identify the evidence they require to see before adding additional assessments of psychosocial factors in future waves of data collection within their cohorts. Taken together, the qualitative results that follow from these interviews inform a theory of change that provides a roadmap for future psychosocial research methods that we theorize will generate more prominent and impactful psychosocial investigations within epidemiological research.

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167 **METHODS**

169 *Defining “Psychosocial”*

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171 Psychosocial research encompasses many possible topics and is used in myriad studies,
172 although definitions are rarely offered. In this article, we begin by offering a definition, or at
173 least a point of reference, that will serve as a useful starting point for understanding
174 psychosocial dimensions of life. The American Psychological Association (APA) Dictionary of
175 Psychology²² lists several different definitions that can help us triangulate a working meaning.
176 “Psychosocial factors” are defined as “social, cultural, and environmental phenomena and
177 influences that affect mental health and behavior” (**Figure 1**). A psychosocial stressor, more
178 specifically, is defined by the APA as “a life situation that creates an unusual or intense level of
179 stress that may contribute to the development or aggravation of mental disorder, illness, or
180 maladaptive behavior. Examples of psychosocial stressors include divorce, the death of a child,
181 prolonged illness, unwanted change of residence, a natural catastrophe, or a highly competitive
182 work situation.”

183 This definition of psychosocial is broad, and encompasses experiences throughout the
184 lifecourse. It is important to note that the term psychosocial in itself does not refer just to
185 adverse life events, but more broadly to the confluence of social, cultural, and environmental
186 factors that come together to affect our biology, physiology, and psychology. Consequently, the
187 term psychosocial captures both negative stressors and positive sources of resiliency,

engagement, and community. This includes factors such as social support, religion and/or spirituality (R/S), and healthy neighborhood conditions.

Research Team

The research team members carrying out interviews (AES and TAB, both female, PhD-level) and data analysis (AES, TAB, MAA, BS, SNP, the final 3 of which were Masters-level/pre-doctoral level) were uniquely positioned as having training and experience in qualitative, clinical, and epidemiological research. The team was therefore well-suited to anticipate and address the dual demands of both maintaining qualitative rigor while also trying to gather and analyze information that is ultimately meant for an epidemiological audience.

AES directs a research center that conducts transdisciplinary research aimed at elucidating the underlying causes of health disparities, investigating ways to reduce health disparities, and addressing ethical and social implications of genomics research. TAB is a radiation oncologist with a longstanding interest in understanding the ways in which patients' religious or spiritual beliefs and practices influence their health care decision-making, particularly at the end of life. MAA is a medical anthropologist and population health researcher currently in the final year of a PhD in population health, and BS is a medical geneticist and MD candidate. Both MAA and BS have worked with AES over the past 5 years to conduct epidemiological and population health research on health inequality, with a particular focus on investigating psychosocial factors. SNP has training in cultural anthropology and is a

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3 209 DO candidate. She has conducted research with TAB for over 2 years focused on understanding
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6 210 the impact of religion and spirituality on health.
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8 211 The research team sought to mitigate bias stemming from any interests that the
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10 212 investigators brought to the investigation by using good interviewing practices in which
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13 213 questions were asked without providing examples or steering the discussion in ways that were
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15 214 apt to introduce bias. Data coding and analysis was carried out using a hypothesis-free,
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18 215 grounded theory approach such that themes and theories presented in this article were only
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20 216 those that emerged from the empirical data and are not reflective of previous priorities or
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23 217 interests of the investigators. These methods, in addition to data triangulation procedures, are
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25 218 described further in the Data Analysis section.
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30 220 **Participants and Recruitment**
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35 222 This study was carried out as part of a larger project investigating the perspectives of PIs
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37 223 on both psychosocial factors and R/S. PIs were contacted, recruited, and then interviewed
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39 224 about these two topics simultaneously. The results concerning R/S specifically are published in
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42 225 a separate manuscript (cite in press).
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45 226 Because of our interest in generating new knowledge useful for reducing health
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47 227 disparities, we first developed an initial list of NIH-funded cohort studies that included large,
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49 228 national samples of racial/ethnic minority communities. Additional cohorts were identified
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52 229 through the published literature, NIH resources, and consultation with epidemiologist advisors
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55 230 to the project. We then developed a ranked list of 30 cohort studies based on the following
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criteria: (1) racial/ethnic composition of cohort; (2) length of time cohort had received competitive funding (as a proxy for influence of the PI); (3) clinical conditions covered; and (4) inclusion of a large, nationally representative sample.

The PI of each of these 30 studies was invited via email to participate in this qualitative study. None of the study investigators had had a previous relationship with the PIs. Telephone calls were scheduled with those interested in learning more, during which 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. 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. All but two participating PIs refused the honorarium. Based on our prior work,²³⁻²⁸ we anticipated that 20 interviews would be a sufficient number to achieve thematic saturation.

Data Collection

One-hour, semi-structured interviews were conducted with each participating PI by the Principal Investigator of our qualitative study (AES) or jointly by two members of the study team (AES and TAB) in 2015. During interviews, PIs were invited to consider psychosocial stress and factors in the broadest possible sense, although they were not given an exact definition to follow. PIs were not instructed to focus on specific psychosocial experiences or variables, and therefore unless specific types of experiences are given as examples in a PI's response, we interpret their answers to refer generally to the whole field of psychosocial factors. Interview

questions addressed: (1) PIs' experiences with and exposure to research on psychosocial factors; (2) reasons why their cohort has collected psychosocial measures in the past; (3) assessment of the quality and value of existing psychosocial research; (4) assessment of the importance of psychosocial factors in understanding disease etiology; (5) beliefs regarding the pathways or mechanisms through which they imagine psychosocial factors might operate to affect human health, if at all; and (6) the evidence they would need to see before being willing to invest additional cohort resources in collecting new psychosocial measures.

Data Analysis

All interviews were recorded and transcribed. Transcripts were analyzed using a grounded theory approach.^{29,30} The interviewers and two research assistants (RAs; BS and SNP) independently 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), and any emergent themes or discrepancies brought to the investigators for resolution. Data were analyzed using content analysis to identify major concepts and themes, and axial coding to group and connect related data.^{28,30,31} Within each topic area, we identified 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.³² 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.

Patient and Public Involvement

As this was a targeted investigation into the perspectives of specific cohort study PIs, no patients or members of the public were involved in the design or recruitment of our study, nor in the dissemination of results. Our 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).

Ethics Approval

Institutional Review Board approval for this study was obtained from the Partners Human Research Committee (Protocol # 2015P000014/MGH).

RESULTS

The final study sample of 20 PIs included men and women from several different racial/ethnic communities, although the vast majority were white. PIs represented a wide range of ages, although few were younger than 55 years old. Most PIs had led only one prospective cohort study in their career, although some had served as PI for more than one study. Collectively, the 20 PIs interviewed for this study represent longitudinal health data on nearly 3.2M individuals across 24 cohorts, or roughly 1.25 out of every 100 adults in the U.S. aged 18 or over. This includes data on every major racial group in the U.S., including approximately 400,000 African Americans and 120,000 Hispanics/Latinos (**Figure 2**).

Importance of the psychosocial domain

PIs’ shared similar views regarding the importance of psychosocial influences on health outcomes. When asked about the importance of psychosocial measures more broadly, one PI responded with:

I mean, I think it is very, very important. We’ve tried to pay a lot of attention to it in our own cohort...I think it’s very important to pay a lot of attention to this, because I feel that many psychosocial variables are definitely modifying factors for disease risk, and can also be causally associated.

PIs with clinical experience often cited their observations of the influence of psychosocial experience on their patients’ outcomes: “I think it’s based on my clinical

321 experience...if you don't address the psychosocial factors, you'll never be able to help improve
322 that person's treatment, and their care for diabetes." Those with clinical experience also
323 seemed to appreciate the complex ways in which psychosocial factors interact with other
324 "traditional" risk factors:

Certainly, my feeling is that there's probably some complex interplay between
psychosocial factors and, for lack of a better word, more traditional factors --
say, for instance, a blood level of cholesterol or blood pressure...In my clinic, I
can certainly see that some of these psychosocial factors have enormous impact
on the other potent, traditional risk factors.

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331 Others viewed psychosocial measures in general as "soft" measures that would never be
332 as informative as "hard" biological measures, but even these PIs believed that to ignore
333 psychosocial influences would be a mistake:

This [psychosocial influences] is not a solid measure of exposure. But I do think
that to ignore it, when you're talking about symptoms and presentation of
disease, is a mistake, because it's all together...I think it all goes together to
create this person's sense of well-being, and you can't ignore it.

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339 Others noted tensions within the field of epidemiology regarding the importance of
340 psychosocial factors in disease etiology, particularly regarding the extent to which psychosocial
341 factors were captured in other measures of behavior or social support already collected. As one
342 PI explained:

I think there's two camps...The skeptics feel it's not an independent risk factor,
and you can account for it with all the other factors and behaviors like smoking,
alcohol use, etc. But there's a very strong camp that believe that these are
upstream of the lifestyle behaviors, and if you don't measure them correctly, you
may be artificially saying that they are all explained by behaviors, and that they
may actually be independently related to disease outcomes.

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Despite a general acceptance of the importance of psychosocial factors in health expressed by the majority of PIs, some were more positive about certain psychosocial domains over others. While PIs were often quick to accept the importance of measuring factors such as social support, abuse, and discrimination, many were far less certain about the contribution of religion and spirituality (R/S) as a source of psychosocial resilience, for example, since it has been less extensively studied in cohort studies. Among our PI informants, three believed that R/S were not important to study in research on human health, eight were open to the possibility that R/S may be important to health but believed that the “jury is still out,” and nine felt that R/S likely had an important impact on health.

The need for psychosocial research using clinically-relevant biomarkers

The vast majority of PIs suggested that for future psychosocial research to gain greater currency among epidemiologists, it would need to explore clinically-relevant biomarkers and biological mechanisms. As one PI put it, “I think the emphasis today in epidemiological sciences is to delineate a clear biological mechanism.” Some offered ideas about creative avenues for exploring these relationships: “I would love to see studies on the effect of psychosocial stress on the microbiome, because of stress’s influence on the immune system.”

When asked where they see the field of psychosocial research going in the future, one PI responded, “I think it is moving into trying to be more anchored in actual biologic changes...to identify people who are actually more likely to have a biologic response in relation to some external stressor.” One PI noted that recent studies investigating psychosocial stress in

372 relationship to biological variables are changing epidemiologists' opinions on the importance of
373 psychosocial stress to health:

374 Studying psychosocial factors and stressors is relatively new, and [was] met with
375 a lot of skepticism until fairly recently... But I think what's changed...[is] there's
376 now biological evidence that stressors may affect various biomarkers.

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378 Another PI emphasized that psychosocial research should ideally be framed in terms of a
379 biological pathway:

380 I wouldn't require that you would have the whole pathway – that is, exposure to
381 intermediates to health outcome – because that's probably the kind of link we're
382 looking for in studies. But having something between the intermediate and
383 health outcome, and having something between the determinant and something
384 along that initial pathway, I think would be very helpful to justify doing
385 [psychosocial] measures in a cohort study.

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387 Although all PIs discussed the value and contribution of conducting future research to
388 elucidate the biological mechanisms through which psychosocial factors operate, several also
389 had concerns about potential directions this kind of research could take when connected to the
390 health of minority and underrepresented communities. As one PI articulated, it's "a little
391 frightening to think about genes and behavior, or genes and things in the psychological realm.
392 You know, some sinister images can pop up...it frightens some people that, you know, you can
393 look at a genome, characterize somebody, and discriminate against them." Other PIs shared
394 similar worries about genomics research with a focus on psychosocial factors. The concern was
395 that if researchers establish correlations between genetic variants (or other biological
396 characteristics) and psychosocial factors such as educational attainment, living in a poor
397 neighborhood, experiencing discrimination, or other factors, that these results might be used to

justify discrimination against these groups. In other words, these sorts of results might be used by those who don't understand the nuances and limitations of these research findings to try to claim that certain groups in society who experience adversity or inequality are genetically or biologically inferior.

