

Implementing Evidence-Based Suicide Prevention Strategies for Greatest Impact

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Suicide remains a leading cause of death in the United States and globally. In this review, epidemiological trends in mortality and suicide risk are presented, with consideration given to the impact of the COVID-19 pandemic. A public health model of suicide prevention with a community and clinical framework, along with advances in scientific discovery, offer new solutions that await widespread implementation. Actionable interventions with evidence for reducing risk for suicidal behavior are presented, including universal and targeted strategies at community, public policy, and clinical levels. Clinical interventions include screening and risk assessment;

brief interventions (e.g., safety planning, education, and lethal means counseling) that can be done in primary care, emergency, and behavioral health settings; psychotherapies (cognitive-behavioral, dialectical behavior, mentalization therapy); pharmacotherapy; and systemwide procedures for health care organizations (training, policies, workflow, surveillance of suicide indicators, use of health records for screening, care steps). Suicide prevention strategies must be prioritized and implemented at scale for greatest impact.

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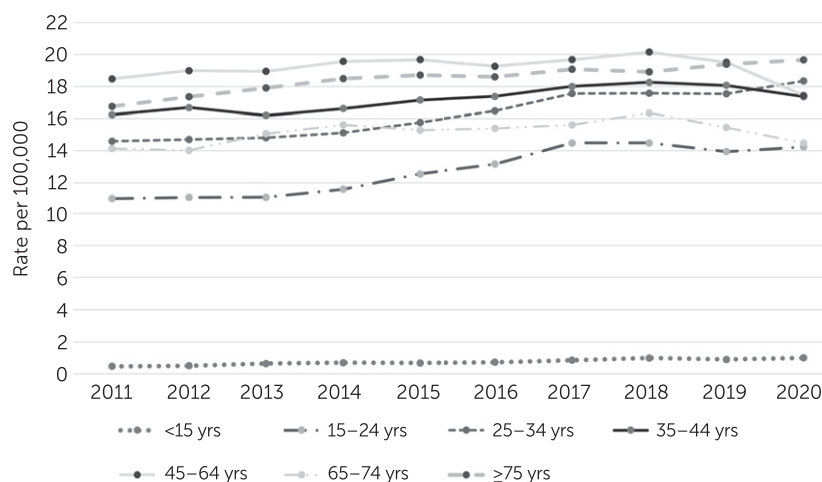
Suicide is a leading cause of death in the United States. More than half of U.S. adults endorse being personally affected by suicide—through loss, lived experience, or the suicidal experiences of loved ones. Attitudes and beliefs are changing rapidly, while stigma diminishes through advocacy efforts amounting to a nationwide movement. Improvements in attitudes, however, do not equate fully to changes in knowledge or action, which could be considered a necessary next step in deepening the public's mental health and suicide prevention literacy. Although research efforts are providing new discoveries and actionable strategies for community and clinical suicide risk reduction, implementation of these interventions and programs has lagged and must be prioritized in a way that is sustainable, evidence-based, cross-sectoral, and scaled to address the multifactorial health outcome of suicide. The objectives of this review are to present epidemiological trends in U.S. suicide and suicidal behavior, along with the top evidence-based strategies to reduce suicide risk, with an emphasis on clinically based strategies.

EPIDEMIOLOGY OF SUICIDE AND SUICIDAL BEHAVIOR IN THE UNITED STATES

According to the Centers for Disease Control and Prevention (CDC), 48,183 people died by suicide in the United States in 2021, making it the 12th leading cause of death. Following year-over-year increases in the national rate in the nearly 2 decades from 1999 to 2018 (when suicide was the 10th leading cause of death), there were 2 consecutive years of decreasing rates in 2019 (by –2.3%) and in 2020 (by –3%).

CDC data for 2021 unfortunately indicate a year-over-year increase of 4.8%, with an overall rate of 14.1 suicides per 100,000 population (versus 14.2 in 2018, the most recent 4-decade high) (1).

Suicide rates are disproportionately distributed by sex, age, and race-ethnicity. In 2020, suicide rates were highest among those ages ≥ 85 (age-adjusted rate per 100,000 of 20.9) (2) but had been highest among middle-age adults (ages 45–54) for the previous decade (see Figure 1). Suicide, however, is the third leading cause of death among youths and the second among those ages 10–14 (3). These rates are consistent with the latest global estimates from 2019, when suicide constituted the fourth leading cause of death worldwide among youths ages 15–19, and self-harm was the third leading cause of disability-adjusted life-years among youths ages 10–24 worldwide (4, 5). Suicide rates continue to be four times higher among U.S. males (age-adjusted rate of 22 per 100,000) compared with U.S. females (age-adjusted rate of 5.5 per 100,000). American Indian and Alaska Native (age-adjusted rate of 28.1 per 100,000) and White individuals (age-adjusted rate of 17.4 per 100,000) showed the highest rates of suicide in 2021 (1) (see Figure 2 for last decade's trends by race-ethnicity). More than 50% of suicide deaths were implemented via firearms (52.8% of deaths), followed by suffocation (27.2%) and poisoning (12%). Whereas suicide rates decreased among non-Hispanic White individuals, non-Hispanic Black and non-Hispanic American Indian and Alaska Native individuals showed increases of 4.0% and 6.2%, respectively, between 2019 and 2020 (3). Similarly, suicide attempt rates have risen among Black and Hispanic

FIGURE 1. U.S. suicide rates by age, 2011–2020

youths (6). Risk factors thought to contribute to these disparities in suicide risk include limited access to mental health care, economic disadvantage, disparities in traumatic experiences (e.g., exposure to neighborhood violence), and perceptions and stigma related to mental health conditions and treatment. However, our understanding of individual-, family-, and neighborhood-level risk and protective factors in these populations is relatively lacking in these historically understudied populations.

