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Stress Measurement in Primary Care: Conceptual Issues, Barriers, Resources, and Recommendations for Study

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Abstract

Objective: Exposure to stressors in daily life and dysregulated stress responses are associated with increased risk for a variety of chronic mental and physical health problems, including anxiety disorders, depression, asthma, heart disease, certain cancers, and autoimmune and neurodegenerative disorders. Despite this fact, stress exposure and responses are rarely assessed in the primary care setting and infrequently targeted for disease prevention or treatment.

Method: In this narrative review, we describe the primary reasons for this striking disjoint between the centrality of stress for promoting disease and how rarely it is assessed by summarizing the main conceptual, measurement, practical, and reimbursement issues that have made stress difficult to routinely measure in primary care. The following issues will be reviewed: (1) assessment of stress in primary care; (2) biobehavioral pathways linking stress and illness; (3) the value of stress measurements for improving outcomes in primary care; (4) barriers to measuring and managing stress; and (5) key research questions relevant to stress assessment and intervention in primary care.

Results: Based on our synthesis, we suggest several approaches that can be pursued to advance this work, including feasibility and acceptability studies, cost-benefit studies, and clinical improvement studies.

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Conclusions: Although stress is recognized as a key contributor to chronic disease risk and mortality, additional research is needed to determine how and when instruments for assessing life stress might be useful in the primary care setting, and how stress-related data could be integrated into disease prevention and treatment strategies to reduce chronic disease burden and improve human health and wellbeing.

Keywords

Life stress; Assessment; Measurement; Screening; Primary care; Risk; Treatment

Introduction

The idea that exposure to life stressors and the responses to them can make us ill is popular in American and other cultures and has been the focus of substantial research [1, 2]. In the clinical practice of primary care, however, healthcare providers have little guidance, time, or incentive to assess stress-related factors. This lack of assessment persists despite evidence that life stressors can alter biological processes that promote the onset and progression of our most common and costly chronic illnesses, including diabetes, obesity, heart disease, and depression [3–6]. Stress also has been linked to increased utilization of primary care services [7] and to the rising mortality rates and shrinking life expectancy in the U.S. [8] but, again, this has not led to widespread assessment or targeted interventions.

Stress is rarely assessed in clinical practice in part because of a lack of consensus on how best to assess this construct. This is true even though numerous instruments exist for assessing stress-related constructs (see https://www.stressmeasurement.org/measurement-toolbox). Some of these measures have been adapted for use in clinical practice, but no guide exists for choosing among these many instruments. Another barrier is the lack of consensus on working definitions of stress-related constructs that are relevant for clinical practice. For example, scientists do not agree on the boundaries between “good”, “tolerable”, and “toxic” stressors or stress responses. Moreover, psychological *outcomes* of life stressor exposure, such as anxiety and depression, are often confused with, or used as markers of, life stressor exposure. Consequently, stress is a coin with no clear measurement guidelines on one side and no clear definitions on the other.

A fact that further complicates the translation of stress measurement into clinical practice is the variability in needs and resources across clinical settings. Whereas clinicians sometimes need to assess exposure to stressors to estimate disease risk, other times they need to measure stress responses to monitor treatment progress. Furthermore, clinical needs can vary with patient populations, with some populations potentially benefiting from a different stress assessment approach than others.

To address these challenges and help translate the assessment of stress into better clinical practice, we first briefly review studies assessing stress in primary care. Second, we summarize the main biobehavioral pathways linking stress and illness. Third, we discuss the value of stress measurements for improving outcomes in primary care. Fourth, we describe barriers to measuring and managing stress in primary care. Finally, we identify key research questions for addressing issues of feasibility and clinical improvement. In doing so, we

aim to address the concerns of health services researchers interested in improving outcomes for common chronic illnesses, health policy decision-makers considering demonstration projects for cost reduction in chronic illness care, and primary care clinicians seeking quality improvements in their clinical practices.