Psychosocial research as an important domain for potential interventions

Roughly half of the PIs interviewed also discussed psychosocial research as potentially helpful in developing public health interventions. One PI articulated this particularly well:

We've had half a century of risk factor epidemiology that tends to focus on the individual as the driver of behavior change. I think this field of stress and psychosocial stress is one that can help us look at the social context and other environments in which people live, and help us think about interventions.

Another PI echoed this enthusiasm, but also expressed concerns about how to actually operationalize insights about psychosocial research for public benefit. As he explained, "So to the extent that observing that racial discrimination increases stress and can impact high blood pressure...that's a useful, almost intuitive observation. But then what?...How do we then break that influence on health?"

PIs' abilities to envision how psychosocial research would translate into improved public health interventions varied by the type of psychosocial domain discussed. Some PIs, for example, had difficulty seeing how R/S research could be used to develop interventions to improve health. As one PI explained:

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.

Challenges in the field

Despite expressing uniform appreciation for the potential of psychosocial factors influencing disease onset or survival, many PIs described a number of circumstances that they see as inhibiting their own cohorts, and the larger epidemiological community, from engaging in robust assessments of psychosocial factors.

Challenging funding landscapes

Several PIs mentioned that despite their own interest or the interest of their colleagues, a lack of relevant funding mechanisms, or even a lack of certainty about future NIH cohort funding in general, has prevented efforts to investigate psychosocial factors. Several made off-hand comments similar to this one: "Oh, we're always open to new projects. So we'd be happy to ask questions if there was funding available." Many PIs also described that their funding organizations had specific scientific priorities and expectations for the parameters of their cohort's questionnaires, which would limit their ability to add in survey questions on psychosocial stress. Several cohort PIs also noted that they do not currently have funding from NIH lined up for another wave of data collection.

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Reproducibility and consensus surrounding measures of psychosocial factors

Several PIs noted that for researchers to be able to reproduce robust research on psychosocial variables and health, it would be a priority that multiple cohorts collect the same psychosocial measures. Describing the field of psychosocial research at large, one PI recounted, “My sense is that...it’s still very broad. And different people are doing different types of psychosocial stressors...I’m hoping that the field might narrow a little bit if we’re able to do this kind of linkage [between cohort studies].”

PIs often articulated that this would necessitate pooled analyses across cohorts and racial/ethnic groups:

I think the kind of data that I would like to see are large, multicentric, multiethnic cohorts, with reasonable duration of power -- of follow-up, with adequate statistical power, with appropriate characterization of the exposure with validated instruments, appropriate adjustment for multiple layers of confounding.

As another PI described, however, the downside is that “we always go back to the least common denominator when we pool. And to do gene environment interactions, you almost have to pool cohorts...You’re going to lose quality if people don’t ask the question in a manner that you can pool across studies.” Clearly, the lack of similar or harmonized psychosocial measures across multiple cohorts to facilitate larger-scale, pooled analyses, is seen by most PIs as a limiting factor for current psychosocial research.

DISCUSSION

The PIs we interviewed almost unanimously agreed that future research on psychosocial domains is likely important, but emphasized the need to elucidate the biological and behavioral mechanisms through which psychosocial factors impact health in order to convince the epidemiological community more broadly to invest resources in investigating psychosocial stress and resilience. To conduct this kind of rigorous psychosocial research using biomarkers and mechanisms, investigators will need to have access to both robust and clinically-relevant biological data as well as comprehensive psychosocial, socioeconomic, behavioral, and health outcome or clinical data on their study participants. Data are also needed at both the individual and neighborhood levels to properly assess a person's environment. These comprehensive data are currently most reliably found in prospective cohort studies, but robust numbers of psychosocial measures are not yet found consistently across cohorts.

One striking finding from our study is the extent to which the selection of psychosocial measures to be collected by cohorts is a nonlinear process determined by the interests and biases of particular research teams. It seems that all cohorts did not set out to systematically identify all psychosocial factors and domains that are important to health and should be included in their data collection efforts. Instead, cohorts seem to have only collected psychosocial factors if and when they support other analyses for more traditional outcome or lifestyle variables, or if an investigator within the cohort has gotten funding or support to investigate a subset of psychosocial factors, often in an ancillary study. Thus, successful psychosocial research depends on champions within established epidemiological cohorts who

can convince colleagues to commit resources for collecting further psychosocial variables and completing psychosocial analyses.

Our interviews also showed that many cohort PIs see psychosocial research as an important area to investigate for developing potential public health interventions. Indeed, behavioral, lifestyle, and resilience factors have been shown to mitigate the impact of stress on developing disease.^{11,33} Despite this enthusiasm exhibited by PIs, however, our interviews also highlighted challenges to the feasibility of this research. In particular, the lack of targeted funding and the lack of consensus on key measures to be collected and/or harmonized across cohort studies were identified as key barriers that need to be overcome to advance psychosocial research.

Our study had several limitations worth noting. While the 20 PIs interviewed represented diverse ethnicities, ages, and clinical domains of interest, they may not fully capture the diversity in PIs' attitudes towards psychosocial research. According to NIH institute websites, there are 70 cohort studies currently funded by NCI and NHLBI, and thus our results reflect roughly a quarter of all NIH-funded cohorts. Future research could survey PIs nationally to quantitatively assess a broader array of perspectives. We also recognize that there may seem to be a methodological disconnect in conducting a qualitative, grounded theory study to provide insight for a quantitative, epidemiological audience. We believe, however, that in depth interviews with cohort PIs is a highly strategic approach that is essential to understanding the on-the-ground demands and challenges of conducting epidemiological research with cohort study data, and is crucial to developing a *theory of change* for epidemiological psychosocial research. We further believe that our multi-disciplinary team of investigators who have training

and experience in qualitative and epidemiological research has allowed us to bridge these two different methodologies approaches and epistemologies.

Despite these limitations, this study provides the first assessment of cohort PIs' attitudes and beliefs regarding the influence of psychosocial factors on disease etiology, and identifies challenges for the field from the perspective of these thought leaders in epidemiology. Our results provide a strategic and pragmatic roadmap for future psychosocial researchers to draw upon in designing and proposing researching studies to be conducted within epidemiological settings, and for identifying strategies to engage cohort studies in future research to advance knowledge regarding the role of psychosocial influences in disease etiology.

CONCLUSION

Looking forward, our interviews with cohort PIs emphasized that: (1) future research will need to investigate biological and behavioral pathways through which psychosocial factors influence disease; (2) funding bodies need to create funding mechanisms and requests for proposals that specifically support these types of analyses as a scientific priority; and (3) psychosocial research will need to be carried out with a focus on building consensus within the greater epidemiological community regarding optimal scales and measures of key psychosocial domains, in order to encourage reproducibility and improve power. PIs also emphasized that future psychosocial research that follows these steps may be particularly impactful in identifying novel public health interventions. By understanding the mechanisms through which

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534 psychosocial factors—including both stress and resources for resilience—operate to affect
535 vulnerability to disease across diverse populations, researchers will not only gain new insight
536 into the etiology of many chronic diseases, but will also generate new insight into how health
537 disparities in the U.S. are produced and identify new leverage points for addressing them.

For peer review only

FIGURES

[Figure 1 here]

Figure 1. Model of psychosocial influences on health. Note: these three domains of life (social, cultural, environmental) converge on individual “health,” which indicates both physical and mental health, as well as intermediate biological and physiological pathways and processes that influence health.

[Figure 2 here]

Figure 2. Total number of adult study participants (aged 18 or over) represented by participating PIs’ cohorts, including breakdown by race/ethnicity.

AUTHORS’ CONTRIBUTIONS

AES and TB completed interviews. AES, TB, BS, and SNP completed interview data analysis. BS, SNP, TB, and MAA indexed qualitative transcripts, MAA wrote initial drafts of the manuscript and created figures. All authors read and approved the final manuscript.

DATA SHARING

Interview transcripts are available, upon reasonable request, by emailing the corresponding author directly.

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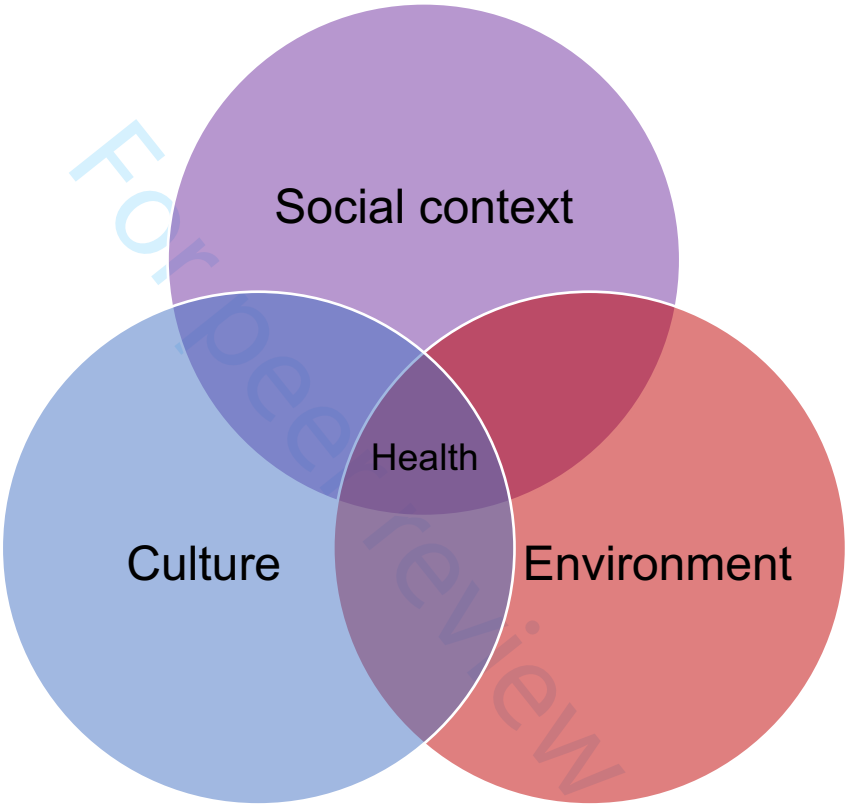
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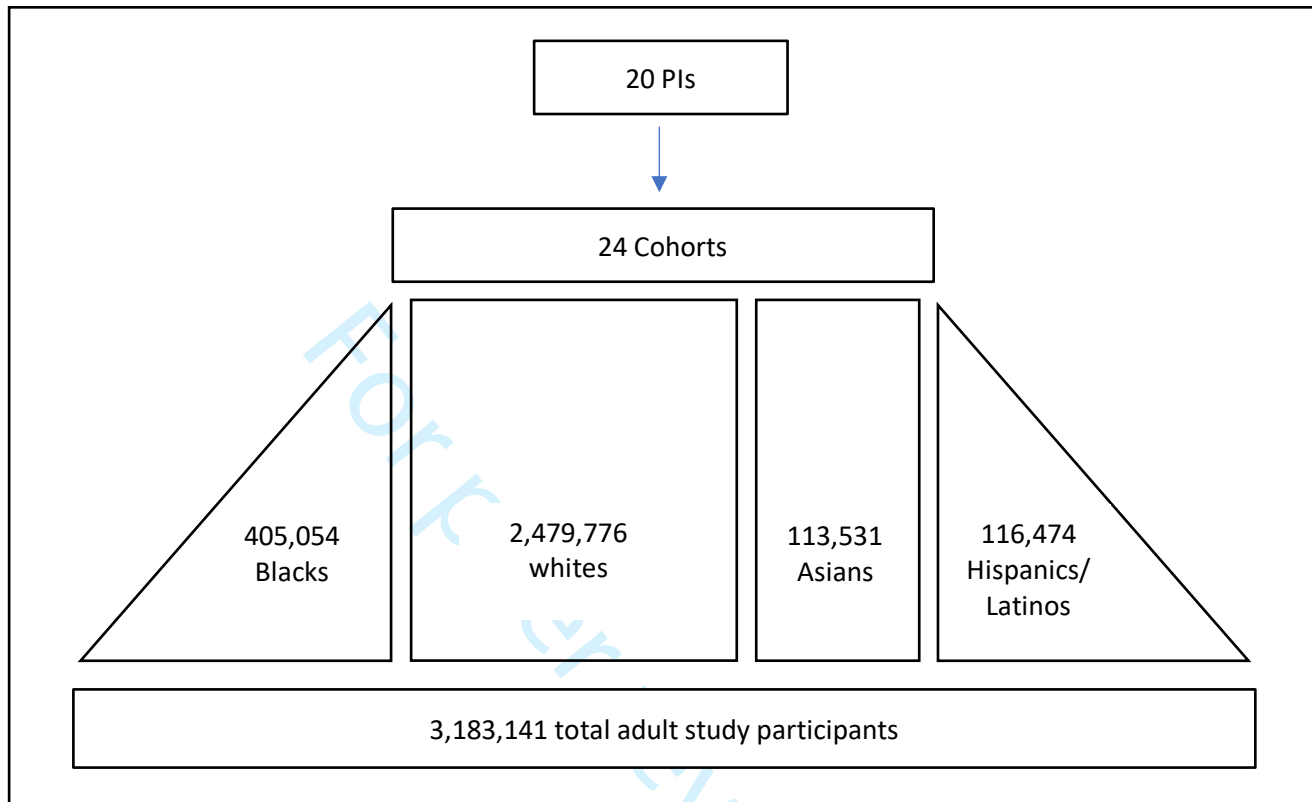
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- Social support or isolation
- Marital status and family relationships
- Abuse and trauma
- Discrimination
- Education
- Socioeconomic status



