10

A Peek Inside the Black Box of Stress

Modern medicine is flush with profiles. The medical assistant who ushers you into your annual checkup is collecting a profile of your vital signs: weight, height, blood pressure, heart rate, and temperature. These vital signs offer a crude picture of how you're doing on a few selected physical measures, a starting point for your conversation with your doctor.

That questionnaire you just filled out in the waiting room provides another profile of your current symptoms. It will find its way into your medical record along with the medical history taken by your astute doctor. That history leads to her revising your problem list, which is also a profile of possible priorities for your treatment plan.

The problem list of Ted Daley, the PR and marketing man at Carnegie Mellon whom we met earlier, and who was taking part in the SHINE study, is short: sleep apnea and overweight. The problem list of Teresa Langford, the disabled veteran, is long: hypertension,

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obesity, low back pain, diabetes, ADHD, obstructive sleep apnea, abdominal hernia, and alcohol use disorder in remission. Those are two very different and useful profiles that guide the planning of treatment.

Both patients are likely to stop at the lab on the way out to give blood for a comprehensive metabolic panel, another profile that will sketch the state of their livers, kidneys, bones, and pancreases through a list of numbers and ranges of normal. Somewhere in her chart Teresa might have a number for her Framingham Heart Index, a profile of her already moderate risk for coronary heart disease based on her age, gender, lipid levels, blood pressure, glucose levels, and smoking.

Modern medicine values these profiles because they help healthcare providers see patterns across several organ systems – a skill that relies on art, science, and a wise doctor's experience and intuition. Each profile provides a different lens trained on a different focal point to answer a specific set of questions.

But where's the profile that captures patterns of toxic stress? Most primary care docs will tell you they don't know of such a profile, much less one they routinely use in practice.

The absence of a standard stress profile contributes to the invisibility of the stress response system. Our difficulty "seeing" this part of our bodies is a reminder that not so long ago it was also difficult for us to see specific types of mental impairment, such as dyslexia, learning disabilities, early dementia, and attention deficit disorder, at a level that could guide treatment.

Profiling the Brain

One of the more useful profiles in medicine is a battery of tests to assess how the mind and brain are working. For example, a young woman struggles with staying organized at home and at work and

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her boss is threatening to fire her. She had a traumatic brain injury from a car accident two years ago, but she has also coped with ADHD and severe anxiety since her teens. Are her current troubles a part of her brain injury, her attention disorder, her anxiety, or some combination of all three?

For her, testing can help identify what is interfering with her memory, attention, and problem solving. It can also point to treatment approaches that may help her keep her job. Primary care doctors use neuropsychological testing to help assess the mental capacities of a patient with traumatic brain injury, stroke, dementia, learning problems, autism, Parkinson's disease, and other neurologic or psychiatric conditions.

Obtaining a neuropsychological profile can be expensive in time (six to twelve hours) and money ($1,600 to $3,000) for a psychologist to complete this battery of tests over several half-day testing sessions. The battery includes measures of IQ, perceptual acuity, short-term memory, immediate recall, attention, spatial orientation, and problem solving, to name a few. The menu of tests varies depending on the questions that need to be answered, but it can include twenty to thirty different tests.

The report summarizing this battery of tests can take a few weeks for the specialist to prepare, and often the report is four to five pages long, single-spaced, including the assessment and recommendations. This report provides a useful profile of the patient's cognitive functioning in relation to behavior and emotions – usually worth the time and money.

Today, most major medical centers in the US keep a neuropsychological testing service busy full-time. But this profile of brain functioning is a recent advance, the product of the mushrooming discipline of cognitive neuroscience.

In the 1980s neuropsychological testing services were rare, even in large medical centers. No wonder we knew so little then about the various types of intellectual disability, attention deficit disorder,

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traumatic brain injury, stroke, autism spectrum issues, and the "software" problems imposed by psychiatric disorders like depression and bipolar disorder.[1]

As complex as the brain is, the stress response system is even more complex because it consists not only of the central nervous system but most of the other major organ systems (endocrine, immune, cardiovascular, as we have discussed). Perhaps it's not surprising then that no such profile for the stress response system exists yet in clinical practice.