The present work represents the consensus viewpoints of the authors, who met monthly from 2018–2020 as members of the American Psychosomatic Society's (APS) Task Force on Stress Measurement in Primary Care. The Task Force was charged with the goal of developing recommendations for improving the measurement of stress in primary care. Members were solicited from the APS 2018 Annual Meeting and by word of mouth. We strived for a balance of disciplines, ages, genders, and cultural backgrounds. A draft of this report was reviewed by the APS Leadership Council, which recommended revisions. Since our aim did not lend itself to meta-analysis, our methods followed standard procedures for a narrative literature review, and recommendations were derived from consensus discussions. This final report was read and approved by the APS Leadership Council but does not represent an official position of the APS.

Current Studies of Stress Measurement in Primary Care

In contrast with a sizeable literature on how stress affects health, relatively few articles have examined issues related to the measurement of stress and, to our knowledge, none have done so in the context of primary care. Along these lines, a recent review of instruments for assessing exposure to early life adversity [9] identified 32 measures, of which 14 were recommended for use in pediatric practice. The authors found that most of the measures identified lack published psychometric data and they concluded by describing several challenges related to the adversity categories assessed, target populations studied, administration methods, reliability, and validity. In addition, two recent commentaries emphasized the urgent need to improve both the practice of measuring exposures to childhood adversity in primary care and research on the risks and benefits of these measurement practices [10, 11]. Beyond this work, we know of no reviews examining issues related to assessing life stress in primary care.

One different but related analysis was conducted by the National Comprehensive Cancer Network, which recommended systematically assessing patients' distress levels at each clinical visit using the Distress Thermometer, which measures self-reported distress using a 0–10 Likert scale. When using the Distress Thermometer, patients also complete a checklist of five possible sources of distress—namely, practical, family, emotional, spiritual/religious, and physical problems [12, 13]. In 2014, a meta-analysis of 42 studies found the Distress Thermometer to be a valid measure with good sensitivity and specificity [14]. Using the Distress Thermometer reduces the chances of missing depression and anxiety disorders [15], and it is also sensitive to changes in distress over time [16]. Moreover, the instrument appears to be helpful for reducing healthcare utilization. For example, cancer centers that assessed distress reported 18% fewer emergency department visits and 19% fewer hospitalizations in the 2 months following the screening (https://ascopost.com/News/57837). Partly as a result of these findings, in 2015 the Commission on Cancer established

accreditation standards that included a requirement for distress screening and appropriate clinical response [17].

In addition to a Danish study showing a dose-response association between psychological distress and primary services utilization [7], a review of psychological distress in frequent primary care and emergency department users found that psychological distress was associated with high medical service utilization and should thus be assessed for both intervention and cost containment reasons [18]. However, the review did not evaluate the measurement practices used, and the high frequency with which primary care clinicians are asked to counsel about stress [19] underscores the pressing need for reliable and useful instruments.

Evidence Linking Stress and Illness: Biological and Behavioral Mechanisms

Why should primary care practices bother with measuring stress, especially when they are already overburdened? And why should health services researchers study the measurement of stress in primary care? One main reason is that adverse childhood experiences (ACEs) and chronic adulthood stressors are relatively common experiences that portend the development of a variety of costly and burdensome mental and physical health problems. For example, the ACEs Scale has been found to robustly predict 40 health outcomes in adulthood, typically in a dose-response manner [3, 20, 21]. In addition, stressors and dysregulated stress responses have been associated with a 25–50% increase in risk for coronary heart disease, a 2-fold greater risk of Type 2 diabetes, and changes in cellular and humoral immunity that increase risk for infectious diseases [22–25].

Although a complete overview of the pathways linking stress exposure and health is beyond the scope of this review, identifying such pathways can lead to novel assessment targets, with some being more easily modifiable or measurable in primary care than others. These pathways include: (1) Genes and epigenetics, including the impact of stress on gene expression profiles that affect disease risk [26–29]; (2) Risky health behaviors, including smoking, unhealthy diet, poor sleep, and sedentary behaviors [30]; (3) Unsafe social interactions, including abusive, threatening, and neglectful relationships [31]; (4) Autonomic nervous system imbalance, caused by stress-induced patterns of excessive sympathetic and insufficient parasympathetic activity [32–34]; (5) Glucocorticoid receptor insensitivity or resistance, which can promote the development of depression and metabolic disorders [35, 36]; and (6) Chronic inflammation, caused by stress-related dysregulation in immune system processes that promote chronic, low-grade inflammatory processes [36–39].