- Acculturation
- Language barriers
- Religion and/or spirituality
- Technological change
- Stigma
- Beliefs

- Air pollution
- Neighborhood conditions
- Green space
- Physical deprivation
- Workplace conditions
- Natural disasters



COREQ (CONsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	
Credentials	2	What were the researcher’s credentials? E.g. PhD, MD	
Occupation	3	What was their occupation at the time of the study?	
Gender	4	Was the researcher male or female?	
Experience and training	5	What experience or training did the researcher have?	
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	
Sample size	12	How many participants were in the study?	
Non-participation	13	How many people refused to participate or dropped out? Reasons?	
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	
Field notes	20	Were field notes made during and/or after the inter view or focus group?	
Duration	21	What was the duration of the inter views or focus group?	
Data saturation	22	Was data saturation discussed?	
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	
Software	27	What software, if applicable, was used to manage the data?	
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	
Clarity of major themes	31	Were major themes clearly presented in the findings?	
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

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A Roadmap for Conducting Psychosocial Research in Epidemiological Studies: Perspectives of Cohort Study Principal Investigators

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The authors declare no conflicts of interest.

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ABSTRACT

Background. Psychosocial adversity disproportionately affects racial/ethnic and socioeconomic minorities in the U.S., and therefore understanding the mechanisms through which psychosocial stress and resilience influence human health can provide meaningful insights into addressing U.S. health disparities. Despite this promise, psychosocial factors are infrequently and unsystematically collected in U.S. prospective cohort studies.

Methods. We sought to understand prospective cohort Principal Investigators' (PIs') attitudes regarding the importance of psychosocial influences on disease etiology, in order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research. One-hour, semi-structured qualitative interviews were conducted with 20 PIs representing 24 U.S. prospective cohort studies funded by the National Institutes of Health (NIH), collectively capturing health data on 1.25 of every 100 American adults. A hypothesis-free, grounded theory approach was used to analyze and interpret interview data.

Results. Most cohort PIs view psychosocial factors as an important research area to further our understanding of disease etiology, and agree that this research will be crucial for future public health innovations. Virtually all PIs emphasized that future psychosocial research will need to elucidate biological and behavioral mechanisms in order to be taken seriously by the epidemiological community more broadly. A lack of pertinent funding mechanisms and a lack of consensus on optimal scales and measures of psychosocial factors were identified as additional barriers to advancing psychosocial research.

Conclusions. Our interviews emphasized the need for: (1) high-quality, longitudinal studies that investigate biological mechanisms and pathways through which psychosocial factors influence health; (2) effort among epidemiological cohorts to broaden and harmonize the measures they use across cohorts, to facilitate replication of results; (3) and the need for targeted funding opportunities from NIH and other grant-making institutions to study these domains.

KEYWORDS

Qualitative Research; Epidemiology; Public Health; Social Medicine

ARTICLE SUMMARY

Strengths and Limitations of the study

- We conducted qualitative interviews with 20 prospective cohort study Principal Investigators (PIs) to better understand barriers and opportunities for greater inclusion of psychosocial factors in high-quality epidemiological research.
- Interviews and data analysis were performed by a multi-disciplinary team with training and expertise in both qualitative methodology and epidemiology.
- Interviewing PIs from major cohort studies is a strategic choice that provides insight into the priorities and concerns of those who decide the research priorities for 24 U.S. cohort studies that collectively include roughly 3.2 million American adults.
- Findings from this qualitative study provide a roadmap for how to conduct future, high-impact epidemiological research on psychosocial factors.
- Findings from this qualitative study can also be used as a guide on how to engage leading U.S. cohort studies in future psychosocial research.

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124 **INTRODUCTION**

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126 Psychosocial factors encompass a broad set of experiences, including childhood
127 adversity, isolation and loneliness, job-related stress, discrimination, trauma, religious and
128 spiritual experiences, social support, healthy neighborhoods, and many other dimensions of
129 life. While acute stressors normally elicit a healthy and adaptive stress response, severe or
130 prolonged psychosocial stress can lead to long-term dysregulation of the stress reactivity
131 system and disease.^{1,2} In particular, psychosocial stress has been implicated as a factor
132 contributing to cardiovascular disease,^{3,4} hypertension,⁵ type 2 diabetes (T2D),⁶ obesity,⁷ and
133 cancer,⁸ among other conditions. Likewise, positive psychosocial factors are also important
134 sources of resilience, support, and engagement that can have positive impacts on mitigating
135 stress and improving health.⁹⁻¹¹

136 Despite the important role that psychosocial factors may play in disease etiology, they
137 are not often assessed comprehensively in epidemiological research, particularly within
138 prospective cohort studies. Furthermore, a lack of precise and operational definitions and
139 clinical cut-off points for many psychosocial exposures has kept them from being incorporated
140 more routinely into clinical guidelines and practice.^{12,13} The influence of psychosocial factors on
141 disease etiology potentially encompasses both acute and chronic experiences, occurring
142 throughout the lifecourse in both childhood and adulthood, that may associate with human
143 disease through many different biological pathways.^{6,14} Since psychosocial experiences are
144 complex phenomena that span many dimensions and timepoints within a person’s life, this
145 poses difficulties for quantitative assessment in epidemiological research. It is therefore

important that epidemiological investigators critically evaluate the measurement and investigation of these domains in a systematic and thoughtful way.

Given that psychosocial adversity and stress are often experienced more frequently by racial/ethnic and socioeconomic minority populations in the U.S.,¹⁵ understanding the mechanisms through which psychosocial stress influences human health may also provide crucial insight into the production of health disparities in the U.S. Psychosocial stress may function both as a key factor driving disproportionate burdens of disease among underrepresented populations,¹⁶⁻¹⁸ and also serve as a key mediator or pathway through which experiences of inequality – such as difficult socioeconomic environments^{19,20} or poor sleep,²¹ among others – influence disease or disease-related behaviors. Likewise, fostering tools for psychosocial resilience and community building among underrepresented populations may also have a positive impact on health inequality.¹¹

In order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research, we conducted qualitative interviews with 20 Principal Investigators (PIs) representing 24 different U.S. prospective cohort studies funded by the National Institutes of Health (NIH). These interviews were used to probe PIs' beliefs and opinions on the impact of psychosocial factors on health, and were also used to identify the evidence they require to see before adding additional assessments of psychosocial factors in future waves of data collection within their cohorts. Taken together, the qualitative results that follow from these interviews inform a theory of change that provides a roadmap for future psychosocial research methods that we theorize will generate more prominent and impactful psychosocial investigations within epidemiological research.

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168 **METHODS**

170 ***Defining “Psychosocial”***

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172 Psychosocial research encompasses many possible topics and is used in myriad studies,
173 although definitions are rarely offered. In this article, we begin by offering a definition, or at
174 least a point of reference, that will serve as a useful starting point for understanding
175 psychosocial dimensions of life. The American Psychological Association (APA) Dictionary of
176 Psychology²² lists several different definitions that can help us triangulate a working meaning.
177 “Psychosocial factors” are defined as “social, cultural, and environmental phenomena and
178 influences that affect mental health and behavior” (**Figure 1**). A psychosocial stressor, more
179 specifically, is defined by the APA as “a life situation that creates an unusual or intense level of
180 stress that may contribute to the development or aggravation of mental disorder, illness, or
181 maladaptive behavior. Examples of psychosocial stressors include divorce, the death of a child,
182 prolonged illness, unwanted change of residence, a natural catastrophe, or a highly competitive
183 work situation.”

184 This definition of psychosocial is broad, and encompasses experiences throughout the
185 lifecourse. It is important to note that the term psychosocial in itself does not refer just to
186 adverse life events, but more broadly to the confluence of social, cultural, and environmental
187 factors that come together to affect our biology, physiology, and psychology. Consequently, the
188 term psychosocial captures both negative stressors and positive sources of resiliency,

engagement, and community. This includes factors such as social support, religion and/or spirituality (R/S), and healthy neighborhood conditions.

Research Team

The research team members carrying out interviews (AES and TAB, both female, PhD-level) and data analysis (AES, TAB, MAA, BS, SNP, the final 3 of which were Masters-level/pre-doctoral level) were uniquely positioned as having training and experience in qualitative, clinical, and epidemiological research. The team was therefore well-suited to anticipate and address the dual demands of both maintaining qualitative rigor while also trying to gather and analyze information that is ultimately meant for an epidemiological audience.

AES directs a research center that conducts transdisciplinary research aimed at elucidating the underlying causes of health disparities, investigating ways to reduce health disparities, and addressing ethical and social implications of genomics research. TAB is a radiation oncologist with a longstanding interest in understanding the ways in which patients' religious or spiritual beliefs and practices influence their health care decision-making, particularly at the end of life. MAA is a medical anthropologist and population health researcher currently in the final year of a PhD in population health, and BS is a medical geneticist and MD candidate. Both MAA and BS have worked with AES over the past 5 years to conduct epidemiological and population health research on health inequality, with a particular focus on investigating psychosocial factors. SNP has training in cultural anthropology and is a

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3 210 DO candidate. She has conducted research with TAB for over 2 years focused on understanding
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6 211 the impact of religion and spirituality on health.
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8 212 The research team sought to mitigate bias stemming from any interests that the
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10 213 investigators brought to the investigation by using good interviewing practices in which
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13 214 questions were asked without providing examples or steering the discussion in ways that were
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15 215 apt to introduce bias. Data coding and analysis was carried out using a hypothesis-free,
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17 216 grounded theory approach such that themes and theories presented in this article were only
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19 217 those that emerged from the empirical data and are not reflective of previous priorities or
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21 218 interests of the investigators. These methods, in addition to data triangulation procedures, are
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23 219 described further in the Data Analysis section.
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30 221 **Participants and Recruitment**
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35 223 This study was carried out as part of a larger project investigating the perspectives of Pls
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37 224 on both psychosocial factors and R/S. Pls were contacted, recruited, and then interviewed
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39 225 about these two topics simultaneously. The results concerning R/S specifically are published in
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41 226 a separate manuscript.²³
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45 227 Because of our interest in generating new knowledge useful for reducing health
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47 228 disparities, we first developed an initial list of NIH-funded cohort studies that included large,
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49 229 national samples of racial/ethnic minority communities. Additional cohorts were identified
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51 230 through the published literature, NIH resources, and consultation with epidemiologist advisors
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54 231 to the project. We then developed a ranked list of 30 cohort studies based on the following
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criteria: (1) racial/ethnic composition of cohort; (2) length of time cohort had received competitive funding (as a proxy for influence of the PI); (3) clinical conditions covered; and (4) inclusion of a large, nationally representative sample.