For every suicide death, there are an estimated four hospitalizations for suicide attempts, eight emergency department (ED) visits related to suicide, and 27 self-reported suicide attempts (7). In 2020, prevalence of suicide attempt in the past year among adults ages 18 and older was 0.5%, translating to 1.2 million adults affected; prevalence of attempts was highest among young adults ages 18–25 (1.9%) (8). The overall rate for seriously thinking about suicide was 4.9% and was higher among those ages 18–25 (11.3%) (8). According to the Youth Risk Behavior Survey (9), the rate of suicide attempts among high school students was alarming, with 9% of high school students reporting a suicide attempt in the past 12 months; those identifying as lesbian, gay, or bisexual (23.4%) had rates that were four times higher than those of heterosexual youths (6.4%). The transgender population is perhaps the most at-risk population, with more than 40% of trans adults attempting suicide at some point in their lives (compared with less than 5% for the general population) (10).

There has been an unprecedented surge in suicidal thoughts and behaviors (STBs) among youths that has been exacerbated by the pandemic, leading the U.S. Surgeon General to issue an advisory of a mental health crisis among youths in December 2021. Studies and systematic reviews have reported an increase in STBs among youths during the pandemic, with rates as high as 31.3%; and ED visits for suspected suicide attempt were 51% higher among adolescent females in early 2021 compared with early 2019. Loneliness and isolation, lack of connectedness, time spent on

screens (including exposure to news about the pandemic and racial violence), time spent on social media, sleep changes, experiences with virtual schooling, reductions in psychiatric services early during the pandemic, parental or caregiver's death due to COVID-19, and housing and financial problems likely led to increases in mental health distress, including mood and anxiety symptoms, likely exacerbating STBs among youths. These risk factors and others have disproportionately affected racial-ethnic minority populations during the pandemic, with suicide rates heralding new, concerning trends for a number of minoritized populations, as well as youths and young adults.

PATHOPHYSIOLOGY OF SUICIDAL BEHAVIOR

Many biological systems are implicated in risk for suicidal behavior. The most commonly studied systems include the serotonergic system, the hypothalamic-pituitary-adrenal (HPA) axis, and inflammatory pathways.

Serotonergic Systems

Antidepressants' mechanisms of action in augmenting serotonin neuron firing and release in the brain resulted in a focus on the serotonergic system in mood disorders and risk for suicidal behavior. Selective serotonin reuptake inhibitors (SSRIs) have been reported to downregulate serotonin (5-HT_{1A}) receptor binding, which has been found to reverse within 2 weeks of discontinuation of medication. This downregulation has been hypothesized to mediate the action of SSRIs (11–13). In addition, higher pretreatment 5-HT_{1A} receptor binding has been associated with antidepressant treatment response (13). Reduced serotonin production and release in the brain have been reported among individuals with mood disorders and at risk for suicidal behavior (12, 13). A meta-analysis of positron emission tomography (PET) imaging studies (14) reported lower 5-HT_{1A} receptor binding in the mesiotemporal cortex of patients with depression compared with healthy individuals.

Other PET studies, including some newer ones (15–18), however, have reported elevated binding in depression and in the offspring of parents with major depression, with higher binding found to predict suicidal ideation 1 year following the scan. It is not clear whether the discrepancy in these results was caused by differences in biological phenotypes related to risk or resilience for mood disorders or suicidal behavior or to methodological differences in PET imaging data acquisition, processing, and analyses.

HPA Axis Activity

Suicidal behavior most often occurs in the context of stressors; therefore, studies have focused on the HPA axis as

a potential mechanism implicated in the pathophysiology of suicidal behavior. A stress diathesis model has been proposed, which posits a preexisting vulnerability or diathesis for suicidal behavior that is exacerbated by an acute stressor (19). Stressors of various sources, whether physical, emotional, or immunological, result in activation of the HPA axis. Meta-analyses have shown impaired HPA axis feedback on the dexamethasone suppression test to be associated with a 4.6-fold increased risk for suicide (20). Both HPA axis hypo- and hyperactivity and reactivity to stress have been described in suicidal ideation and behavior and have been reported by relatives of suicide decedents. Our previous work (21) showed blunted HPA axis activity among youths who had attempted suicide compared with that of other high-risk individuals during an experimental stressor (Trier Social Stress Task). In addition, youths who were offspring of parents with a history of suicide attempt showed lower HPA axis activity than those without parental history of attempt (21). These results were replicated in another study (22), and blunted HPA axis activity was found to predict suicidal ideation a month later. We extended these findings (23), by comparing hair cortisol concentrations of psychiatric inpatients admitted for suicide attempt, psychiatric inpatients admitted for suicidal ideation, and healthy control individuals, to show that this blunted HPA axis activity precedes suicidal behavior. Blunted HPA axis activity was also found to prospectively predict suicide attempt among adolescent females (24). These results are consistent with recent meta-analyses (25, 26) showing blunted HPA axis profiles among individuals who attempted suicide compared with psychiatric control patients. Individuals with a history of childhood abuse also show dysregulations in HPA axis function, myelination, plasticity, and signaling. Epigenetic alterations in gene expression may mediate the relationship between childhood abuse, brain function, and mental disorders (27).