These pathways are complex and interact at all levels of the biopsychosocial model, from genes to organ systems to psychology to social relationships and environments. Since no single measure can capture all aspects of the stress-illness association, the process of measuring stress for clinical benefit may require serial measurements by different measures. As in much of medicine, the stress measurement has to progress in a stepped care fashion from the initially broad and simple level in primary care to the detailed and complex in specialty care.

Value of Stress Measurement for Improving Outcomes in Primary Care

Assessing stress in primary care may also be useful insofar as it can help identify patients who would benefit from stress management. Managing stress, especially in conjunction with other behavioral interventions, has shown promise for reducing risk for a variety of chronic conditions commonly encountered in primary care, including cardiovascular disease, diabetes, obesity, and chronic pain syndromes [40]. Effective stress management techniques include mindfulness-based stress reduction, other forms of relaxation training, low-grade exercise training, cognitive behavioral therapy, sleep management, and group support, with each showing evidence of helping to improve patients' quality of life [41], delay or reverse the progression of disease [42], or reduce the risk of mortality [43].

Along similar lines, research has shown that stress reduction improves the course and prognosis of coronary heart disease. The Ornish intensive cardiac rehabilitation program also has been shown to yield long-lasting improvements in cardiovascular risk [44, 45], and incorporates intensive stress management including yoga and meditation, vegetable-based diet, daily physical activity, and weekly psychosocial group support. Significant improvement in clinical outcomes include levels of triglycerides, low-density lipoprotein (LDL), total cholesterol, blood pressure, and BMI [46]. Psychological interventions also appear to help prevent clinical coronary heart disease in patients who otherwise have a healthy lifestyle (i.e., nonsmoking, eating a balanced diet) [47]. One such program reduced medical service utilization by 43%, and is estimated to save from $640 - $25,500 per person in healthcare costs [48].

In addition, stress reduction has been recommended as a behavioral management for hypertension in the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [49]. There is also evidence that transcendental meditation can yield clinically significant reductions in systolic blood pressure [50, 51], and that multicomponent stress reduction therapies significantly reduce blood pressure [52, 53]. However, more research is needed to determine the longer-term efficacy beyond a 3–6 month follow-up, as well as an improvement in ambulatory blood pressure, especially since existing evidence is limited to blood pressure measured in doctors' offices.

Mindfulness, cognitive restructuring, and acceptance and commitment therapies have all been found to improve HbA1C levels in patients with type 2 diabetes [54–56], and a recent meta-analysis suggested that psychosocial interventions may lead to decreases in harmful immune system function and to improvements in beneficial immune system function [57]. Stress management interventions also yield long-term cost reduction, with reduced serum cholesterol at 12 months and savings of $137 per patient, which is modest when compared to other interventions [58, 59].

The value of measuring perceived stress in clinical settings to help inform and improve healthcare also has been demonstrated in initiatives by the Institute of Medicine (IOM) to establish standardized measurement of sociodemographic, psychosocial, and behavioral factors that affect health. The IOM recommended including measures of stress along

with depression, social connectedness, and intimate partner violence [60, 61]. These recommendations were based on assessing the usefulness of constructs for managing population health and individual patient care, psychometric properties, and burden and possible discomfort or risks of disclosure. However, the efficient use of scarce resources requires that we identify people who might benefit most from intensive stress management interventions.

Target Populations

The common pathways from stress to illness described above suggest that several target populations may benefit from the assessment of stress exposures and responses in primary care, including those with (a) high levels of ACEs, (b) any stress-related chronic health condition, (c) metabolic syndrome, (d) multiple comorbid medical and psychiatric disorders, and (e) persons with persistent unexplained medical symptoms. These populations, which likely comprise a majority of the adult primary care population, are most likely to benefit from screening and monitoring of stress exposures and responses as well as stress management. They are also the populations that incur high costs in the healthcare system [62–64].