The field of stress neuroscience today may be similar in its development to the field of neuropsychology fifty years ago. Then, neuropsychologists had lots of measures of cognitive function but no standards of practice, no consensus on the essential elements of a comprehensive neuropsychological assessment, and few norms for interpreting results.

In the last chapter we looked at some of the reasons for the current gap between the science of stress and the clinical practice of stress assessments. In this chapter we look at the ways that a stress profile could become a useful part of your next doctor visit. It does not have to be expensive, intrusive, or exhaustive to be useful. But it should strive to be comprehensive, blending some essential components of all stress profiles with some measures that are specific to needs of the individual patient.

Building the Stress Profile

We can organize the stress profile into four groups of measures, each of which overlaps with the others: subjective distress, cumulative life stress exposures and responses, physiologic stress measures, and social determinants of health. The Distress Thermometer summarizes this process by listing some options for selecting measures in each of these groups.

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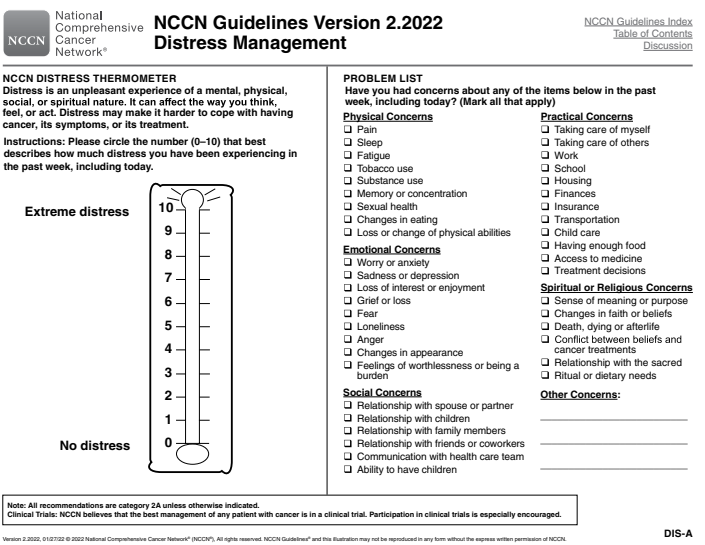
The assessment of toxic stress begins with measures of subjective distress – the psychological dimension of the process of adapting to high demands. The logic of this starting point rests partly in the importance of current distress as a motivator for behavior change.

People are most motivated to change high-risk health behaviors when they believe those changes could relieve their distress. A clear understanding of the patterns of discomfort over the recent months can indicate the need for a plan to reduce the distress, and this pattern can readily be assessed with a visit to a primary care doctor. The Distress Thermometer combines your overall estimate of distress with some guesses about the sources of the distress, which are often social factors like financial problems or unemployment or lack of childcare.

In 1997 the National Cancer Center Network adopted a guideline for the systematic assessment of distress at every visit, using


National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Distress Management

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Discussion

NCCN DISTRESS THERMOMETER
Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect the way you think, feel, or act. Distress may make it harder to cope with having cancer, its symptoms, or its treatment.

Instructions: Please circle the number (0–10) that best describes how much distress you have been experiencing in the past week, including today.

Extreme distress
10
9
8
7
6
5
4
3
2
1
0
No distress

PROBLEM LIST
Have you had concerns about any of the items below in the past week, including today? (Mark all that apply)

Physical Concerns
- ❑ Pain
- ❑ Sleep
- ❑ Fatigue
- ❑ Tobacco use
- ❑ Substance use
- ❑ Memory or concentration
- ❑ Sexual health
- ❑ Changes in eating
- ❑ Loss or change of physical abilities

Emotional Concerns
- ❑ Worry or anxiety
- ❑ Sadness or depression
- ❑ Loss of interest or enjoyment
- ❑ Grief or loss
- ❑ Fear
- ❑ Loneliness
- ❑ Anger
- ❑ Changes in appearance
- ❑ Feelings of worthlessness or being a burden

Social Concerns
- ❑ Relationship with spouse or partner
- ❑ Relationship with children
- ❑ Relationship with family members
- ❑ Relationship with friends or coworkers
- ❑ Communication with health care team
- ❑ Ability to have children

Practical Concerns
- ❑ Taking care of myself
- ❑ Taking care of others
- ❑ Work
- ❑ School
- ❑ Housing
- ❑ Finances
- ❑ Insurance
- ❑ Transportation
- ❑ Child care
- ❑ Having enough food
- ❑ Access to medicine
- ❑ Treatment decisions

Spiritual or Religious Concerns
- ❑ Sense of meaning or purpose
- ❑ Changes in faith or beliefs
- ❑ Death, dying or afterlife
- ❑ Conflict between beliefs and cancer treatments
- ❑ Relationship with the sacred
- ❑ Ritual or dietary needs

Other Concerns:

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

DIS-A

Figure 10.1 The distress thermometer.