Inflammation

The nervous and endocrine systems work closely with the immune system to maintain homeostasis. Our work (23) has shown that blunted HPA axis activity, together with increased inflammation, differentiates youths who have attempted suicide, and that blunted HPA axis activity precedes suicidal behavior. Co-occurring low HPA axis activity and high inflammation have been also reported to be associated with chronic interpersonal stressors among adolescent females and have been associated with increased risk for suicidal behavior (28, 29). Indeed, meta-analyses (30) have reported increased inflammation in cerebrospinal fluid and peripheral blood among suicidal patients, with increased IL-6 and IL-1 β to be the most robust findings. Dysregulations in the expression of inflammatory genes, genes implicated in immune system responses, and

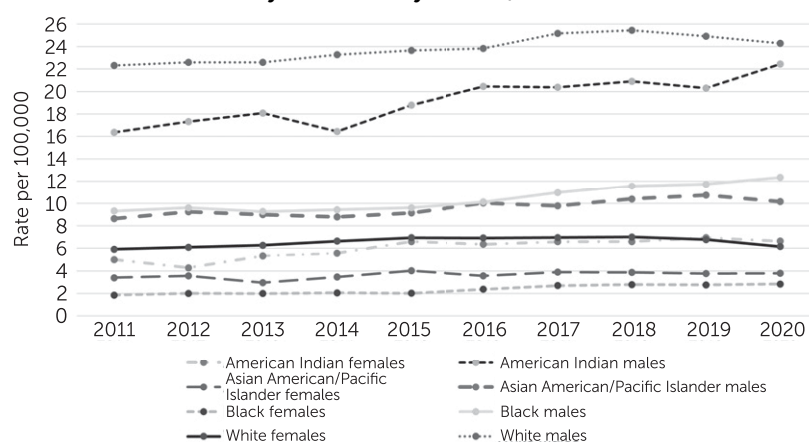
microglia have also been reported in postmortem studies of brains of people who died by suicide (31–34). Specifically, increased expression of IL-1 β , IL-6, TNF- α , and upregulation of toll-like receptors 3 and 4 mRNA have been reported in the prefrontal cortex of adolescents and adults who died by suicide (35–37). Differential expression for inflammatory genes has also been reported in peripheral blood of individuals at risk for suicidal behavior (23, 38).

There are several mechanisms by which inflammation may influence suicidal behavior (39). Circulating cytokines can access the brain through a number of pathways, including active or passive transportation across the blood-brain barrier; cytokines can also be secreted in the brain by microglia, astrocytes, and endothelial cells (40). The prefrontal cortex and hippocampus play an important role in cognitive and emotional processes (40). Animal studies have supported an association between peripheral inflammation and cytokine levels in these brain regions, where IL-6 receptors are concentrated (41). An inverse relationship between peripheral IL-6 and hippocampal gray matter volume also has been reported (42). Peripheral inflammation also has been associated with impaired cognitive processes, including learning and memory (43). In addition, inflammation interacts with the serotonergic and HPA axis systems, whereby proinflammatory cytokines (44) and environmental stressors and glucocorticoids (45) result in activation of the kynurenine pathway, which metabolizes tryptophan (TRP) into an array of neuroactive metabolites that modulate neuroinflammation and glutamate neurotransmission, resulting in TRP depletion and reducing TRP availability for serotonin synthesis. Converging evidence from plasma, cerebrospinal fluid, and postmortem brain studies implicates the kynurenine pathway in suicidal ideation and behavior (46).

Role of Decision-Making Brain Processes in Suicidal Behavior

The reviewed literature suggests that impairments in medial and lateral ventrolateral prefrontal cortex (VLPFC) regions and their connections may be important in the excessive

FIGURE 2. Suicide rates by race-ethnicity and sex, 2011–2020



negative and blunted positive internal states that can stimulate suicidal ideation, and that impairments in the dorso-lateral prefrontal cortex (DPFC) and inferior frontal gyrus system may be important in suicidal behaviors. A combination of VPMC and DPFC system disturbances may lead to the transition from suicidal ideation to lethal actions via decreased top-down inhibition of behavior and maladaptive, inflexible decision-making and planning. The dorsal anterior cingulate cortex and insula may have important roles in switching between the VPMC and DPFC systems, possibly contributing to the transition from suicidal thoughts to behaviors (47). Indeed, dysregulations in decision-making processes are consistently reported in suicidal behavior, with riskier decision making observed among people who attempt suicide compared with other patients and healthy control individuals (48).