Barriers to the Measurement and Management of Stress in Primary Care

Barriers that have prevented clinicians from assessing and treating stress fall under four main categories: (a) definitions of stress, (b) measurement-related barriers, (c) provider-related barriers, and (d) patient-related barriers.

Effective Working Definitions of Stress in Primary Care

The term *stress* has been a barrier to effective stress measurement because stress has historically been used as a noun, verb, and adjective, as well as to describe both a stimulus (e.g., life stressor) and a response (e.g., anxiety, depression). This has led to substantial debate and confusion, and prevented the development of precise assessment and standardized approaches to the measurement and treatment of stress-related health problems [65, 66].

To address these terminology and definitional issues, we recommend that clinicians and researchers only use the term *stress* when referring to general, non-specific adaptive biopsychosocial responses that are essential for responding to environmental challenges. In turn, *stressor* should be used to refer to a specific acute (i.e., short-term, episodic) or chronic (i.e., long-term, persistent) event, situation, or environment that can elicit a psychological, biological, or behavioral response, with those that persist being more likely to degrade health-sustaining biological stress systems [67, 68]. Finally, *stress response* is a general term that refers to the personal experience or appraisal of a stressor and the ensuing cognitive, emotional, psychological, biological, and behavioral response.

The *physiological activation* component of a stress response can involve the autonomic, neuroendocrine, and immune systems, which help individuals adequately manage a stressor and regain homeostasis [69]. This activation is likely not dangerous when engaged

infrequently; when activated frequently or chronically, however, these stress systems may become dysregulated, altering the functioning of the autonomic, neuroendocrine, and immune systems [70]. Indeed, what appears to be more predictive of disease than the magnitude of the stress response is the duration of the response or the time required to recover [71]. Slower recovery can amplify the burden on the stress response system, and, if persistent, it can hasten the development of disease [72, 73]. The characteristics of acute and chronic stressors and stress responses are described in Table 1.

Measurement-Related Barriers

Even with clear definitions, it can be difficult for clinicians to assess stress processes in primary care because of a lack of consensus on how to efficiently, reliably, and validly measure the relevant constructs. Acute and chronic stressor exposure is often assessed using questionnaires or interviews that inquire about the frequency, timing, and/or duration of stressors. Researchers have also relied on life event checklists, where individuals report which stressful events (e.g., death of a loved one, job loss) have happened to them over a designed time period. Using these instruments, clinicians and researchers can create a score for *cumulative lifetime stress exposure*, or the sum of all the acute and chronic stressors that a person has experienced over the life course. Questionnaires and checklists tend to be brief, cheap, and easy to administer. However, they are often unreliable, imprecise, and biased [74]. In comparison, interview-based techniques demonstrate superior validity relative to checklists, but are more costly and time consuming [67].

Methods for measuring acute stress responses depend on the stress response domain of interest. Questionnaires and interviews can be used to assess cognitive and emotional responses. For example, a measure can ask whether a stressor occurred then inquire about a person's perceptions of and/or current emotions related to their experience. Assessing a person's perceptions of a stressor can be particularly useful, as some research has shown that individuals' subjective perceptions of a stressor may be more strongly related to health than whether a stressor has occurred [75]. However, subjective stress response assessments may be affected by factors like *socially desirable responding* (i.e., responding with socially acceptable answers rather than being truthful) and *recall bias* (i.e., misremembering or recalling prior experiences).

Researchers also measure acute physiologic stress responses using a physical exam, laboratory-based challenge tasks, or ambulatory recordings. Physiologic measures such as heart rate, blood pressure, and neuroendocrine and inflammatory markers can be collected during laboratory-based mental stress tasks to quantify a person's acute stress response [76–78]. Wearables that continually track vital signs and more complex physiologic markers of stress (e.g., heart rate variability) are still in development but will one day provide more ecologically valid assessments of ambulatory acute stress responses [79]. However, for each of these laboratory or ambulatory measures, single values may be confounded by extraneous factors other than psychological stress, such as health behaviors or obesity, that need to be taken into account. Therefore, ensuring the accuracy and reliability of these measures for capturing acute stress responses in the general population is an important task for future research.