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the Distress Thermometer. The NCCN has published guidelines for patients and doctors over the years on the measurement and management of *distress*, a term they define simply as "an unpleasant experience of a mental, physical, social, or spiritual nature."

The NCCN use of the term *distress* is broad and includes mental and emotional responses to stress exposures of any kind. Think of the thermometer as rating your stress responses over the past week and the Problem List as identifying some possible types of exposures to stressful events or threats or social determinants of health.

The impact of the Distress Thermometer on the care of cancer patients has been helpful in some specific ways. In one recent study the cancer centers that followed the screening protocols for the Distress Thermometer reported 18 percent fewer emergency department visits and 19 percent fewer hospitalizations during the two months after the distress screening, suggesting better care and lower costs.

In primary care settings the benefits and barriers to routine screening for distress are likely to be similar to those in cancer centers. However, the proven benefits of this simplest of all stress measures make it the place to start. For those who screen positive by scoring over 4 on several successive assessments, the Distress Thermometer initiates the conversation on what's going on with you. In other words, it's not just the knee pain but the worry about not being able to get around.

This is particularly helpful for those with severe and persistent distress over six months. The Distress Thermometer provides the sensitive first step to identifying those in greatest need, which is one of the key roles of primary care. It points the way to the second step for those who screen positive: referral to a health psychology service that selects and collects the data from more specific measures for the remainder of the stress profile.

Measures of distress may also include brief self-report inventories of symptoms of depression or anxiety, along with a measure

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of resilience, such as the Brief Resilience Scale.[2] These symptom measures can identify the patients who are in need of a full stress profile.

Cumulative Life Stress

What more would a patient and doctor want to know about risks for illness if a screening measure such as the Distress Thermometer suggested a high risk for illness? As we saw in the last chapter, a meaningful measure of stress should include both the events we've been exposed to and our responses to those exposures. And any period less than the person's full lifespan captures only a fraction of the toll on the stress response system.

The Adverse Childhood Experiences (ACE) Scale. One measure that captures part of the process (exposures) over part of the lifespan (childhood) is worth mentioning again because it has had an impact on recent clinical practice, at least in the US. Ten years after the first ACE study report was published in 1998, Nadine Burke Harris, MD, discovered that report when a psychologist she had hired to work in her fledgling pediatrics clinic recommended she read it.

Reading that report turned on a lightbulb that shifted her approach to patients with complex illnesses in her practice. She realized she needed a clinical procedure that her mentors at Stanford had not known about or taught her: a profile for the impact of childhood trauma on health and illness. She discovered the power of applying arithmetic to childhood adversity experiences.

The ACE consists of ten items about possible adverse experiences in childhood. The items include some common experiences, such as divorce or living with a relative who was a problem drinker or had a mental illness, and some less common experiences, such as the threat of sexual or physical injury. No single question alone would be considered unusual in a routine pediatric evaluation.

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Adverse Childhood Experiences (ACE) Questionnaire
Finding Your ACE Score

While you were growing up, during your first 18 years of life:

1. Did a parent or other adult in the household **often . . .**
   Swear at you, insult you, put you down, or humiliate you?
   or
   Act in a way that made you afraid that you might be physically hurt?
   Yes No If yes enter 1 _____

2. Did a parent or other adult in the household **often . . .**
   Push, grab, slap, or throw something at you?
   or
   Ever hit you so hard that you had marks or were injured?
   Yes No If yes enter 1 _____

3. Did an adult or person at least 5 years older than you **ever . . .**
   Touch or fondle you or have you touch their body in a sexual way?
   or
   Try to or actually have oral, anal, or vaginal sex with you?
   Yes No If yes enter 1 _____

4. Did you **often** feel that . . .
   No one in your family loved you or thought you were important or special?
   or
   Your family didn't look out for each other, feel close to each other, or support each other?
   Yes No If yes enter 1 _____