Psychological Theories on the Causes of Suicide

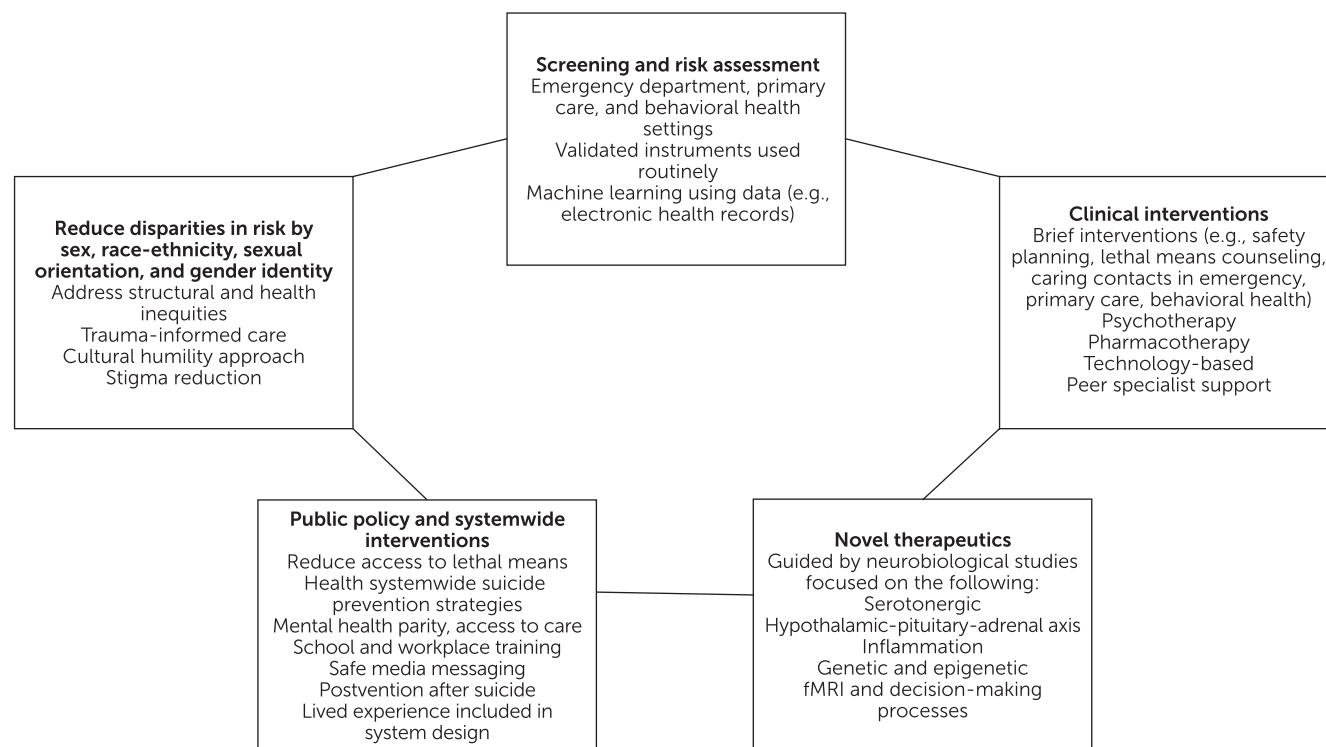
Several psychological theories offer frameworks for understanding suicide. Psychological theories of suicide have generally focused on suicide as a response to overwhelming pain, isolation, or hopelessness. Most current theories assume consensus about these experiences as relevant to suicide and shift the focus to explaining why some people who have these experiences move from ideation to action (49–53). The interpersonal theory of suicide is the most well-known and posits that stressors lead to suicide when three key experiences converge and intensify to drive behavioral action: low belongingness (feeling isolated, disconnected), burdensomeness (feeling like a burden to others), and acquired capability (reduced sensitivity to physical pain, fearlessness of death, ready access to lethal means). The integrated motivational-volitional model builds on the interpersonal theory and focuses on entrapment (feeling trapped) and defeat (social humiliation) as primary drivers and explains how people with risk factors and precipitating events progress from ideation to behavior (54). The Three-Step Theory proposes that suicide occurs related to experiences of pain and hopelessness, when the person's pain is greater than their capacity for connection with others, and the person acquires the capability for suicide (53). Although these psychological constructs seem distinct from the aforementioned neurobiological research findings, there are likely correlates between these psychological experiences and the physiological processes associated with suicide.

PREDICTION, SCREENING, AND IDENTIFICATION OF HIGH-RISK PATIENTS

In clinical practice, identifying which patients will attempt suicide is a challenge. Our ability to predict suicidal behavior is modest (55), although, recent studies, including our work (56, 57), have resulted in models with improved performance among youths. However, these studies have either focused on self-report measures, a wide age range, or long-term

prediction of suicidal behavior. Machine learning approaches have been applied to the prediction of suicidal behavior among children, adolescents, and adults. These approaches also have been applied to large electronic health records data sets and have been found to have high predictive utility, with an area under the curve of 0.83 to 0.93 for predicting suicidal behavior among adults and adolescents (58–60). Although these models have low positive predictive value, given the low base rate of suicidal behavior in the population (59), they are useful as a complement to the clinical picture in identifying those who may be at high risk in the shorter term, so that additional personalized resources can be provided.

At the clinical level, universal screening for depression and suicide risk is increasingly recommended to identify adolescents and adults at risk and is becoming the standard of care. For example, the American Academy of Pediatrics' Bright Futures periodicity schedule recently recommended routine universal suicide screening in outpatient primary care for youths ages 12 and older. Although the 2022 U.S. Preventive Service Task Force released recommendations finding insufficient evidence for recommending routine suicide screening for youths, as well as for adults, many suicide prevention experts do not agree with this recommendation, finding ample evidence for valid, effective screening and evidence-based or evidence-informed care steps that can reduce suicide risk (61). In 2019, The Joint Commission released its National Patient Safety Goal on suicide prevention, requiring all health care organizations to screen and provide care steps for patients with a mental health concern, and universally in behavioral health settings. Increasingly, primary care practices are using various instruments, including the nine-item Patient Health Questionnaire (PHQ-9), to screen for depression and using item nine (thoughts that one would be better off dead or of hurting oneself in some way) to screen for suicidal thoughts. Although screening for depression is important, it can miss suicide risk; 32% and 58% of youths who screened negative on the PHQ-9 and on item nine, respectively, screened positive for risk for suicide using the Ask Suicide–Screening Questions (ASQ) toolkit (61). Therefore, suicide risk can be missed if only a depression screening instrument is used, especially among youths. Thus, suicide screening should be implemented in addition to depression screening, rather than requiring a positive screen result for depression before implementing suicide screening (61). In addition, 39% of suicide attempts and 36% of suicide deaths occur within 30 days after denying ideation on the PHQ-9 (62). This finding may be particularly salient for Black youths, who are less likely than White youths to report suicidal ideation prior to a suicide attempt (63). Additional screening tools used to screen for suicidal ideation and behavior include the Suicidal Behaviors Questionnaire–Revised (SBQ-R) (64) and the Columbia–Suicide Severity Rating Scale (C-SSRS) (65). The ASQ includes four questions, and its use has been validated among youths and adults across various medical settings,