Chronic stress responses can be assessed by combining measures of endocrine, immune, metabolic, and cardiovascular functioning into an index called the *allostatic load index* [80, 81], which is possible to do in the lab but challenging to accomplish in a primary care setting. Nevertheless, doing so is an important goal, as both cumulative lifetime stressor exposure and allostatic load have been found to predict accelerated biological aging and the onset and progression of common chronic illnesses, such as heart disease and diabetes [80, 82, 83]. However, uniform procedures need to be identified that ensure the physiologic indices are reflecting chronic stress and not long-term effects of other health issues (e.g., diabetes, cardiovascular disease) that may occur either separately from or alongside stressor exposure.

The issue of balancing measurement efficiency with reliability (i.e., consistency) and validity (i.e., accuracy) is compounded by the lack of focus on what qualifies as a clinically significant stress exposure or response. Therefore, there is a need for employing measures that combine the simplicity of self-report assessments with the validity and reliability of interview measures. These measurement-related barriers have deterred or precluded primary care clinicians from accurately evaluating the contribution of stress exposures and responses to the stress-related disorders they manage.

Provider-Related Barriers

The ability for primary care clinicians to assess patients' stressors and stress responses is influenced by several factors, including limited time, training, reimbursement, resources, and expectations about priorities and scope of practice. Adding stress measurement and management to patient visits can be viewed as economically questionable due to the lack of current evidence that stress assessment and management tools directly improve clinical outcomes. Providers and hospital systems may be less likely to implement stress screening and care when there is no reimbursement for these services from insurance providers and it costs patients money out of pocket. Many primary care clinicians may feel they have not received adequate education and training to efficiently assess and manage stress exposures and responses [84]. Even providers who are comfortable responding to patients who report high levels of stress by probing further and providing resources and referrals may find it takes valuable time from the many other tasks they must accomplish in a time-limited visit. Therefore, stress screening will be influenced by providers' beliefs about its importance and their ability to act on the outcome.

An extension of provider-related barriers includes limitations in access to mental health specialty services, social work resources, and community programs. In systems such as the Veterans Affairs health care program, with integrated primary and mental healthcare, these barriers may be reduced. However, for many patients and providers, it may be challenging to connect patients with the care and support they need to respond to high levels of stress and ongoing stressors. The growing adoption over the past decade of services that integrate mental health care into primary care (e.g., co-location, collaborative care, and blended models) provides promising new clinical settings for overcoming many of these provider-related barriers by facilitating the assessment and the management of stress and stress-related conditions. However, more will need to be done.

These provider and system-level barriers are critical considerations. Indeed, for depression screening, prior recommendations from the United States Preventative Services Task Force were to conduct screening *only* "when staff-assisted depression care supports are in place to assure accurate diagnosis, effective treatment, and follow-up" [85]. Given the increasing availability of these resources, the guidelines were updated in 2016 to recommend routine depression screening in the general adult population [86]. As we discuss below, more research is needed to establish appropriate procedures for stress screening and responses and to evaluate the cost and benefit of screening and treatment programs.

Patient-Related Barriers

Beyond measurement- and provider-related barriers, patients' unique backgrounds and the interaction between patients and the medical system can play a role in stress measurement and management. Depending on the stress measurement used, a patient may misinterpret the content or intent of a measure or of a specific item, causing them to provide misleading or false responses that bias or confuse the assessment of stress [74]. For example, *demand characteristics* (i.e., assumptions of the purpose of an assessment and a desire to give the "right" answer) can cause patients to provide false information they believe will be helpful. Further, medically underserved patients from marginalized backgrounds may experience bias, stigma, and discrimination in their medical systems that engenders mistrust in clinicians and impedes stress measurement by self-report and participation in stress management [87]. Finally, some patients may not want to complete stress measurements due to the time required or the person not understanding its value.