The PI of each of these 30 studies was invited via email to participate in this qualitative study. None of the study investigators had had a previous relationship with the PIs. Telephone calls were scheduled with those interested in learning more, during which 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. 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. All but two participating PIs refused the honorarium. Based on our prior work,²⁴⁻²⁹ we anticipated that 20 interviews would be a sufficient number to achieve thematic saturation.

Data Collection

One-hour, semi-structured interviews were conducted with each participating PI by the Principal Investigator of our qualitative study (AES) or jointly by two members of the study team (AES and TAB) in 2015. During interviews, PIs were invited to consider psychosocial stress and factors in the broadest possible sense, although they were not given an exact definition to follow. PIs were not instructed to focus on specific psychosocial experiences or variables, and therefore unless specific types of experiences are given as examples in a PI's response, we interpret their answers to refer generally to the whole field of psychosocial factors. Interview

questions addressed: (1) PIs’ experiences with and exposure to research on psychosocial factors; (2) reasons why their cohort has collected psychosocial measures in the past; (3) assessment of the quality and value of existing psychosocial research; (4) assessment of the importance of psychosocial factors in understanding disease etiology; (5) beliefs regarding the pathways or mechanisms through which they imagine psychosocial factors might operate to affect human health, if at all; and (6) the evidence they would need to see before being willing to invest additional cohort resources in collecting new psychosocial measures.

Data Analysis

All interviews were recorded and transcribed. Transcripts were analyzed using a grounded theory approach.^{30,31} The interviewers and two research assistants (RAs; BS and SNP) independently 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), and any emergent themes or discrepancies brought to the investigators for resolution. Data were analyzed using content analysis to identify major concepts and themes, and axial coding to group and connect related data.^{29,31,32} Within each topic area, we identified 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.³³ 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.

Patient and Public Involvement

As this was a targeted investigation into the perspectives of specific cohort study PIs, no patients or members of the public were involved in the design or recruitment of our study, nor in the dissemination of results. Our 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).

Ethics Approval

Institutional Review Board approval for this study was obtained from the Partners Human Research Committee (Protocol # 2015P000014/MGH).

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297 **RESULTS**

298
299 The final study sample of 20 PIs included men and women from several different
300 racial/ethnic communities, although the vast majority were white. PIs represented a wide range
301 of ages, although few were younger than 55 years old. Most PIs had led only one prospective
302 cohort study in their career, although some had served as PI for more than one study.
303 Collectively, the 20 PIs interviewed for this study represent longitudinal health data on nearly
304 3.2M individuals across 24 cohorts, or roughly 1.25 out of every 100 adults in the U.S. aged 18
305 or over. This includes data on every major racial group in the U.S., including approximately
306 400,000 African Americans and 120,000 Hispanics/Latinos (**Figure 2**).

308 ***Importance of the psychosocial domain***

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310 PIs’ shared similar views regarding the importance of psychosocial influences on health
311 outcomes. When asked about the importance of psychosocial measures more broadly, one PI
312 responded with:

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314 I mean, I think it is very, very important. We’ve tried to pay a lot of attention to it
315 in our own cohort...I think it’s very important to pay a lot of attention to this,
316 because I feel that many psychosocial variables are definitely modifying factors
317 for disease risk, and can also be causally associated.

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319
320 PIs with clinical experience often cited their observations of the influence of
321 psychosocial experience on their patients’ outcomes: “I think it’s based on my clinical

322 experience...if you don't address the psychosocial factors, you'll never be able to help improve
323 that person's treatment, and their care for diabetes." Those with clinical experience also
324 seemed to appreciate the complex ways in which psychosocial factors interact with other
325 "traditional" risk factors:

Certainly, my feeling is that there's probably some complex interplay between
psychosocial factors and, for lack of a better word, more traditional factors --
say, for instance, a blood level of cholesterol or blood pressure...In my clinic, I
can certainly see that some of these psychosocial factors have enormous impact
on the other potent, traditional risk factors.

331
332 Others viewed psychosocial measures in general as "soft" measures that would never be
333 as informative as "hard" biological measures, but even these PIs believed that to ignore
334 psychosocial influences would be a mistake:

This [psychosocial influences] is not a solid measure of exposure. But I do think
that to ignore it, when you're talking about symptoms and presentation of
disease, is a mistake, because it's all together...I think it all goes together to
create this person's sense of well-being, and you can't ignore it.

339
340 Others noted tensions within the field of epidemiology regarding the importance of
341 psychosocial factors in disease etiology, particularly regarding the extent to which psychosocial
342 factors were captured in other measures of behavior or social support already collected. As one
343 PI explained:

I think there's two camps...The skeptics feel it's not an independent risk factor,
and you can account for it with all the other factors and behaviors like smoking,
alcohol use, etc. But there's a very strong camp that believe that these are
upstream of the lifestyle behaviors, and if you don't measure them correctly, you
may be artificially saying that they are all explained by behaviors, and that they
may actually be independently related to disease outcomes.

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351 Despite a general acceptance of the importance of psychosocial factors in health
352 expressed by the majority of PIs, some were more positive about certain psychosocial domains
353 over others. While PIs were often quick to accept the importance of measuring factors such as
354 social support, abuse, and discrimination, many were far less certain about the contribution of
355 religion and spirituality (R/S) as a source of psychosocial resilience, for example, since it has
356 been less extensively studied in cohort studies. Among our PI informants, three believed that
357 R/S were not important to study in research on human health, eight were open to the
358 possibility that R/S may be important to health but believed that the “jury is still out,” and nine
359 felt that R/S likely had an important impact on health.

361 ***The need for psychosocial research using clinically-relevant biomarkers***

363 The vast majority of PIs suggested that for future psychosocial research to gain greater
364 currency among epidemiologists, it would need to explore clinically-relevant biomarkers and
365 biological mechanisms. As one PI put it, “I think the emphasis today in epidemiological sciences
366 is to delineate a clear biological mechanism.” Some offered ideas about creative avenues for
367 exploring these relationships: “I would love to see studies on the effect of psychosocial stress
368 on the microbiome, because of stress’s influence on the immune system.”

369 When asked where they see the field of psychosocial research going in the future, one
370 PI responded, “I think it is moving into trying to be more anchored in actual biologic
371 changes...to identify people who are actually more likely to have a biologic response in relation
372 to some external stressor.” One PI noted that recent studies investigating psychosocial stress in

373 relationship to biological variables are changing epidemiologists' opinions on the importance of
374 psychosocial stress to health:

375 Studying psychosocial factors and stressors is relatively new, and [was] met with
376 a lot of skepticism until fairly recently... But I think what's changed...[is] there's
377 now biological evidence that stressors may affect various biomarkers.

378
379 Another PI emphasized that psychosocial research should ideally be framed in terms of a
380 biological pathway:

381 I wouldn't require that you would have the whole pathway – that is, exposure to
382 intermediates to health outcome – because that's probably the kind of link we're
383 looking for in studies. But having something between the intermediate and
384 health outcome, and having something between the determinant and something
385 along that initial pathway, I think would be very helpful to justify doing
386 [psychosocial] measures in a cohort study.

387
388 Although all PIs discussed the value and contribution of conducting future research to
389 elucidate the biological mechanisms through which psychosocial factors operate, several also
390 had concerns about potential directions this kind of research could take when connected to the
391 health of minority and underrepresented communities. As one PI articulated, it's "a little
392 frightening to think about genes and behavior, or genes and things in the psychological realm.
393 You know, some sinister images can pop up...it frightens some people that, you know, you can
394 look at a genome, characterize somebody, and discriminate against them." Other PIs shared
395 similar worries about genomics research with a focus on psychosocial factors. The concern was
396 that if researchers establish correlations between genetic variants (or other biological
397 characteristics) and psychosocial factors such as educational attainment, living in a poor
398 neighborhood, experiencing discrimination, or other factors, that these results might be used to

justify discrimination against these groups. In other words, these sorts of results might be used by those who don't understand the nuances and limitations of these research findings to try to claim that certain groups in society who experience adversity or inequality are genetically or biologically inferior.

Psychosocial research as an important domain for potential interventions

Roughly half of the PIs interviewed also discussed psychosocial research as potentially helpful in developing public health interventions. One PI articulated this particularly well:

We've had half a century of risk factor epidemiology that tends to focus on the individual as the driver of behavior change. I think this field of stress and psychosocial stress is one that can help us look at the social context and other environments in which people live, and help us think about interventions.

Another PI echoed this enthusiasm, but also expressed concerns about how to actually operationalize insights about psychosocial research for public benefit. As he explained, "So to the extent that observing that racial discrimination increases stress and can impact high blood pressure...that's a useful, almost intuitive observation. But then what?...How do we then break that influence on health?"

PIs' abilities to envision how psychosocial research would translate into improved public health interventions varied by the type of psychosocial domain discussed. Some PIs, for example, had difficulty seeing how R/S research could be used to develop interventions to improve health. As one PI explained:

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.

Challenges in the field

Despite expressing uniform appreciation for the potential of psychosocial factors influencing disease onset or survival, many PIs described a number of circumstances that they see as inhibiting their own cohorts, and the larger epidemiological community, from engaging in robust assessments of psychosocial factors.

Challenging funding landscapes

Several PIs mentioned that despite their own interest or the interest of their colleagues, a lack of relevant funding mechanisms, or even a lack of certainty about future NIH cohort funding in general, has prevented efforts to investigate psychosocial factors. Several made off-hand comments similar to this one: "Oh, we're always open to new projects. So we'd be happy to ask questions if there was funding available." Many PIs also described that their funding organizations had specific scientific priorities and expectations for the parameters of their cohort's questionnaires, which would limit their ability to add in survey questions on psychosocial stress. Several cohort PIs also noted that they do not currently have funding from NIH lined up for another wave of data collection.

Reproducibility and consensus surrounding measures of psychosocial factors

Several PIs noted that for researchers to be able to reproduce robust research on psychosocial variables and health, it would be a priority that multiple cohorts collect the same psychosocial measures. Describing the field of psychosocial research at large, one PI recounted, “My sense is that...it’s still very broad. And different people are doing different types of psychosocial stressors...I’m hoping that the field might narrow a little bit if we’re able to do this kind of linkage [between cohort studies].”

PIs often articulated that this would necessitate pooled analyses across cohorts and racial/ethnic groups:

I think the kind of data that I would like to see are large, multicentric, multiethnic cohorts, with reasonable duration of power -- of follow-up, with adequate statistical power, with appropriate characterization of the exposure with validated instruments, appropriate adjustment for multiple layers of confounding.

As another PI described, however, the downside is that “we always go back to the least common denominator when we pool. And to do gene environment interactions, you almost have to pool cohorts...You’re going to lose quality if people don’t ask the question in a manner that you can pool across studies.” Clearly, the lack of similar or harmonized psychosocial measures across multiple cohorts to facilitate larger-scale, pooled analyses, is seen by most PIs as a limiting factor for current psychosocial research.

DISCUSSION

The PIs we interviewed almost unanimously agreed that future research on psychosocial domains is likely important, but emphasized the need to elucidate the biological and behavioral mechanisms through which psychosocial factors impact health in order to convince the epidemiological community more broadly to invest resources in investigating psychosocial stress and resilience. To conduct this kind of rigorous psychosocial research using biomarkers and mechanisms, investigators will need to have access to both robust and clinically-relevant biological data as well as comprehensive psychosocial, socioeconomic, behavioral, and health outcome or clinical data on their study participants. Data are also needed at both the individual and neighborhood levels to properly assess a person's environment. These comprehensive data are currently most reliably found in prospective cohort studies, but robust numbers of psychosocial measures are not yet found consistently across cohorts.