FIGURE 3. Intervention strategies for an integrated approach to reducing suicide risk

including inpatient, outpatient, ED, and primary care settings. Similarly, the SBQ-R includes four items and is used for adolescents and adults. The C-SSRS (65) is an assessment instrument used for triage and screening, with six items—including a question about prior history of suicidal behavior—one of the most important predictors of suicidal behavior. Other screening tools include the Computerized Adaptive Screen for Suicidal Youth (66) and the Computerized Adaptive Test Suicide Scale (CAT-SS) (67) for suicidal behavior, which have shown high accuracy in prediction of suicide attempt among youth and adult samples.

PREVENTION OF SUICIDE AND SUICIDAL BEHAVIOR

This section reviews evidence-based strategies to reduce the public health burden of suicide and suicidal behavior. We index intervention strategies to our above-noted integrated approach to suicide prevention (see Figure 3). Universal prevention enhances protective factors or targets risk factors common to a broad spectrum of the population. A significant proportion of studies have focused on the treatment of acutely suicidal individuals, with the goal of decreasing suicidal ideation and/or reducing the likelihood that at-risk individuals will act on their suicidal urges. These interventions include ultra-brief services that focus on safety planning, linkage to mental health care, and provision of nonspecific supportive contacts via letters, postcards, or texts. We then discuss psychotherapeutic approaches to the management of suicidal patients; use of apps, games, and

online interventions; and somatic treatments. Finally, we discuss systemic interventions, including those that target and support primary care physicians' role in detecting and caring for at-risk individuals, multicomponent suicide prevention initiatives, restriction of access to lethal agents, and health systems interventions designed to improve access and continuity of care for individuals at risk for suicide.

Universal Prevention

A public health framework for reducing complex health outcomes can be applied to suicide prevention, which includes a stratified approach that incorporates universal, primary prevention along with more targeted approaches. Whereas the suicide research community is making strides on short-term risk prediction, clinicians currently have limited ability to identify who is at highest risk and when that risk for suicidal behavior will manifest. Key examples of universal prevention are two types of school-based interventions with a 3–12-month delivery time frame that significantly reduce suicidal ideation and attempts: first, a mindfulness intervention for early adolescent students, and second, curriculum-based interventions. The latter interventions promote recognition of mental health distress among oneself and one's friends, increase the likelihood of help-seeking, and model how to respond supportively to friends who disclose depression or suicidal thoughts. Meta-analyses have found that the odds ratio of ideation and attempts after these two interventions were 0.76 and 0.58,

TABLE 1. Safety plan components

Safety plan component	Example
Identify triggers for suicidal urges	Argument with significant other; intoxication
Develop personal ways to avoid triggers	Try to avoid controversial topics; engage in temporary abstinence; limit time with certain individuals
Identify personal ways to cope with suicidal urges	Distractions, such as taking a walk, listening to music; relaxation through slow breathing
Identify interpersonal ways to cope with suicidal urges	Call or meet a friend
Contact professional or crisis services	Call therapist, emergency department, crisis services; contact 988 (call, text, or chat) or crisis text line (text "TALK" to 741741)
Secure environment	Remove or secure firearms, medications, substances, sharps, cleaning supplies

respectively (68). The single largest school-based clinical trial tested a curriculum called Youth Aware of Mental Health (YAM), gatekeeper training, and screening for suicide risk (followed by referral as needed), compared with a bibliotherapy (exposure to six posters about mental disorders and accessing care) control group, among >11,000 European secondary school students. Only YAM was superior to bibliotherapy, cutting the rate of suicidal ideation and attempt by half at 12-month follow-up (69). The Good Behavior Game, a teacher-led classroom-based social skills intervention for first-graders, reduced occurrence of suicidal ideation and attempt by half, 20 or more years post-intervention, when the teachers delivering the intervention received weekly supervision (69). Gatekeeper training, which involves training professionals and nonprofessionals most likely to encounter individuals at risk for suicide, has been widely disseminated and endorsed as a suicide prevention approach, but has demonstrated limited effect on gatekeeper behavior and on suicidal behavior. One recent quasi-experimental study of an American Foundation for Suicide Prevention teacher education program, called "More Than Sad," showed that, in addition to improving knowledge and self-efficacy, gatekeeper training of school personnel increased referrals for suicide-related issues (70). In addition, gatekeeper training has shown promise as part of multimodal interventions, discussed below (71).

Brief Interventions for Suicidal Patients

Patients who arrive in an ED with suicidal ideation, or who are discharged from a psychiatric inpatient unit after being hospitalized for suicidal ideation or attempt, are at high risk for subsequent suicidal behavior in the days to weeks following discharge. Brief interventions that encourage linkage to mental health care, safety planning, and caring contacts have been shown to decrease risk of a subsequent attempt

(odds ratio [OR]=0.69) and to increase the likelihood of accessing follow-up care (OR=3.0) (72). Screening and referring to behavioral health care on their own, however, are less likely to affect subsequent attempts compared to when safety planning is included for patients who screen positive for suicide risk.