Key Research Questions

With these incentives and barriers in mind, below, we identify research questions that we believe are most fundamental for understanding how to improve the measurement of stress-related factors in primary care. Then, we describe example study designs that could help answer these questions.

Feasibility and Acceptability:

Is it feasible to regularly assess life stressors in a primary care setting? And is such measurement acceptable to primary care patients? What is the most feasible method of identifying severe and persistent stressors or stress responses across a broad range of primary care practices? Important considerations when answering questions of feasibility include measure selection, efficiency of procedures, scoring, data recording, and management of the results.

Cost-Benefit:

What are the costs and benefits of systematically assessing stressors and stress responses in primary care? Is the value added worth the additional cost? Which methods are most cost effective?

Improvement in Care:

Does systematic screening for early life and/or adulthood stressors in primary care improve risk stratification for specific chronic illnesses, such as diabetes, hypertension, or coronary heart disease?

Answering these questions and others will help the field better understand whether systematically measuring stressors or stress responses can improve the practice of primary care. Addressing the feasibility and cost-effectiveness questions, in turn, will provide a basis for considering the application of stressor measurement to risk stratification.

Recommended Studies

Feasibility and Acceptability Studies

A first step in studying the assessment of stressors in primary care involves feasible and the selection of suitable measures. As with any complex medical processes, initial assessments must be quick and simple. More complex assessments [e.g., 83] may be needed as a patient progresses up the stepped-care ladder, either in primary or specialty care. We thus propose that an instrument be recommended for use in primary care if it meets most or all of the following criteria: (1) Brief (e.g., 15 items or less; max 5 min response time); (2) Free or inexpensive; (3) Face-value scoring and interpretation, with clear cutoffs for clinical actions; (4) Easy to administer; (5) Supported by evidence for its clinical benefit as a stress exposure or response measure; and (6) Clear indications for use as (a) risk screen, (b) diagnostic guide, and/or (c) change measure.

Although these criteria may provide a rough guide for selecting measures, some measures that do not qualify could be adapted to fit these criteria (e.g., a short form could be created; scoring cutoffs could be made more straightforward). As an illustrative example, we present in Table 2 a selection of a few common instruments that meet most or all of these criteria, along with some distinguishing features. Reviews of the psychometric properties of each measure are available in the cited references.

We propose that one top-priority study is to compare the feasibility of different stressor assessment methods across primary care settings. Focus groups including patients, physicians, nurses, and other medical staff at multiple sites are needed to assess opinions on the expected value of selected measures with respect to efficiency, acceptability, and utility.

Cost-Benefit Studies

The economic value of screening programs for any health condition increases with the prevalence of the condition being screened and the availability of effective treatment programs for those who screen positive [88]. Severe and persistent stress responses are a common condition in primary care, and there are effective stress management programs for reducing the risks of specific chronic illnesses. However, there are currently no published studies assessing the cost-benefit of systematic screening for severe stress exposures in primary care [10].

We recommend that studies of the cost-benefit of stress screening and monitoring in primary care examine the effects of stress screening procedures on the rates at which patients engage in proven effective stress management programs. Following the example of the National Cancer Center Network, which has established the value of systematic Distress Thermometer screening for improving outcomes and reducing costs of cancer care [14–16], we recommend that large primary care centers investigate the value of systematic stress screening and monitoring for improving the outcomes and reducing the costs of common chronic illnesses, where effective stress management approaches are available. Examples of proven chronic disease management programs that include stress management interventions are the Ornish Undo It! Program for coronary heart disease [44, 45], National Diabetes Prevention Program for pre-diabetes [89], University of Washington's collaborative care programs for depression and diabetes or heart disease [90, 91], and Veterans Affairs programs for post-traumatic stress disorder (https://www.ptsd.va.gov/understand_tx/index.asp). Longitudinal studies that assess patients' stress levels, symptom profiles, and healthcare utilization statistics will be most helpful in this context, as they will shed light on whether patients' improve clinically following adequate life stress assessment and, additionally, what the cost-benefit is of including such assessments in routine care.