5. Did you **often** feel that. . .
   You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you?
   or
   Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?
   Yes No If yes enter 1 _____

6. Were your parents **ever** separated or divorced?
   Yes No If yes enter 1 _____

7. Was your mother or stepmother:
   Often pushed, grabbed, slapped, or had something thrown at her?
   or
   Sometimes or often kicked, bitten, hit with a fist, or hit with something hard?
   or
   Ever repeatedly hit over at least a few minutes or threatened with a gun or knife?
   Yes No If yes enter 1 _____

8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?
   Yes No If yes enter 1 _____

9. Was a household member depressed or mentally ill or did a household member attempt suicide?
   Yes No If yes enter 1 _____

10. Did a household member go to prison?
    Yes No If yes enter 1 _____

Now add up your "Yes" answers: _____ This is your ACE Score.

Figure 10.2 The ACE Questionnaire.

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What is novel and powerful about this scale is the collecting of scores on these ten items tapping abuse, neglect, or dysfunction in the family, adding up the scores, and using the sum of these childhood exposures to estimate risks for later illness.

Imagine how this simple questionnaire could have identified childhood experiences with Mrs. B and with Teresa Langford?

In 2018, another ten years after her realization about the impact of childhood adversity on health, Dr. Harris and selected colleagues in the region adopted this scale as a standard screening measure. She and her foundation, the Center for Youth Wellness, have collaborated with colleagues in the Bay Area through the PEARLS study to examine the impact of systematic ACE screening in primary care on health outcomes. Since 2014, her vocal advocacy for screening for adverse childhood experiences in primary care pediatric populations has earned her the attention of her mayor, Gavin Newsome, who, as the newly elected governor of California in 2019, promptly appointed her the state's first Surgeon General.

As an early screening step in the process of building a stress profile, the ACE scale offers a promising complement to the Distress Thermometer. The ACE screens for past childhood stress *exposures*, while the Distress Thermometer reflects current adult stress *responses*.

There are plenty of measurement shortcomings in the ACE scale. It does not specify the age of exposure or quantify the frequency or severity of these exposures. It does not ask about the severity of the person's responses to them. It gives equal weight to parental separations, sexual abuse, and not feeling loved. Yet in spite of these psychometric shortcomings, responses to this list of exposures have proven to predict many of our most important public health outcomes in adults, not only in the initial Kaiser sample in San Diego, but also in twenty-five states around the country.[3]

Aside from age, no other risk factor can claim such predictive power. The secret of this power lies in part in its simple addition. It

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recognizes that each of us has a limit to the burdens we can manage during the formative stages of our childhood.

The Life Stress Test. Questionnaires about cumulative life stress tend to be affordable but long, whereas interviews are expensive and often longer. Ideally, we need a way to combine the best of both methods for collecting information about cumulative life stress.

In one of the more innovative efforts to combine the convenience of questionnaires with the validity and depth of interviews, George Slavich, PhD, and his team at UCLA have spent over a decade creating an interactive online assessment of stress exposures and responses called the STRAIN or the Life Stress Test.[4] After developing this measure through over a hundred studies in research settings, the researchers have recently begun looking at how the Life Stress Test can be adopted into clinical practice.

The Life Stress Test is an easy measure to complete, but to make sense of the results you need a clinician who is certified to interpret the results. You can try it at www.lifestresstest.com. It will take you twenty to thirty minutes, and it generates four sets of results to help you and the certified clinician make sense of your cumulative stress level: number of stressors, severity of stressors, stress exposure by life domain, and resilience.

Why is the Life Stress Test one of the better measures among the few available for assessing cumulative exposures and responses in the doctor's office? It asks not only about the number and types of events, but when they happened, how frequently, at what ages, and how you responded. It can collect a lot of relevant data on both stress exposures and responses in a relatively short time because it selects questions according to the answers provided to stem items. For example, it avoids asking a thirty-year-old unmarried male about retirement and grandchildren.