One striking finding from our study is the extent to which the selection of psychosocial measures to be collected by cohorts is a nonlinear process determined by the interests and biases of particular research teams. It seems that all cohorts did not set out to systematically identify all psychosocial factors and domains that are important to health and should be included in their data collection efforts. Instead, cohorts seem to have only collected psychosocial factors if and when they support other analyses for more traditional outcome or lifestyle variables, or if an investigator within the cohort has gotten funding or support to investigate a subset of psychosocial factors, often in an ancillary study. Thus, successful psychosocial research depends on champions within established epidemiological cohorts who

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491 can convince colleagues to commit resources for collecting further psychosocial variables and
492 completing psychosocial analyses.

493 Our interviews also showed that many cohort PIs see psychosocial research as an
494 important area to investigate for developing potential public health interventions. Indeed,
495 behavioral, lifestyle, and resilience factors have been shown to mitigate the impact of stress on
496 developing disease.^{11,34} Despite this enthusiasm exhibited by PIs, however, our interviews also
497 highlighted challenges to the feasibility of this research. In particular, the lack of targeted
498 funding and the lack of consensus on key measures to be collected and/or harmonized across
499 cohort studies were identified as key barriers that need to be overcome to advance
500 psychosocial research.

501 Our study had several limitations worth noting. While the 20 PIs interviewed
502 represented diverse ethnicities, ages, and clinical domains of interest, they may not fully
503 capture the diversity in PIs' attitudes towards psychosocial research. According to NIH institute
504 websites, there are 70 cohort studies currently funded by NCI and NHLBI, and thus our results
505 reflect roughly a quarter of all NIH-funded cohorts. Future research could survey PIs nationally
506 to quantitatively assess a broader array of perspectives. While we have outlined in this paper
507 the types of research that will be persuasive to cohort PIs in evaluating psychosocial research,
508 future research could also investigate PIs views on what the quantitative threshold – in terms
509 of numbers of new studies, health conditions investigated, or other criteria – might be for a
510 persuasive evidence base of psychosocial research. Our grounded theory approach limited our
511 analyses and focus to the empirical data gathered, and did not allow us to offer deeper
512 interpretation or explanations for why PIs may hold the views that they reported. We also

recognize that there may seem to be a methodological disconnect in conducting a qualitative, grounded theory study to provide insight for a quantitative, epidemiological audience. We believe, however, that in depth interviews with cohort PIs is a highly strategic approach that is essential to understanding the on-the-ground demands and challenges of conducting epidemiological research with cohort study data, and is crucial to developing a *theory of change* for epidemiological psychosocial research. We further believe that our multi-disciplinary team of investigators who have training and experience in qualitative and epidemiological research has allowed us to bridge these two different methodologies approaches and epistemologies.

Despite these limitations, this study provides the first assessment of cohort PIs' attitudes and beliefs regarding the influence of psychosocial factors on disease etiology, and identifies challenges for the field from the perspective of these thought leaders in epidemiology. Our results provide a strategic and pragmatic roadmap for future psychosocial researchers to draw upon in designing and proposing researching studies to be conducted within epidemiological settings, and for identifying strategies to engage cohort studies in future research to advance knowledge regarding the role of psychosocial influences in disease etiology.

CONCLUSION

Looking forward, our interviews with cohort PIs emphasized that: (1) future research will need to investigate biological and behavioral pathways through which psychosocial factors influence disease; (2) funding bodies need to create funding mechanisms and requests for

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proposals that specifically support these types of analyses as a scientific priority; and (3)
psychosocial research will need to be carried out with a focus on building consensus within the
greater epidemiological community regarding optimal scales and measures of key psychosocial
domains, in order to encourage reproducibility and improve power. PIs also emphasized that
future psychosocial research that follows these steps may be particularly impactful in
identifying novel public health interventions. By understanding the mechanisms through which
psychosocial factors—including both stress and resources for resilience—operate to affect
vulnerability to disease across diverse populations, researchers will not only gain new insight
into the etiology of many chronic diseases, but will also generate new insight into how health
disparities in the U.S. are produced and identify new leverage points for addressing them.

FIGURES

[Figure 1 here]

Figure 1. Model of psychosocial influences on health. Note: these three domains of life (social, cultural, environmental) converge on individual “health,” which indicates both physical and mental health, as well as intermediate biological and physiological pathways and processes that influence health.

[Figure 2 here]

Figure 2. Total number of adult study participants (aged 18 or over) represented by participating PIs’ cohorts, including breakdown by race/ethnicity.

AUTHORS’ CONTRIBUTIONS

AES and TB completed interviews. AES, TB, BS, and SNP completed interview data analysis. BS, SNP, TB, and MAA indexed qualitative transcripts, MAA wrote initial drafts of the manuscript and created figures. All authors read and approved the final manuscript.

DATA SHARING

Transcripts of the full interviews with cohort PIs are not available due to the ease with which study participants could be identified. Anonymized and redacted interview transcripts are available, upon reasonable request, by emailing the corresponding author directly.

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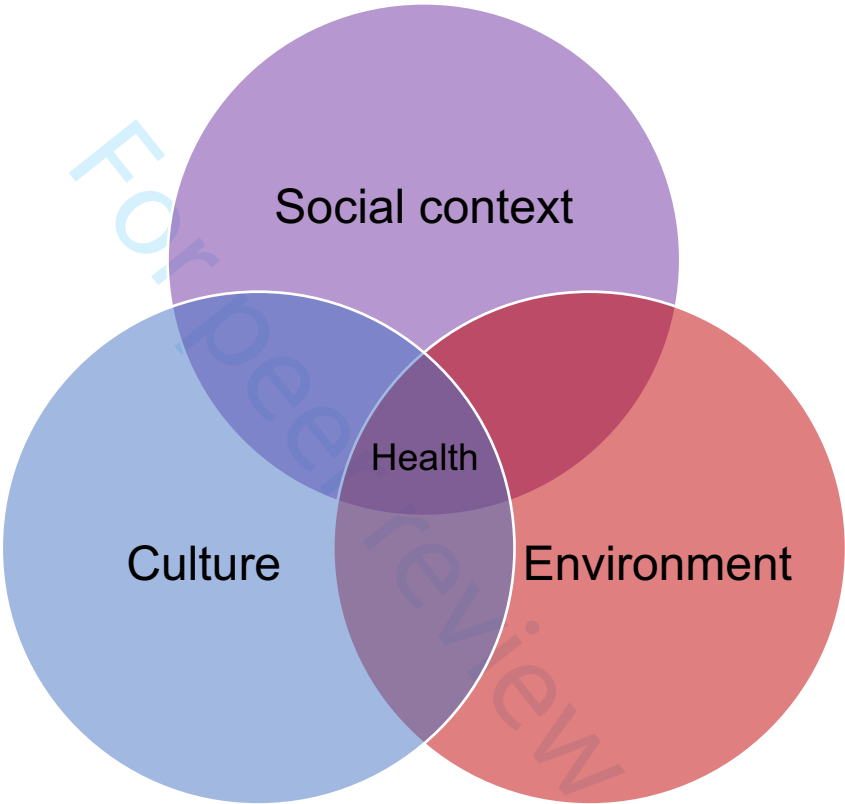
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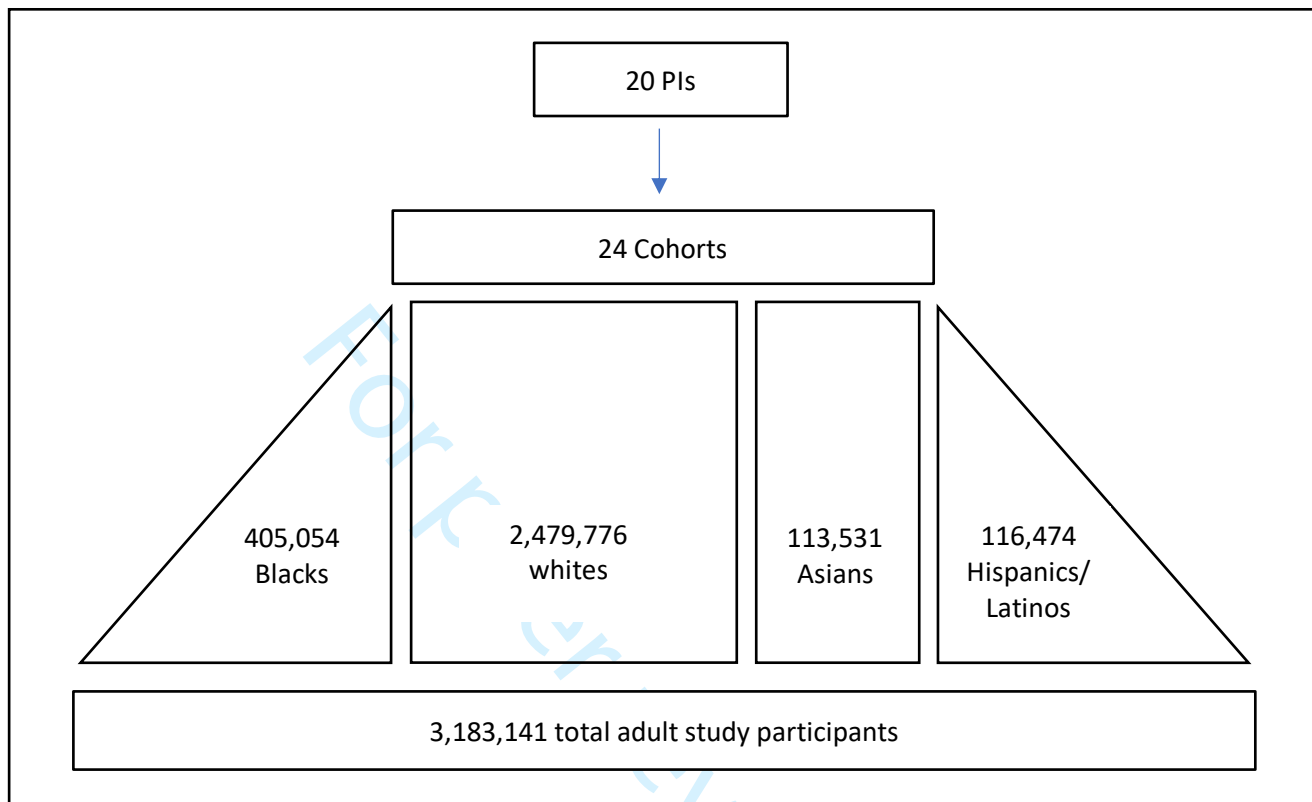
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- Social support or isolation
- Marital status and family relationships
- Abuse and trauma
- Discrimination
- Education
- Socioeconomic status



- Acculturation
- Language barriers
- Religion and/or spirituality
- Technological change
- Stigma
- Beliefs

- Air pollution
- Neighborhood conditions
- Green space
- Physical deprivation
- Workplace conditions
- Natural disasters



COREQ (CONsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	
Credentials	2	What were the researcher’s credentials? E.g. PhD, MD	
Occupation	3	What was their occupation at the time of the study?	
Gender	4	Was the researcher male or female?	
Experience and training	5	What experience or training did the researcher have?	
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	
Sample size	12	How many participants were in the study?	
Non-participation	13	How many people refused to participate or dropped out? Reasons?	
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	
Field notes	20	Were field notes made during and/or after the inter view or focus group?	
Duration	21	What was the duration of the inter views or focus group?	
Data saturation	22	Was data saturation discussed?	
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	
Software	27	What software, if applicable, was used to manage the data?	
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	
Clarity of major themes	31	Were major themes clearly presented in the findings?	
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

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A Roadmap for Conducting Psychosocial Research in Epidemiological Studies: Perspectives of Cohort Study Principal Investigators

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COMPETING INTERESTS

The authors declare no conflicts of interest.

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49 **ABSTRACT**

52 **Background.** Psychosocial adversity disproportionately affects racial/ethnic and socioeconomic
53 minorities in the U.S., and therefore understanding the mechanisms through which psychosocial
54 stress and resilience influence human health can provide meaningful insights into addressing
55 U.S. health disparities. Despite this promise, psychosocial factors are infrequently and
56 unsystematically collected in U.S. prospective cohort studies.