Clinical Improvement Studies

The systematic assessment of stress could bring to the primary care of chronic illness improved risk stratification in a primary care population that does not yet have a chronic illness [92]. For example, does systematic stress assessment improve risk stratification for coronary heart disease? The Framingham Heart Index predicts about half of all first myocardial infarctions (MI). What other factors could improve the identification of people at high risk for MIs?

Studies on this topic could address several questions, including, do the rates of incident MI and other cardiovascular endpoints in the high stress quartile differ significantly from the rates in the lowest stress quartile, while controlling for patients' Framingham Heart Index score? If so, how much does systematic stressor assessment improve the prediction of incident coronary heart disease over and above the Framingham Heart Index alone? And, do some stressor measures improve risk stratification more so than others?

These example studies could serve as a template for similar studies examining the effect of systematic stress assessments in other high-risk groups for improving the prediction of other chronic illness outcomes, such as patients with hypertension who may be at risk for stroke. For example, how much does a pattern of severe or persistent stress responses increase the risk for stroke in patients with hypertension?

Other Possible Studies

We have selected a few of what we consider to be high-priority studies for advancing the application of stress assessment to the practice of primary care. Before concluding, it is worth noting some other important topics of inquiry.

As Campbell argues [10], the ultimate value of screening in primary care for ACEs and other forms of toxic stress depends on evidence that the poor health outcomes predicted by

these exposures can be prevented. Eventually, the argument for measuring exposure to life stressors in primary care must be anchored in clinical trials showing that poor outcomes can be prevented in high-risk groups using interventions available in primary care settings. One likely effect of such a series of clinical trials will be a sharpening of focus on the most discriminating measures for specific target populations who have the most preventable outcomes. The foundation for these clinical trials will include research on sound methods for screening, assessing, and monitoring toxic stress.

Among the possibilities for stress measures that may improve the risk stratification of chronic illness, we do not yet know what the best predictive measures are. Is a measure of biological aging or allostatic load as good as, or better than, the assessment of cumulative lifetime stressor exposure by the Stress and Adversity Inventory [93]? Is telomere length a cost-efficient biomarker for identifying high-risk individuals? Is a combination of these biologic and psychosocial assessments necessary, or is the briefer ACEs Scale sufficient and more cost-effective? Studies comparing methods of assessing stress will add to the validity of stress measurement.

The recent interest in social determinants of health as a predictor of poor health outcomes is closely related to the literature on toxic stress as a contributor to chronic illness. They are complementary and overlapping concepts that deserve comparative investigation. For example, is the value of systematic stress assessments for risk stratification improved by also assessing social determinants of health? Does the procedure recommended by the Institutes of Medicine report [61] of abstracting from the electronic medical record measures of ten selected social determinants of health provide a measurable benefit for the allocation of resources for stress management to high risk patients?

Is there an optimal age for stress screening? We do not yet know the optimal age for intervening to prevent incident metabolic disorders in persons at high risk. If the aim is the prevention of chronic illness among those at risk, we need studies that better define the optimal age of the target populations for whom systematic stress screening adds a measurable benefit. Systematic stress screening or monitoring can also be helpful in relapse prevention planning for people with stress-related conditions, but when such screenings should take place also remains unknown.

Conclusion

In conclusion, based on available research examining the role of severe and persistent stress in the onset and progression of our most common chronic diseases, there is little doubt that the measurement of stress in primary care deserves our careful attention. Unlike most risk factors for chronic disease, stressor exposure does not just increase individuals' risk for a few select behavioral or health outcomes, but rather is associated with a variety of serious disorders and chronic conditions that dominate our current morbidity and mortality rates. Stressor exposure is also strongly related to chronic pain, fatigue, burnout, and poor health behaviors and medication adherence, which are prevalent in the primary care setting. Moreover, there is evidence of bidirectional links between stress responsivity and Illness, whereby stress can increase a person's risk of disease but disease can also result in

increased psychological distress. Primary care settings are uniquely positioned to intervene in this potential vicious circle to improve population health, and assessing patients' stressor exposure and/or response is a critical step in achieving this potential.