The Life Stress Test provides an immediate tally of your stress data in a form that is easy to read as a profile that charts your lifetime stress levels across nine domains relative to other people of

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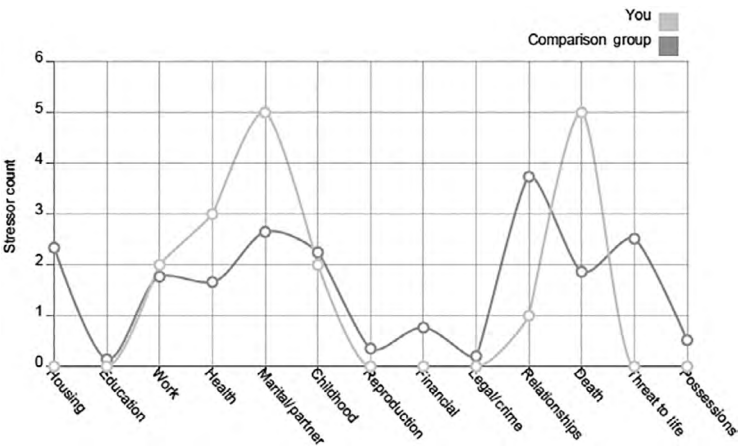

Figure 10.3 Lifetime stress exposures by domain.

your age and gender. These features make it attractive for use in clinical practice.

Compared to a neuropsychology test battery or a colonoscopy, the Life Stress Test is quick, cheap, and easy. And a lot less stressful. In a short time at low cost with minimal effort invested by professionals, the therapist and patient can obtain a stress profile that is both specific and measurable. The Life Stress Test can help you and your doctor focus your stress reduction treatments on the specific domains of the stress profile that are of greatest risk to your future health, whether it's sleep, time management, risky relationships, or unhealthy habits.

The Body Keeps the Score

But something is still missing from this stress profile. In addition to subjective measures of current distress and a profile of cumulative life stress, doctors and patients need to know what's going on in the body.

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My friend and colleague Bessel van der Kolk, MD, has made a strong case in his popular book *The Body Keeps the Score: Brain, Mind, and Body in the Healing of Trauma* for attending to the signals from the body when assessing the impact of trauma over the lifespan. Ideally, physical measures of stress should be a part of anyone's profile.

In a haphazard way we already pay attention to some indirect measures of stress when we focus on weight, blood pressure, hours of sleep per night, and pain or fatigue levels. But a useful complement to our psychosocial measures of the cumulative toll of stress is a measure of the cumulative toll on our body's stress response systems. If it's true that the body keeps the score and chronic stress accelerates aging, is there a way to measure that toll?

Among those who have explored this question, the most vocal and persuasive voice has been that of Bruce McEwen, a neuroendocrinologist who spent his career at the Rockefeller Institute in New York conducting research on various aspects of the stress response system.

Since 2000, he has published at least twenty-four scientific articles with the term *allostatic load* in the title, and has talked at length about stress and health on PBS, CBS, NBC, NPR, and other popular media.

The elusive allostatic load. Dr. McEwen, in the company of other esteemed scientists such as Teresa Seeman, PhD, at UCLA, ventured into the troubled waters of stress measurement in the late 1990s with a proposal for an allostatic load index based on these ten biomarkers, which they proposed could capture the cumulative toll of lifetime stress:[5]

1. Systolic blood pressure (the first number in a normal blood pressure of 120/80)
2. Diastolic blood pressure (the bottom number)
3. Waist–hip ratio
4. Total cholesterol

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5. HDL (high density lipoprotein)
6. Hemoglobin A1C (a measure of glucose levels over three months)
7. Dehydroepiandrosterone (DHEA, an adrenal steroid that counters cortisol)
8. Cortisol
9. Epinephrine
10. Norepinephrine.

Dr. McEwen's concept of an allostatic load index was potent and promising enough that it generated lots of studies that aimed to replicate or improve on the original proposal. Like generativity in nature, generativity in science can be both fruitful and wild. The offspring stray from home. In a recent analysis of many studies of allostatic load in the workplace,[6] the reviewers found that, in summary, the concept of allostatic load has proven both robust and unruly.

One of the practical issues limiting the use of the allostatic load index in clinical practice is the problem of how to collect the data necessary to calculate the index. A definition of allostatic load that requires collecting only a thimble-full of blood is more likely to be used in primary care than one that requires a thimble-full of blood plus twelve hours of urine plus measuring the person's waist and hip circumferences with a tape measure.