58 **Methods.** We sought to understand prospective cohort Principal Investigators' (PIs') attitudes
59 regarding the importance of psychosocial influences on disease etiology, in order to identify
60 barriers and opportunities for greater inclusion of these domains in high-quality epidemiological
61 research. One-hour, semi-structured qualitative interviews were conducted with 20 PIs
62 representing 24 U.S. prospective cohort studies funded by the National Institutes of Health
63 (NIH), collectively capturing health data on 1.25 of every 100 American adults. A hypothesis-
64 free, grounded theory approach was used to analyze and interpret interview data.

66 **Results.** Most cohort PIs view psychosocial factors as an important research area to further our
67 understanding of disease etiology, and agree that this research will be crucial for future public
68 health innovations. Virtually all PIs emphasized that future psychosocial research will need to
69 elucidate biological and behavioral mechanisms in order to be taken seriously by the
70 epidemiological community more broadly. A lack of pertinent funding mechanisms and a lack of
71 consensus on optimal scales and measures of psychosocial factors were identified as additional
72 barriers to advancing psychosocial research.

74 **Conclusions.** Our interviews emphasized the need for: (1) high-quality, longitudinal studies that
75 investigate biological mechanisms and pathways through which psychosocial factors influence
76 health; (2) effort among epidemiological cohorts to broaden and harmonize the measures they
77 use across cohorts, to facilitate replication of results; (3) and the need for targeted funding
78 opportunities from NIH and other grant-making institutions to study these domains.

84 **KEYWORDS**

86 Qualitative Research; Epidemiology; Public Health; Social Medicine

ARTICLE SUMMARY

Strengths and Limitations of the study

- We conducted qualitative interviews with 20 prospective cohort study Principal Investigators (PIs) to better understand barriers and opportunities for greater inclusion of psychosocial factors in high-quality epidemiological research.
- Interviews and data analysis were performed by a multi-disciplinary team with training and expertise in both qualitative methodology and epidemiology.
- Interviewing PIs from major cohort studies is a strategic choice that provides insight into the priorities and concerns of those who decide the research priorities for 24 U.S. cohort studies that collectively include roughly 3.2 million American adults.
- Findings from this qualitative study provide a roadmap for how to conduct future, high-impact epidemiological research on psychosocial factors.
- Findings from this qualitative study can also be used as a guide on how to engage leading U.S. cohort studies in future psychosocial research.

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3134INTRODUCTION

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7136Psychosocial factors encompass a broad set of experiences, including childhood

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9137adversity, isolation and loneliness, job-related stress, discrimination, trauma, religious and

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11138spiritual experiences, social support, healthy neighborhoods, and many other dimensions of life.

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13139While acute stressors normally elicit a healthy and adaptive stress response, severe or

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15140prolonged psychosocial stress can lead to long-term dysregulation of the stress reactivity

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17141system and disease.^{1,2} In particular, psychosocial stress has been implicated as a factor

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19142contributing to cardiovascular disease,^{3,4} hypertension,⁵ type 2 diabetes (T2D),⁶ obesity,⁷ and

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21143cancer,⁸ among other conditions. Likewise, positive psychosocial factors are also important

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23144sources of resilience, support, and engagement that can have positive impacts on mitigating

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25145stress and improving health.⁹⁻¹¹

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28146Despite the important role that psychosocial factors may play in disease etiology, they

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30147are not often assessed comprehensively in epidemiological research, particularly within

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32148prospective cohort studies. Furthermore, a lack of precise and operational definitions and

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34149clinical cut-off points for many psychosocial exposures has kept them from being incorporated

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36150more routinely into clinical guidelines and practice.^{12,13} The influence of psychosocial factors on

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38151disease etiology potentially encompasses both acute and chronic experiences, occurring

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40152throughout the lifecourse in both childhood and adulthood, that may associate with human

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42153disease through many different biological pathways.^{6,14} Since psychosocial experiences are

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44154complex phenomena that span many dimensions and timepoints within a person’s life, this

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46155poses difficulties for quantitative assessment in epidemiological research. It is therefore

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48156important that epidemiological investigators critically evaluate the measurement and

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50157investigation of these domains in a systematic and thoughtful way.

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54158Given that psychosocial adversity and stress are often experienced more frequently by

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56159racial/ethnic and socioeconomic minority populations in the U.S.,¹⁵ understanding the

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mechanisms through which psychosocial stress influences human health may also provide crucial insight into the production of health disparities in the U.S. Psychosocial stress may function both as a key factor driving disproportionate burdens of disease among underrepresented populations,¹⁶⁻¹⁸ and also serve as a key mediator or pathway through which experiences of inequality – such as difficult socioeconomic environments^{19,20} or poor sleep,²¹ among others – influence disease or disease-related behaviors. Likewise, fostering tools for psychosocial resilience and community building among underrepresented populations may also have a positive impact on health inequality.¹¹

In order to identify barriers and opportunities for greater inclusion of these domains in high-quality epidemiological research, we conducted qualitative interviews with 20 Principal Investigators (PIs) representing 24 different U.S. prospective cohort studies funded by the National Institutes of Health (NIH). These interviews were used to probe PIs' beliefs and opinions on the impact of psychosocial factors on health, and were also used to identify the evidence they require to see before adding additional assessments of psychosocial factors in future waves of data collection within their cohorts. Taken together, the qualitative results that follow from these interviews inform a theory of change that provides a roadmap for future psychosocial research methods that we theorize will generate more prominent and impactful psychosocial investigations within epidemiological research.

METHODS

Defining “Psychosocial”

Psychosocial research encompasses many possible topics and is used in myriad studies, although definitions are rarely offered. In this article, we begin by offering a definition, or at least a point of reference, that will serve as a useful starting point for understanding

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186 psychosocial dimensions of life. The American Psychological Association (APA) Dictionary of
187 Psychology²² lists several different definitions that can help us triangulate a working meaning.
188 “Psychosocial factors” are defined as “social, cultural, and environmental phenomena and
189 influences that affect mental health and behavior” (**Figure 1**). A psychosocial stressor, more
190 specifically, is defined by the APA as “a life situation that creates an unusual or intense level of
191 stress that may contribute to the development or aggravation of mental disorder, illness, or
192 maladaptive behavior. Examples of psychosocial stressors include divorce, the death of a child,
193 prolonged illness, unwanted change of residence, a natural catastrophe, or a highly competitive
194 work situation.”

195 This definition of psychosocial is broad, and encompasses experiences throughout the
196 lifecourse. It is important to note that the term psychosocial in itself does not refer just to
197 adverse life events, but more broadly to the confluence of social, cultural, and environmental
198 factors that come together to affect our biology, physiology, and psychology. Consequently, the
199 term psychosocial captures both negative stressors and positive sources of resiliency,
200 engagement, and community. This includes factors such as social support, religion and/or
201 spirituality (R/S), and healthy neighborhood conditions.

202
203 **Research Team**

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205 The research team members carrying out interviews (AES and TAB, both female, PhD-
206 level investigators) and data analysis (AES, TAB, MAA, BS, SNP, the final 3 of which were
207 Masters-level/pre-doctoral level researchers) have training and experience in diverse
208 disciplines, including qualitative, clinical, and epidemiological research. The team was thus
209 ideally suited to anticipate and address the dual demands of both maintaining qualitative rigor
210 while also trying to elicit and analyze data intended to engage an epidemiological audience.

AES is a health researcher who directs a research center that conducts transdisciplinary research aimed at elucidating the underlying causes of health disparities, identifying novel strategies to reduce health disparities, and addressing ethical and social issues in genomics research. TAB is a radiation oncologist with a longstanding interest in understanding the ways in which patients' religious or spiritual beliefs and practices influence their health care decision-making, particularly at the end of life. MAA is a medical anthropologist and population health researcher currently in the final year of a PhD in population health, and BS is an MD candidate and medical geneticist. Both MAA and BS have worked with AES over the past 5 years to conduct epidemiological and population health research on health inequality, with a particular focus on investigating psychosocial factors. SNP has training in cultural anthropology and is a DO candidate. She has conducted research with TAB for over 2 years focused on understanding the impact of religion and spirituality on health.

The research team sought to mitigate bias stemming from any prior beliefs or hypotheses the investigators brought to the study by employing good interviewing practices in which questions were asked without providing examples or steering the discussion in ways that were apt to introduce bias. Data coding and analysis was carried out using a hypothesis-free, grounded theory approach such that themes and theories presented in this article were only those that emerged from the empirical data and are not reflective of previous perspectives or interests of the investigators. These methods, in addition to data triangulation procedures, are described further in the Data Analysis section.

Participants and Recruitment

This study was carried out as part of a larger project investigating the perspectives of PIs on both psychosocial and R/S influences on health. PIs were contacted, recruited, and then

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3 236 interviewed about these two topics simultaneously. The results concerning PIs' views on the
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5 237 role R/S specifically are published in a separate manuscript.²³
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7 238 Because of our interest in generating new knowledge useful for reducing health
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9 239 disparities, we first developed an initial list of NIH-funded cohort studies that included large,
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11 240 national samples of racial/ethnic minority communities. Additional cohorts were identified
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13 241 through the published literature, NIH resources, and consultation with epidemiologist
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15 242 colleagues. We then developed a ranked list of 30 cohort studies based on how well they met
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17 243 the following criteria: (1) diverse racial/ethnic cohort composition; (2) long duration of
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19 244 competitive funding (as a proxy for influence of the PI); (3) many diverse clinical conditions
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21 245 covered; and (4) inclusion of large, nationally representative samples of cohort participants.
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24 246 The PI of each of these 30 studies was invited via email to participate in this qualitative
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26 247 study. None of the study investigators had had a previous relationship with the PIs. Telephone
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28 248 calls were scheduled with those interested in learning more, during which PIs were provided
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30 249 with additional information about the study to facilitate informed consent and again invited to be
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32 250 interviewed then or on a future date of their choosing. PIs who agreed to be interviewed were
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34 251 offered a \$100 honorarium. We followed these procedures until we reached our study goal of 20
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36 252 PI interviews. Only one PI with whom we discussed the study declined to participate in the
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38 253 study. All but two participating PIs refused the honorarium. Based on our prior work,²⁴⁻²⁹ we
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40 254 anticipated that 20 interviews would be a sufficient number to achieve thematic saturation.
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45 256 **Data Collection**
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49 258 All one-hour, semi-structured PI interviews were conducted in 2015 by the Principal
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51 259 Investigator of our qualitative study (AES), with a subset conducted jointly by two members of
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53 260 the study team (AES and TAB). During interviews, PIs were invited to articulate their own
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55 261 understanding of psychosocial research and psychosocial influences on health in the broadest
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possible sense, and were not provided a definition by interviewers. PIs were not instructed to focus on specific psychosocial experiences or variables, and therefore unless specific types of experiences are given as examples in a PI's response, we interpret their answers to refer generally to the whole field of psychosocial factors. Interview questions addressed: (1) PIs' experiences with and exposure to research addressing psychosocial influences on health; (2) reasons why their cohort has collected particular psychosocial measures in the past; (3) assessment of the quality and value of existing psychosocial research; (4) assessment of the importance of psychosocial factors in understanding disease etiology; (5) beliefs regarding the pathways or mechanisms through which they imagine psychosocial factors might operate to affect human health, if at all; and (6) the evidence they would need to see before being willing to invest additional cohort resources in collecting new psychosocial measures.

Data Analysis

All interviews were recorded and transcribed. Transcripts were analyzed using a grounded theory approach.^{30,31} The interviewers and two research assistants (RAs; BS and SNP) independently 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), and any emergent themes or discrepancies brought to the investigators for resolution. Data were analyzed using content analysis to identify major concepts and themes, and axial coding to group and connect related data.^{29,31,32} Within each topic area, we identified 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.³³ We incorporated triangulation at two levels. First, we used a multidisciplinary research team for coding and analysis (investigator triangulation). All coding was done using a grounded theory approach, wherein investigators identified themes that emerged from the empirical data irrespective of their own hypotheses, research interests, or priorities. The Kappa score for assessing congruence of coding between coders was 0.95, indicating an extremely high interrater reliability. This strongly suggests that the coding schema developed and applied to interview transcripts reflects themes emergent and plainly evident in the transcripts and does not reflect investigator bias or investigators projecting their own epistemological viewpoints onto the information provided by informants. Second, we included PI participants from diverse communities and disciplines, whose cohort studies also include participants from diverse racial/ethnic communities and geographical regions of the country (data triangulation). This ensured that any significant themes found were reflective of a consistent and broad viewpoint across PIs representing many different kinds of NIH-funded cohort studies.