Safety planning is a key ingredient of almost every psychotherapeutic intervention for patients at risk for suicide and includes the tiered steps or elements outlined in Table 1 (73). "Caring contacts," which are supportive communications from health care providers by letter, postcard, telephone call, or text, reduce hazard for subsequent ideation, attempts, or suicide compared with treatment as usual (74). Collaborative assessment and management of suicidal patients (CAMS) has been widely used and replicated and is a 2–3 session intervention designed to collaborate with the suicidal patient in assessing and managing suicidal thoughts. In studies to date, CAMS has shown a positive effect on suicidal ideation ($d=0.25$) and distress ($d=0.29$), but so far has not demonstrated an effect on subsequent attempts (75). Finally, all health professionals in all settings are recommended to provide suicide-specific education and resources to patients and families for any level of suicide risk. Box 1 provides evidence-informed resources clinicians can use to educate patients and families.

Evidence-Based Psychotherapies for Suicidal Patients

Several types of psychotherapies have shown evidence of efficacy in decreasing suicidal ideation and attempts or the broader category of "self-harm," which combines suicidal behavior and nonsuicidal self-injury (76, 77). Cognitive-behavioral therapy (CBT) focuses on cognitive distortions that lead to suicidal feelings and urges (e.g., hopelessness). CBT also teaches problem solving and substitution of alternative, more adaptive ways of conceptualizing the stresses and emotions that lead to a suicidal crisis. Meta-analyses (78) have shown that CBT reduces recurrent suicidal behavior among adults by about half in the 6 months following treatment (OR=0.52). Dialectical behavior therapy (DBT) focuses on development of emotion regulation, distress tolerance, and interpersonal effectiveness skills to cope with suicidal urges. DBT has been shown effective in preventing suicidal behavior among adolescents (OR=0.46) and has shown a trend for the same among adults (OR=0.65). Mentalizing, a psychotherapeutic approach with roots in psychoanalytic psychotherapy, teaches patients to conceptualize their own and others' behavior in terms of thoughts and emotions. Mentalizing has been found to decrease self-harm among adolescents (OR=0.70) and adults (OR=0.34). Treatment that focuses on emotion regulation and psychodynamic therapy (76, 77, 79) has been shown to reduce incidence of subsequent suicide attempts.

Substance use plays a key role in increasing suicide risk in short- and longer-term ways. For example, intoxication is an important proximal predictor of suicide attempt, and substance use disorder is a mental health condition that elevates suicide

BOX 1. Patient and family suicide prevention resources**To learn more and access resources:**

Suicide Prevention Resource Center, <https://www.sprc.org>
 SAMHSA Help Prevent Suicide, <https://www.samhsa.gov/suicide>
 American Foundation for Suicide Prevention (AFSP), <https://afsp.org>
 Psych Hub Educational Video Library, <https://psychhub.com/resources/videos>
 Blueprint for Youth Suicide Prevention (American Academy of Pediatrics/AFSP), <https://www.aap.org/en/patient-care/blueprint-for-youth-suicide-prevention>
 How to talk with patients and their families about suicide risk (American Academy of Pediatrics), <https://www.aap.org/en/patient-care/blueprint-for-youth-suicide-prevention/strategies-for-clinical-settings-for-youth-suicide-prevention/how-to-talk-about-suicide-risk-with-patients-and-their-families>

To learn about evidence-based treatments for reducing suicide risk:

Suicide Prevention Interventions and Treatment (AFSP), <https://afsp.org/suicide-prevention-interventions-and-treatments>

To help patients find specialized treatment:

Substance Abuse and Mental Health Services Administration Treatment Finder, <https://www.samhsa.gov/find-treatment>

Patient and family education resources:

AFSP "After an Attempt" Family/Patient Resource, <https://afsp.org/after-an-attempt>
 How to start a conversation about mental health, <https://afsp.org/story/how-to-start-and-continue-a-conversation-about-mental-health-a-realconvo-guide-fr>
 If someone tells you they are thinking of suicide, <https://afsp.org/story/if-someone-tells-you-they-re-thinking-about-suicide-a-realconvo-guide-from-afsp>
 AFSP Tips for Parents, <https://afsp.org/teens-and-suicide-what-parents-should-know>
 Mindfulness and Dialectical Behavior Therapy micro-skills, <https://nowmattersnow.org>

After Suicide Loss and Healing:

Suicide Loss Support Groups (AFSP), <https://afsp.org/find-a-support-group>
 Surviving a Suicide Loss: Resource and Healing Guide, <https://aws-fetch.s3.us-east-1.amazonaws.com/flipbooks/survivingASuicideLoss/index.html?page=1>
 Guide for talking with children and teens after suicide: Children, Teens, and Suicide Loss, <https://aws-fetch.s3.amazonaws.com/flipbooks/childrenteenssuicideloss/index.html?page=1>

risk in the longer term. Interventions that decrease the quantity and frequency of alcohol consumption and that target opiate abuse have been shown to decrease subsequent suicide attempts (80). The frequency of alcohol use, for example, increases risk of a suicide attempt among those with suicidal ideation, making the assessment and management of alcohol abuse critical in the prevention of suicidal behavior (81). Moreover, regional health systems that implement treatment programs that target mental and substance abuse disorders together (for individuals with co-occurring disorders) have demonstrated reduced regional suicide rates (82).

Attachment-based family therapy has shown promise as an intervention for suicidal adolescents. However, although subsequent replications in the United States and Norway showed that attachment-based family therapy significantly reduced suicidal ideation, the reductions did not differ from those of other active treatment comparison interventions (83–87).