Dr. McEwen's original ten biomarkers require all three sources of data (the DHEA, cortisol, epinephrine, and norepinephrine come from urine collection). Then someone has to enter the data on all ten biomarkers and calculate the index according to an algorithm that generates the allostatic load index, a number from 0 to 1 that can be used to estimate cumulative physiologic stress and risk for illness.

Primary care clinics usually don't hire people to crunch numbers like this. They count on laboratories to deliver such a service and the number, and so far no commercial laboratory offers such a service for allostatic load.

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Another issue that has limited the use of allostatic load in the clinic for estimating risk is the unresolved debate about which combination of biomarkers offers the best predictive power at the least cost. We know that multiple measures of allostatic load predict poor health better than any single measure, but do fifteen biomarkers predict health outcomes better than ten or five? That question has not been answered yet. Five would be better (cheaper, easier), but which five work best for all populations? Good scientists are studying the question.[7]

Another important limitation to the original list of biomarkers proposed by McEwen and his colleagues has spurred experimentation with new biomarkers. The original list does not include measures of two of the important physiologic systems that we saw in earlier chapters play major roles in acute and chronic stress responses: the immune system and the autonomic nervous system.

What we need but don't yet have is a measure of allostatic load that combines the single best cumulative measures of each of the five main organ systems of the stress response system in a way that is easy to collect and calculate as an index that predicts risk for future illness. Better still, if this measure improves with effective toxic stress reduction and worsens with toxic stress events, it would be a useful guide for monitoring the effectiveness of intensive stress management. That kind of measure will raise the visibility of toxic stress for both patient and clinician.

Biological aging. What if your doctor were able to take a sample of your blood and tell you how old your body is, in contrast to how old you may actually be? We're not too far off.

In a variation on the concept of allostatic load, a group of investigators from Duke University, King's College London, and the University of Otago in Dunedin, New Zealand, have examined a measure of composite physiologic measures, which they call biological aging, in contrast to the person's chronological age.[8]

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From the prospective longitudinal Dunedin study, this team has been able to identify a composite of seventeen physiologic measures of biological aging, five of which overlap with the original measures of McEwen's allostatic load. With this composite measure of biological age collected at three time points before the age of thirty-eight, the researchers found that biological age correlated with physical functioning, self-reported health, and mental decline.

A recent review found that biological aging may be a better measure for predicting risk than other measures,[9] but biological aging is not yet ready for use in primary care.

Recently investigators have found that a more accurate measure of biological aging is the amount of methyl molecules that have accumulated on our DNA, dubbed the DNA methylation process or epigenetic aging because the rate of DNA methylation varies with the epigenetic changes that accelerate the aging process.[10]

This measure suggests the appealing promise of providing the patient and doctor a summary number for a person's biological age, calculated from one blood sample to compare with the chronological age.

Imagine how you would react if, during your routine checkup at age forty, your doctor told you that your biological age was already fifty-three and accelerating? And when you return at forty-five, your biological age is now closer to sixty-five. How would that grab you?

We need a lot of science to fill in the blanks before we can make this kind of conversation a reality, but we already have some promising new ways of seeing the biology of our stress response systems as they slip into trouble.

Telomere lengths. All your life your chromosomes have been slowly fraying at the ends, like the aglets (keep this word handy for Wordle) on your shoelaces, those tightly wrapped tips that begin to fray with the wear and tear of life. And all your life the enzyme telomerase has been trying to repair your fraying aglets.

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As discussed earlier, cumulative stress and the normal aging process are intertwined at every level. Telomeres are the DNA strands at the ends of chromosomes, and telomere length is a measure of biological aging that is also sensitive to cumulative stress loads, including the stress of certain chronic illnesses.

Chronic stress generally inhibits telomerase, and in that way can accelerate cellular aging and cellular death. When telomeres reach a certain shortness, the cell dies. So, the cellular aging process varies with stress exposures and the environment.[11]

Telomere length can be assessed from white blood cells taken from any blood sample. In general, the higher the cumulative stress load, the shorter the telomere length, if you adjust for age.

Telomere length tests are just beginning to be used in clinical settings to guide treatment, but there are at least ten ways to assess telomere length, and the methods differ in their variability and costs, which range from $100 to $400 per sample. Commercial labs that offer telomere tests are not currently regulated by the government, so it can be hard to know what their reports mean.