Patient and Public Involvement

As this was a targeted investigation into the perspectives of NIH-funded cohort study PIs, no patients or members of the public were involved in the design or recruitment of our study, nor in the dissemination of results. Our semi-structured interview guide was developed by AES, with input from the study team and several investigators participating in the National Consortium on Psychosocial Stress, Spirituality, and Health (CoSSH).

Ethics Approval

Institutional Review Board approval for this study was obtained from the Partners Human Research Committee (Protocol # 2015P000014/MGH).

RESULTS

The final study sample of 20 PIs included men and women from several different racial/ethnic communities, although the vast majority were white. PIs represented a wide range of ages, although few were younger than 55 years old. Most PIs had led only one prospective cohort study in their career, although some had served as PI for more than one study. Collectively, the 20 PIs interviewed for this study represent longitudinal health data on nearly 3.2M individuals across 24 cohorts, or roughly 1.25 out of every 100 adults in the U.S. aged 18 or over. This includes data on every major racial group in the U.S., including approximately 400,000 African Americans and 120,000 Hispanics/Latinos (**Figure 2**).

Importance of the psychosocial domain

PIs' shared similar views regarding the importance of psychosocial influences on health outcomes. When asked about the importance of psychosocial measures more broadly, one PI responded with:

I mean, I think it is very, very important. We've tried to pay a lot of attention to it in our own cohort...I think it's very important to pay a lot of attention to this, because I feel that many psychosocial variables are definitely modifying factors for disease risk, and can also be causally associated.

PIs with clinical experience often cited their observations of the influence of psychosocial experience on their patients' outcomes: "I think it's based on my clinical experience...if you don't address the psychosocial factors, you'll never be able to help improve that person's treatment, and their care for diabetes." Those with clinical experience also seemed to appreciate the complex ways in which psychosocial factors interact with other "traditional" risk factors:

Certainly, my feeling is that there's probably some complex interplay between psychosocial factors and, for lack of a better word, more traditional factors -- say, for instance, a blood level of cholesterol or blood pressure...In my clinic, I can certainly see that some of these psychosocial factors have enormous impact on the other potent, traditional risk factors.

Others viewed psychosocial measures in general as "soft" measures that would never be as informative as "hard" biological measures, but even these PIs believed that to ignore psychosocial influences would be a mistake:

This [psychosocial influences] is not a solid measure of exposure. But I do think that to ignore it, when you're talking about symptoms and presentation of disease, is a mistake, because it's all together...I think it all goes together to create this person's sense of well-being, and you can't ignore it.

Others noted tensions within the field of epidemiology regarding the importance of psychosocial factors in disease etiology, particularly regarding the extent to which psychosocial factors were captured in other measures of behavior or social support already collected. As one PI explained:

I think there's two camps...The skeptics feel it's not an independent risk factor, and you can account for it with all the other factors and behaviors like smoking, alcohol use, etc. But there's a very strong camp that believe that these are upstream of the lifestyle behaviors, and if you don't measure them correctly, you may be artificially saying that they are all explained by behaviors, and that they may actually be independently related to disease outcomes.

Despite a general acceptance of the importance of psychosocial factors in health expressed by the majority of PIs, some were more positive about certain psychosocial domains over others. While PIs were often quick to accept the importance of measuring factors such as

social support, abuse, and discrimination, many were far less certain about the contribution of religion and spirituality (R/S) as a source of psychosocial resilience, for example, since it has been less extensively studied in cohort studies. Among our PI informants, three believed that R/S were not important to study in research on human health, eight were open to the possibility that R/S may be important to health but believed that the “jury is still out,” and nine felt that R/S likely had an important impact on health.

The need for psychosocial research using clinically-relevant biomarkers

The vast majority of PIs suggested that for future psychosocial research to gain greater currency among epidemiologists, it would need to explore clinically-relevant biomarkers and biological mechanisms. As one PI put it, “I think the emphasis today in epidemiological sciences is to delineate a clear biological mechanism.” Some offered ideas about creative avenues for exploring these relationships: “I would love to see studies on the effect of psychosocial stress on the microbiome, because of stress’s influence on the immune system.”

When asked where they see the field of psychosocial research going in the future, one PI responded, “I think it is moving into trying to be more anchored in actual biologic changes...to identify people who are actually more likely to have a biologic response in relation to some external stressor.” One PI noted that recent studies investigating psychosocial stress in relationship to biological variables are changing epidemiologists’ opinions on the importance of psychosocial stress to health:

Studying psychosocial factors and stressors is relatively new, and [was] met with a lot of skepticism until fairly recently... But I think what’s changed...[is] there’s now biological evidence that stressors may affect various biomarkers.

Another PI emphasized that psychosocial research should ideally be framed in terms of a biological pathway:

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3 401 I wouldn't require that you would have the whole pathway – that is, exposure to
4 402 intermediates to health outcome – because that's probably the kind of link we're
5 403 looking for in studies. But having something between the intermediate and health
6 404 outcome, and having something between the determinant and something along
7 405 that initial pathway, I think would be very helpful to justify doing [psychosocial]
8 406 measures in a cohort study.

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11 408 Although all PIs discussed the value and contribution of conducting future research to
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13 409 elucidate the biological mechanisms through which psychosocial factors operate, several also
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15 410 had concerns about potential directions this kind of research could take when connected to the
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17 411 health of minority and underrepresented communities. As one PI articulated, it's "a little
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19 412 frightening to think about genes and behavior, or genes and things in the psychological realm.
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21 413 You know, some sinister images can pop up...it frightens some people that, you know, you can
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23 414 look at a genome, characterize somebody, and discriminate against them." Other PIs shared
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25 415 similar worries about genomics research with a focus on psychosocial factors. The concern was
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27 416 that if researchers establish correlations between genetic variants (or other biological
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29 417 characteristics) and psychosocial factors such as educational attainment, living in a poor
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31 418 neighborhood, experiencing discrimination, or other factors, that these results might be used to
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33 419 justify discrimination against these groups. In other words, these sorts of results might be used
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35 420 by those who don't understand the nuances and limitations of these research findings to try to
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37 421 claim that certain groups in society who experience adversity or inequality are genetically or
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39 422 biologically inferior.

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43 424 ***Psychosocial research as an important domain for potential interventions***

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46 426 Roughly half of the PIs interviewed also discussed psychosocial research as potentially
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48 427 helpful in developing public health interventions. One PI articulated this particularly well:

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51 428 We've had half a century of risk factor epidemiology that tends to focus on the
52 429 individual as the driver of behavior change. I think this field of stress and

psychosocial stress is one that can help us look at the social context and other environments in which people live, and help us think about interventions.

Another PI echoed this enthusiasm, but also expressed concerns about how to actually operationalize insights about psychosocial research for public benefit. As he explained, “So to the extent that observing that racial discrimination increases stress and can impact high blood pressure...that’s a useful, almost intuitive observation. But then what?...How do we then break that influence on health?”

PIs’ abilities to envision how psychosocial research would translate into improved public health interventions varied by the type of psychosocial domain discussed. Some PIs, for example, had difficulty seeing how R/S research could be used to develop interventions to improve health. As one PI explained:

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.

Challenges in the field

Despite expressing uniform appreciation for the potential of psychosocial factors influencing disease onset or survival, many PIs described a number of circumstances that they see as inhibiting their own cohorts, and the larger epidemiological community, from engaging in robust assessments of psychosocial factors.

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3 455 Challenging funding landscapes
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7 457 Several PIs mentioned that despite their own interest or the interest of their colleagues,
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9 458 a lack of relevant funding mechanisms, or even a lack of certainty about future NIH cohort
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11 459 funding in general, has prevented efforts to investigate psychosocial factors. Several made off-
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13 460 hand comments similar to this one: “Oh, we’re always open to new projects. So we’d be happy
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15 461 to ask questions if there was funding available.” Many PIs also described that their funding
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17 462 organizations had specific scientific priorities and expectations for the parameters of their
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19 463 cohort’s questionnaires, which would limit their ability to add in survey questions on
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21 464 psychosocial stress. Several cohort PIs also noted that they do not currently have funding from
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23 465 NIH lined up for another wave of data collection.
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28 467 Reproducibility and consensus surrounding measures of psychosocial factors
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32 469 Several PIs noted that for researchers to be able to reproduce robust research on
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34 470 psychosocial variables and health, it would be a priority that multiple cohorts collect the same
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36 471 psychosocial measures. Describing the field of psychosocial research at large, one PI
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38 472 recounted, “My sense is that...it’s still very broad. And different people are doing different types
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40 473 of psychosocial stressors...I’m hoping that the field might narrow a little bit if we’re able to do
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42 474 this kind of linkage [between cohort studies].”
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45 475 PIs often articulated that this would necessitate pooled analyses across cohorts and
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47 476 racial/ethnic groups:
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50 477 I think the kind of data that I would like to see are large, multicentric, multiethnic
51 478 cohorts, with reasonable duration of power -- of follow-up, with adequate
52 479 statistical power, with appropriate characterization of the exposure with validated
53 480 instruments, appropriate adjustment for multiple layers of confounding.
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As another PI described, however, the downside is that “we always go back to the least common denominator when we pool. And to do gene environment interactions, you almost have to pool cohorts... You’re going to lose quality if people don’t ask the question in a manner that you can pool across studies.” Clearly, the lack of similar or harmonized psychosocial measures across multiple cohorts to facilitate larger-scale, pooled analyses, is seen by most PIs as a limiting factor for current psychosocial research.

DISCUSSION

The PIs we interviewed almost unanimously agreed that future research on psychosocial domains is likely important, but emphasized the need to elucidate the biological and behavioral mechanisms through which psychosocial factors impact health in order to convince the epidemiological community more broadly to invest resources in investigating psychosocial stress and resilience. To conduct this kind of rigorous psychosocial research using biomarkers and mechanisms, investigators will need to have access to both robust and clinically-relevant biological data, as well as comprehensive psychosocial, socioeconomic, behavioral, and health outcome or clinical data on their study participants. Data are also needed at both the individual and neighborhood levels to properly capture all of the dimensions of a person’s psychosocial environment. These comprehensive data are currently most reliably found in prospective cohort studies, but robust numbers of psychosocial measures are not yet found consistently across cohorts.

One striking finding from our study is the extent to which the selection of psychosocial measures to be collected by cohorts is a nonlinear process determined by the interests and biases of particular research teams. It seems that cohorts did not set out to systematically identify all psychosocial factors and domains that are important to health and thus should be included in their data collection efforts. Instead, cohorts seem to have only collected

psychosocial factors if and when they support other analyses for more traditional outcome or lifestyle variables, or if an investigator within the cohort advocates for a particular psychosocial measure needed to support their research. Thus, successful psychosocial research depends on champions within established epidemiological cohorts who can convince colleagues to commit resources for collecting further psychosocial variables and completing psychosocial analyses.

Our interviews also showed that many cohort PIs see psychosocial research as an important area to investigate for developing potential public health interventions. Indeed, behavioral, lifestyle, and resilience factors have been shown to mitigate the impact of stress on developing disease.^{11,34} Despite this enthusiasm exhibited by PIs, however, our interviews also highlighted challenges to the feasibility of this research. In particular, the lack of targeted funding and the lack of consensus on key measures to be collected and/or harmonized across cohort studies were identified as primary barriers that need to be overcome to advance psychosocial research.