Online CBT for suicidal patients ameliorates suicidal ideation, with some evidence that concomitant live coaching improves treatment outcomes (87–89). Several apps with reported feasibility and acceptability have been designed for suicidal youths and adults. Only a handful of these apps have been tested in randomized controlled trials (RCTs), however, with most showing no demonstrable effect on suicidal ideation or attempts. LifeBuoy (90), a 6-week telephone app intervention developed on the basis of DBT principles, has been shown to be superior to a sham treatment with respect to suicidal ideation ($d=0.45$) (91). Franklin (91), on the basis of

work by Millner and colleagues (92, 93) developed a game targeting the identification of self with death and suicide. In this game, the patient gets points for pairing images representing the self with positive images and for pairing suicide with negative images. For the first month after exposure to this gaming intervention a marked decrease in suicidal ideation (21%–59%), nonsuicidal self-injury (32%–40%), and attempted suicide (33%–77%) were observed across three trials with young adults recruited via the Internet, but the effects faded within a month after participation ended.

Pharmacotherapy

There is evidence to support the role of antidepressants, lithium, clozapine, and ketamine in reducing suicidal ideation and attempts and suicide. When considering antidepressants, the clinician must weigh the potential for both reducing and increasing risk for suicidal ideation and attempts. The U.S. Food and Drug Administration decision in 2004 to issue a black box warning on antidepressants for people ages 24 and younger was controversial. The decision was based on a meta-analysis of the impact of second-generation antidepressants. The meta-analysis found an increase in suicidal ideation ($OR=1.62$) and suicidal behavior ($OR=2.3$) in RCTs of antidepressants for participants ages 24 and younger with depression (94); however, the analysis did not consider preexisting suicidal behavior or other suicide risk factors. In those $>age 25$, there was a protective effect against suicidal ideation compared with placebo (95).

More specific analyses found that, among adolescents, the only statistically significant increase in suicidal events in placebo-controlled trials occurred among youths treated with venlafaxine (96). One of the few studies comparing risks and benefits of antidepressants in the same study (96) showed that >14 depressed youths would benefit from antidepressant use for each one who experienced a suicidal event.

Pharmacoepidemiologic studies, although not as rigorous as clinical trials, may have more ecological validity. Unlike clinical trials, pharmacoepidemiologic studies do not screen out most suicidal patients. These studies include large enough numbers of individuals to be able to discern effect on suicide as well as on suicidal ideation or attempts. Seven studies in Europe and the United States found regional suicide rates that were inversely proportional to prescription rates for SSRIs, and data from large pharmacological databases have shown a protective effect of both pharmacotherapy and psychotherapy on subsequent suicide attempts (97–100).

Further context on the risks and benefits of antidepressant medications for suicide risk or benefit comes from two more important studies. In a study (99) conducted in a large health care system, the highest incidence of suicide attempts was in the month prior to initiation of an antidepressant. Incidence of suicide attempt declined after initiation of an antidepressant (99). In the Zisook et al. (101) 7-month follow-up study to the Sequenced Treatment Alternatives to Relieve Depression trial, 665 adult outpatients with major depressive disorder took one of three antidepressant medications (no control group). Among patients without suicidal ideation prior to medication initiation, 2.5% had ideation at 4 weeks, 1.3% at 12 weeks, and 1.7% at 28 weeks. Of those with suicidal ideation at baseline, 79% had none at 4 weeks, 83% had none at 12 weeks, and 86% had none at 28 weeks. Overall, Zisook et al. (101) observed that emergence of new suicidal ideation was uncommon (1.3%–2.5% of patients without baseline ideation) and that antidepressant medication was associated with reduction or resolution of suicidal ideation in most cases.

Meta-analyses of RCTs involving lithium versus placebo and versus alternative treatments consistently have shown a protective effect of lithium against suicide and suicide attempts among patients with bipolar and unipolar mood disorders (102). Compared with other active treatments, clozapine has shown a protective effect against suicide attempts among patients with psychosis, with some evidence that clozapine's effect is mediated by its impact on impulsivity and aggression (102, 103).

Public Policy and Systemwide Interventions

Systemic interventions refer to the effects of laws, policies, or methods of organizing health care delivery on population outcomes, such as suicide and suicidal behavior. Evaluation of the impact of systemic interventions is by necessity quasi-experimental and observational.

Interventions designed to train general practitioners in the recognition and management of depression have

demonstrated regional improvement in suicide rates, although ongoing consultation and supervision appears to be more potent than a 1-day seminar (104). Also, identification and treatment of depression through a collaborative care model, in which there is an office-based care manager and an embedded mental health practitioner, has been shown to improve access and outcomes compared with usual care (105).

The Garrett Lee Smith Act (GLSA) was enacted into federal law in 2004, providing states and tribes with funds for youth suicide prevention. The GLSA covers gatekeeper training; continuing education for professionals who interact with children; increased screening and case identification; coordination of care; information linkage across health, mental health, educational, and social agencies involved in the care of vulnerable youths; and support for identification and referral of at-risk youths in schools. Impact of the GLSA was assessed with a quasi-experimental study comparing demographically similar counties that did and did not participate in GLSA activities (71). The study found decreased rates of suicide and suicide attempts in the counties that participated, with the effects identified only among the targeted population of adolescents. The suicide rate was approximately 1.0/100,000 lower in the counties participating in the GLSA, with a 2-year average duration of effect. Effects were stronger in rural areas. These results suggest that ongoing training is necessary to maintain positive effects. Although RCTs do not generally support the efficacy of gatekeeper training, the salutary effects of GLSA were mediated in part by the number of gatekeepers trained (71).