And once again, although the science is good and the concept is sound, the logistics of collecting and testing and interpreting telomere lengths still need to be refined. This test is also not yet ready for you to ask your doctor about.

This absence of a good measure of the cumulative toll on the stress response system, one that is useful for primary care doctors at your regular physical exam, remains a high priority for the translation of stress neuroscience into clinical practice.[12]

Social Determinants of Health

If we are going to measure psychological and biological factors affecting the stress response system, shouldn't we also measure social factors?

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The Institute of Medicine proposed in 2014 a method of estimating risk for common chronic conditions by collecting social and behavioral data through electronic health records.[13] Recognizing that the burden of collecting new information in primary care settings can be prohibitive, this report recommends focusing on twelve measures that either are routinely a part of the medical history-taking process, or could be easily added as specific new items:

1.	Alcohol use	3 questions
2.	Tobacco use	2
3.	Race and ethnicity	2
4.	Residential address	1 (geocoded)
5.	Census tract median income	1 (geocoded)
6.	Education	2
7.	Financial resource strain	1
8.	Depression	2
9.	Stress	1
10.	Intimate partner violence	4
11.	Physical activity	2
12.	Social connections and isolation	4

By calling for all healthcare systems with electronic health records to join in collecting these uniform data at prescribed frequencies, this report recognizes the need for a social profile to measure a common set of exposures to demanding social conditions.[14] Though some of the items tap physiological conditions, such as smoking and physical activity, and others tap psychological conditions, such as depression and perceived stress, this list creates a profile of the social demands on the stress response system.

This social profile may be as effective as the psychological or physiological profiles in estimating a person's risk for developing illness, but that question, too, needs to be studied.

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Stress Testing the Heart

Consider also the role of challenge tests. The most common stress test in clinical practice is the treadmill. This test has become so routine in primary care and cardiology that it is what most doctors assume you're talking about if you mention taking a stress test.

The graded exercise tolerance test assesses how well your heart tolerates increasing or "graded" amounts of exercise on a treadmill up to a brisk walk or slow jog, which usually raises heart rates up to 150 beats per minute or more.[15] The measure of tolerance or the fitness of your heart is the ST segment of the EKG that records your heart activity while you're huffing on the treadmill.

If that ST segment drops down a certain amount, it's a signal that your heart is straining against a dwindling supply of oxygen. It is poetically referred to in the trade as "ST depression" – the prelude to myocardial ischemia, the signature mechanism of heart attacks.

The catch here, and the key to the value of this test in clinical practice, is that most of us don't feel our ST depressions at rest or during exercise. And when we're lying on our backs during a resting EKG, our tracings may look normal. But under the demands of exercise, well before our heart disease causes us shortness of breath or chest pressure or angina, these silent ST depressions, if we're lucky enough to have them measured soon enough, signal the early stages of coronary heart disease, when it's easier to treat and possible to *prevent* heart attacks.

If the modest physical demands of walking on a treadmill and doubling your heart rate can expose the vulnerabilities of early heart disease, what about mental stress?

Since many of us who live in relative physical comfort are more frequently exposed to mental stress than physical stress, wouldn't it be helpful to know how our hearts respond to mental stress?

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Dr. Vaccarino and her team at Emory University have been exploring this question with a focus on women. She wondered if women with heart disease might be more prone to "silent" ischemia (narrowing of arteries) in their hearts during physical and mental stress.

The standard protocol for mental stress – induced myocardial ischemia – is about as simple as walking on a treadmill, but it requires a lab setting. While a six-lead EKG records heart activity, the person performs either a timed arithmetic test or a two-minute speech to strangers in lab coats. This has proved to be sufficiently stressful for most people to trigger measurable and meaningful responses across a variety of mental and physical stress response measures, including measures of transient ischemia or ST depressions on the EKG.

Dr. Vaccarino and others have found that women with coronary heart disease are nearly 40 percent more likely to have mental stress-induced ischemia than men with coronary heart disease. And the difference is more pronounced in women under fifty who have heart attacks.[16]

Why are younger women with heart disease more likely to have silent ischemia under mental stress? Dr. Vaccarino notes that women in general report more mental stress of all kinds (trauma, mental illness, poverty, work stress, discrimination, among others) than men, and the mechanism of their silent ischemia is still unclear.