Our study had several limitations worth noting. While the 20 PIs interviewed represented diverse ethnicities, ages, and clinical domains of interest, they may not fully capture the diversity in PIs' attitudes towards psychosocial research. According to NIH institute websites, there are 70 cohort studies currently funded by NCI and NHLBI, and thus our results reflect the perspective of PIs from roughly a quarter of all NIH-funded cohorts. Future research could survey PIs nationally to quantitatively assess a broader array of perspectives. While we have outlined in this paper the types of research that will be persuasive to cohort PIs in evaluating psychosocial research, future research could also investigate PIs' views on what the quantitative threshold – in terms of numbers of new studies, health conditions investigated, or other criteria – might be for a persuasive evidence base that legitimizes the investment of more cohort resources into psychosocial research. Our grounded theory approach limited our analyses and focus to the empirical data gathered, and did not allow us to offer deeper interpretation or explanations for why PIs may hold the views that they reported. We also recognize that there

may seem to be a methodological disconnect in conducting a qualitative, grounded theory study to provide insight for a quantitative, epidemiological audience. We believe, however, that in-depth interviews with cohort PIs is a highly strategic approach that is essential to understanding the on-the-ground demands and challenges of conducting epidemiological research with cohort study data, and is crucial to developing a *theory of change* for epidemiological psychosocial research. We further believe that our multi-disciplinary team of investigators who have training and experience in both qualitative and epidemiological research has allowed us to bridge these two different methodological approaches and epistemologies.

Despite these limitations, this study provides the first assessment of cohort PIs' attitudes and beliefs regarding the influence of psychosocial factors on disease etiology, and identifies challenges for the field of psychosocial research from the perspective of these thought leaders in epidemiology. Our results provide a strategic and pragmatic roadmap for future psychosocial researchers to draw upon in designing and proposing research studies to be conducted within cohort studies, and for identifying strategies to engage cohort study investigators in future research to advance knowledge regarding the role of psychosocial influences in disease etiology.

CONCLUSION

Looking forward, our interviews with cohort PIs emphasized that: (1) future research will need to investigate biological and behavioral pathways through which psychosocial factors influence disease; (2) funding bodies need to create funding mechanisms and requests for proposals that specifically support these types of analyses as a scientific priority; and (3) psychosocial research will need to be carried out with a focus on building consensus within the greater epidemiological community regarding the most important psychosocial factors to human health and the best measures for capturing these factors, in order to facilitate replication of

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560 results and multi-cohort analyses. PIs also emphasized that future psychosocial research that
561 follows these steps may be particularly impactful in identifying novel public health interventions.
562 By understanding the mechanisms through which psychosocial factors – including both stress
563 and resources for resilience – operate to affect disease across diverse populations, researchers
564 will not only gain new insight into the etiology of many chronic diseases, but will also generate
565 new insight into how health disparities in the U.S. are produced and identify new leverage points
566 for addressing them.

For peer review only

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FIGURES

Figure 1. Model of psychosocial influences on health. Note: these three domains of life (social, cultural, environmental) converge on individual “health,” which indicates both physical and mental health, as well as intermediate biological and physiological pathways that influence health.

Figure 2. Total number of adult study participants (aged 18 or over) represented by participating PIs’ cohorts, including breakdown by race/ethnicity.

AUTHORS’ CONTRIBUTIONS

AES conducted all PI interviews and TAB joined AES in conducting a subset of interviews. BS, SNP, TAB, and MAA indexed qualitative transcripts, and AES, TAB, BS, SNP and MAA completed interview data analysis. MAA wrote the initial draft of the manuscript and created figures. All authors read and approved the final manuscript.

DATA SHARING

Transcripts of the full interviews with cohort PIs are not publicly available due to the ease with which cohort PIs could be identified. However, anonymized and redacted interview transcripts are available, upon reasonable request, by emailing the corresponding author directly.

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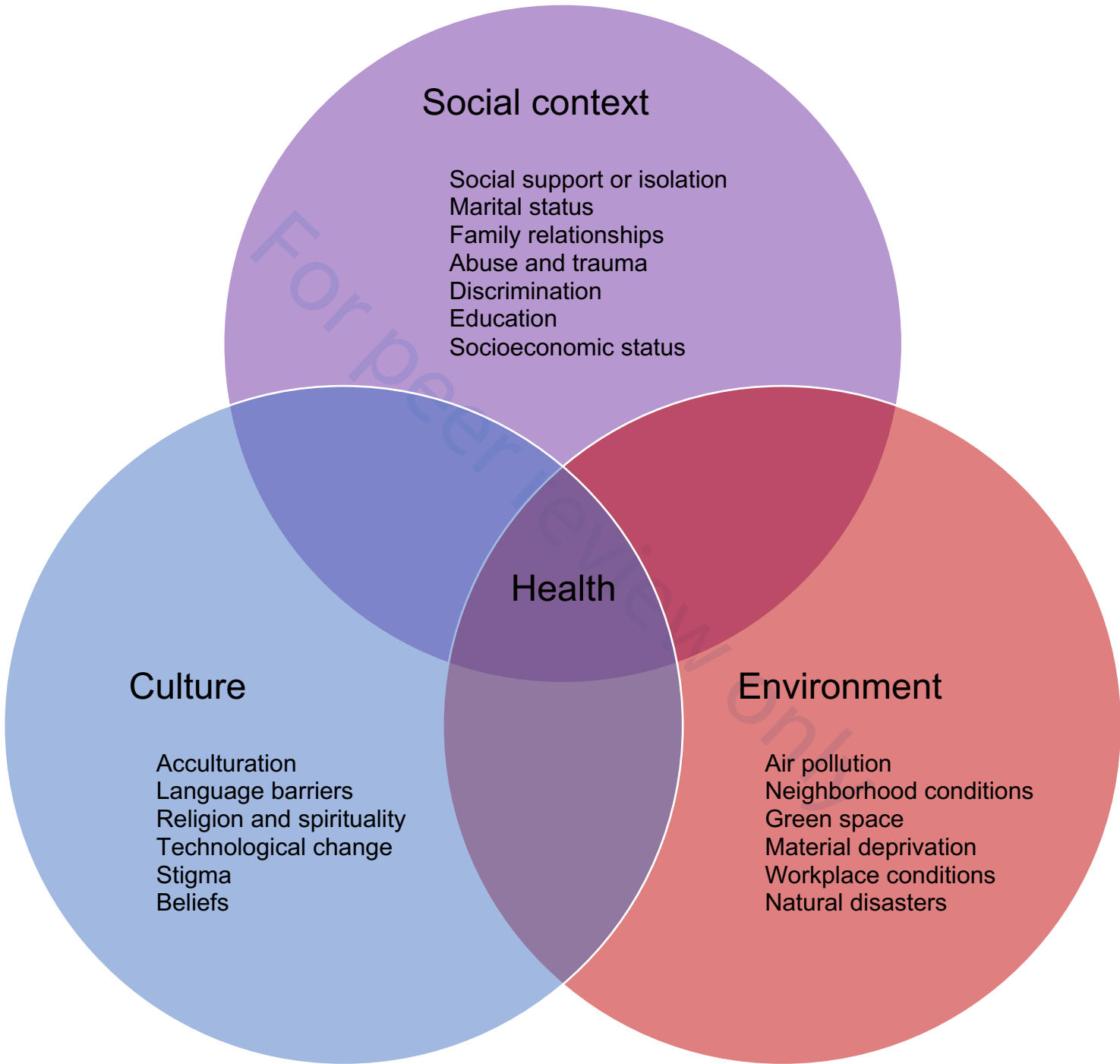
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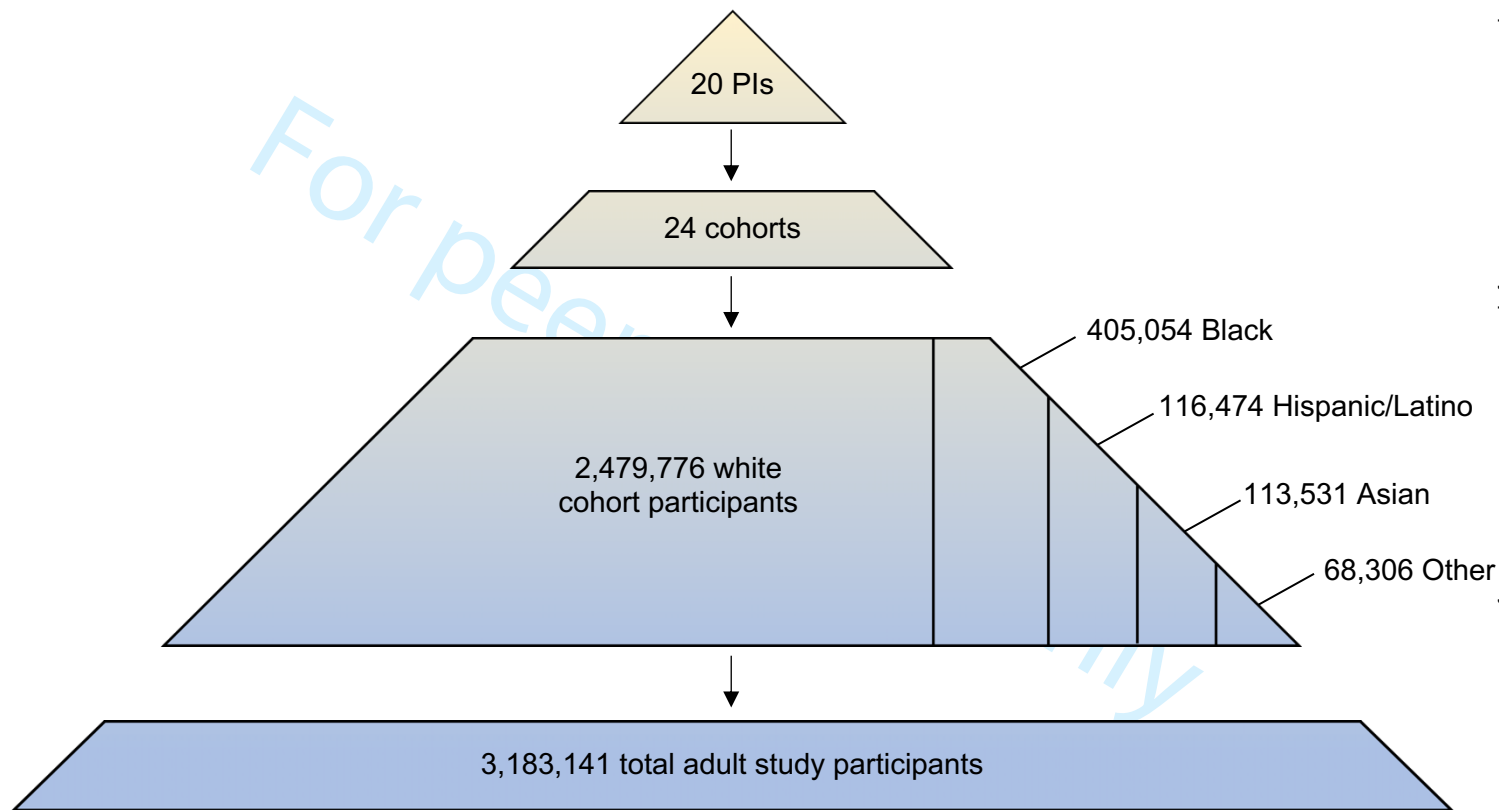
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COREQ (CONsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	
Credentials	2	What were the researcher’s credentials? E.g. PhD, MD	
Occupation	3	What was their occupation at the time of the study?	
Gender	4	Was the researcher male or female?	
Experience and training	5	What experience or training did the researcher have?	
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	
Sample size	12	How many participants were in the study?	
Non-participation	13	How many people refused to participate or dropped out? Reasons?	
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	
Field notes	20	Were field notes made during and/or after the inter view or focus group?	
Duration	21	What was the duration of the inter views or focus group?	
Data saturation	22	Was data saturation discussed?	
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	
Software	27	What software, if applicable, was used to manage the data?	
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	
Clarity of major themes	31	Were major themes clearly presented in the findings?	
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

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