As discussed, there are several good reasons for why primary care providers rarely assess patients' life stressor histories and these reasons span conceptual, measurement, and practical issues. Given the potential benefits of assessing stressors in target populations [92,93], though, we believe that outlining the next steps for careful study of these measurement issues can advance our capacity to prevent and treat the common chronic conditions that currently cause substantial disease burden and mortality. Therefore, in addition to recommending the adoption of standard terminology for all stress studies, we recommend that future studies of stressor measurement in primary care prioritize research investigating the (a) feasibility and acceptability of measurement procedures, (b) cost-benefit analyses, and (c) clinical improvements associated with stress measurements and related interventions.

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Table 1:

Characteristics of acute and chronic life stressors and responses

	Acute	Chronic
Description of Stressors	A life event or acute situation that is time-limited or episodic in nature, and that has a relatively short and identifiable duration (e.g., a few days). In terms of severity, they can range from being relatively minor (e.g., daily hassles) to severe or traumatic, at which point they may involve substantial threat, cognitive upheaval, and/or disruptions to a person's goals, plans, or aspirations for the future.	A long-term exposure to forms of adversity that are threatening, distressing, or demanding, and that persist or frequently recur for several weeks, months, or years. Over time, these stressors can lead to substantial changes in the activity or regulation of patients' stress systems that increase risk for the development of stress-related chronic disease conditions (e.g., "allostatic load").
Examples of Stressors	Minor daily events: Minor arguments, traffic, rushing to make deadlines Major life events: Job loss, getting divorced, death of a close loved one Traumatic events: Serious natural disaster, being attacked, physically abused, or sexually assaulted	Ongoing physical or sexual abuse; emotional abuse or neglect; financial strain; housing or food insecurity; having a parent or spouse with a severe mental illness; caregiving; discrimination
Stress Responses	The experience or appraisal of a stressor and ensuing short-term cognitive, emotional, behavioral, and biological changes. A defining characteristic of the acute stress response is its identifiable peak and recovery to homeostasis over a relatively short period of time. For example, autonomic reactions to acute stressors typically last for the duration of the stressor (e.g., minutes), while HPA axis and immune system reactions and recovery times last for hours to days. Cognitive, emotional, and behavioral responses are similar, with a distinct response and recovery period. Major life events and traumatic events are more likely to lead to long-term activation of, or changes in, the human stress response than are lower-severity acute stressors.	Long-term changes in psychological, physiological, and behavioral processes due to chronic stressor exposure, or the cumulative burden of many acute stressors occurring over the lifetime. Often referred to as "allostatic load", these chronic stress responses can be viewed as the accumulated "wear and tear" on the body. The chronic stress response can be prolonged and last longer than the duration of the initiating stressor itself. Chronic stress responses (e.g., sustained negative thinking about the self or world) can also engender other acute or chronic stressors in a person's life (e.g., relationship problems), which further compounds their negative effects on human health and behavior.

Table 2.

Examples of Stress Measures Suitable for Primary Care

Measure	Description	Assesses	Time to Complete	Number of Items	Free	Cutoffs
Adverse Childhood Experiences (ACEs) Scale [3]	Screening measure of self-reported major life stressors occurring during childhood.	Exposure to Stressors	3–4 minutes	10	Yes	No
Stress and Adversity Inventory Screener for Adults (Adult STRAIN Screener) [93]	Screening measure of self-reported major lifetime stressors that predict high risk for stress-related health problems; positive screen suggests the full STRAIN may be helpful.	Exposure to Stressors	3–4 minutes	10	Yes	Yes
Distress Thermometer [17]	Screening measure of stress burden over the past week; identifies sources of stress in five areas; serial administrations for change measure.	Stress Responses	1 minute	6	Yes	No
Perceived Stress Scale 4 (PSS-4) [94, 95]	Screening measure of self-reported stress perceptions over the past week; serial administrations for change measure. A 10-item version has been recommended as part of the NIH toolbox of measures [95].	Stress Responses	1–2 minutes	4	Yes	No