Dr. Vaccarino's group has also shown in the largest and most rigorous study of its kind that mental stress-induced ischemia is a more powerful predictor of worsening heart disease than physical stress.[17] The cardiologist's traditional stress test on the treadmill may have focused over the last fifty years on the less predictive kind of stress. It's time now to add mental stress tests to the physical stress tests that identify those most at risk for heart attacks.

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Studies like these of mental stress-induced ischemia are making the case for adding this kind of stress measurement to the routine assessments of heart disease.[18] They remind us of how much we don't know. Wouldn't you like to know what your road rage or those too frequent arguments with your spouse are doing to your heart? If you have high blood pressure or Crohn's disease or diabetes, wouldn't you like to know if your mental stress is aggravating your condition?

For now, this kind of challenge test is not readily available to doctors to order for their patients when assessing a stress profile, and then there are the barriers of technology, cost, and data interpretation.

The Stress Profile Service

In primary care, the first step is to identify those people with severe and persistent distress. For those who screen positive for distress, the next step requires deciding who needs what kinds of help: who may need the help of a social worker for housing or financial problems, who needs a mental health specialist for managing a mental disorder, and who may benefit more from a regimen of exercise, sleep management, and meditation.

This second step requires a more in-depth assessment of stress exposures and responses, specific trouble spots, and which social situations causing the current problems could be modified.

As we'll see in the next few chapters, guidance about stress measurement depends on the patient's stress profile, and this process works best when the primary care provider is guided by a mental health specialist, such as a health psychologist, who knows how to keep it simple and useful for each patient.

Given the complexity of the assessment process and the clinical judgment required to translate the findings into recommendations

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for treatment, the creation of the stress profile should be the responsibility of a certified health psychologist. Similar to the neuropsychology testing report, the stress profile could be generated by the standard consultation process for patients with known stress-related conditions or with high risks for developing stress-related conditions.

Copies of the stress profile would go to the patient and the primary care doctor or the specialist who requested the consultation, to be placed in the patient's medical record. Because health psychologists are also the specialists who deliver most of the stress management interventions, these reports will be written in terms that translate readily into treatment plans.

Although this seems like a logical process that would follow traditional consultation procedures, it is still rare that any large medical center in the US provides a health psychology consultation service for these kinds of stress profiles.

Peering into the Well

Nadine Burke Harris reminds us in *The Deepest Well* of a few lessons about the measurement of stress that she has learned since her eyes were opened to the role of childhood trauma and adversity in health and illness.

Dr. Harris makes the point that our current understanding of how toxic stress in childhood dysregulates the stress response system is comparable to the understanding of infections in the nineteenth century before germ theory. At that time the leading theories about how infections operate focused on poisonous vapors and the "miasmas," but these were just guesses.

The observations of John Snow about cholera around the London water pump and Joseph Lister about the impact of hand-washing to reduce infection rates during surgery came long before the confirmation that certain microbes were the culprits.

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Early in the course of changing the way medicine understands complex processes such as infection or toxic stress, any measure that improves vision advances the field: the thermometer, the microscope, the blood pressure cuff. And I will add the ACE scale as one measurement tool that has improved our ability to recognize a toxic combination of stress exposures in early life that predict later poor health outcomes.

Consider the advances in our understanding of cancer and its treatments over the past half-century. In 1966 during my ninth-grade year, Craig, one of our forty-five classmates, died of Hodgkin's lymphoma. Two years later another of our classmates, Peter, died of acute lymphoblastic leukemia (ALL). In those days, half of patients with ALL died within six months of the diagnosis; my friend was one of the lucky ones to last two years. Now 85 percent of children with ALL are cured.

These advances in childhood cancer over the last half-century have required unprecedented collaborative research networks and funding from basic science to the bedside across many cancer centers worldwide.

This example of progress in treating a complex set of processes shows the way forward for the 15 to 20 percent of us who live with persistent toxic stress. Though our current level of understanding of the dysregulation of the stress response system may resemble our basic understanding of cancer in the 1960s, nonetheless the stress measures we currently have can guide the next steps in that journey and help us offer effective treatments. That requires facing two tough questions: How can we treat a dysregulated stress response system? And how much does it improve the course of a chronic illness to relieve distress and reduce the psychosocial risks for that illness?

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