Several multicomponent suicide prevention programs have focused on elderly populations. Interventions have ranged from telehealth appointments for suicidal elders to depression screening paired with linkage to mental health and/or primary care evaluation and treatment, all of which have shown some evidence of regional reduction in suicide among women, compared with similar regions where these programs were not deployed (104–106).

Legislation and policy change restricting access to lethal agents consistently result in decreases in suicides carried out through these methods, which are not offset by method substitution. This effect has been documented with respect to access to pesticides (a leading method for suicide in South Asia), acetaminophen, carbon monoxide from cars and heating gas (107), and laws promoting safe storage or access to firearms (108, 109). Laws promoting rights and protecting against harassment toward sexual and gender minority populations have been tied to reductions in disparities in suicidal behavior between sexual and gender minority and nonminority youth populations (108, 109).

Kapur and colleagues (82) translated their groundbreaking work on facilitators of and barriers to suicide into recommendations for how mental health care should be delivered to reduce suicide rates. Among their recommendations for health care systems were the following: easily accessible crisis services, assertive follow-up of patient recidivism, services

treating co-occurring conditions, coordination of patient transition across levels of care or transition from adolescent to adult services, adherence to treatment guidelines for depression, and open inquests into patient suicides that include all care parties and surviving family members. The extent to which these recommendations were followed was related to a 20%–30% decline in regional suicide rates (82). This work inspired the Zero Suicide Initiative, which was first pilot tested in the United States within the Henry Ford Health system and resulted in a dramatic decline in suicide among patients accessing specialty mental health care (104, 105). In newer implementations of health systemwide suicide prevention efforts, other key actions have included engaging leadership; making suicide and suicidal behavior reduction ongoing priorities with workflow protocols and health record modifications to ensure outcomes tracking; training all personnel in suicide prevention; implementing safety planning; providing lethal means safety counseling; and implementing caring contacts on a systematic basis (110, 111).

Health Equity Solutions

Health inequity and disparities are driven by societal, systemic, clinician, and patient factors. Legislation aiming at shoring up inclusivity and equal protections has been associated with decreases in suicide-related disparities among sexual and gender minority populations. Ensuring equal access to care can be lifesaving. For example, for suicidal youths discharged from a psychiatric hospital, having an outpatient mental health appointment within 1 week of discharge was found to be protective against suicide (112). Black youths were less likely to have follow-up appointments, accounting in part for suicide-related health disparities. Provision of mental health services in primary care may help reduce disparities in access and outcomes (113). Provision of services that have substantial input from and reflect the cultural values of patients can result in better uptake and outcomes, as is the case for interventions designed with, and for, patients from indigenous communities (114). Finally, we need to increase the diversity of our mental health workforce, and the cultural humility of mental health clinicians.

CONCLUSIONS

Suicide remains a critical public health priority, with potentially preventable loss of life continuing, despite advances in science and advocacy. Arguably, scientifically based solutions are at an early stage of translation and dissemination into community and clinical settings. Most of the programs and interventions with promise or evidence for reducing suicide risk included in this review are not yet widely accessible to the public. Overcoming real-world barriers to achieve full implementation of suicide prevention strategies is one of the greatest needs and opportunities in suicide prevention. With continued focus on broad-scale implementation of the programs and interventions discussed in

this article, we hope to see reduced suffering and suicide mortality in the future.

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REFERENCES

1. Stone DM, Mack KA, Qualters J: Notes from the field: recent changes in suicide rates, by race and ethnicity and age group—United States, 2021. *MMWR Morb Mortal Wkly Rep* 2023; 72:160–162. <http://dx.doi.org/10.15585/mmwr.mm7206a4>. Accessed Feb 10, 2023
2. Ehlman DC, Yard E, Stone DM, et al: Changes in suicide rates—United States, 2019 and 2020. *MMWR Morb Mortal Wkly Rep* 2022; 71:306–312
3. WISQARS (Web-Based Injury Statistics Query and Reporting System). Atlanta, Centers for Disease Control and Prevention, 2021. <https://www.cdc.gov/injury/wisqars/index.html>. Accessed Dec 27, 2022
4. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; 396:1204–1222
5. Global, regional, and national mortality among young people aged 10–24 years, 1950–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2021; 398:1593–1618
6. Lindsey MA, Sheftall AH, Xiao Y, et al: Trends of suicidal behaviors among high school students in the United States: 1991–2017. *Pediatrics* 2019; 144:e20191187
7. Key Substance Use and Mental Health Indicators in the United States: Results From the 2020 National Survey on Drug Use and Health. Pub no. PEP21-07-01-003, NSDUH Series H-56. Rockville, MD, Substance Abuse and Mental Health Services Administration, 2020. <https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFRPFDWHTMLFiles2020/2020-NSDUHFRPFDW102121.pdf>
8. NSDUH Annual National Report. Rockville, MD, National Survey on Drug Use and Health, 2021. <https://www.samhsa.gov/data/report/2020-nsduh-annual-national-report>
9. High School YRBS. Youth Online. Atlanta, Centers for Disease Control and Prevention. <https://nccd.cdc.gov/Youthonline/App/Default.aspx>. Accessed Sep 11, 2022
10. Goldblum P, Testa RJ, Plüm S, et al: The relationship between gender-based victimization and suicide attempts in transgender people. *Prof Psychol Res Pr* 2012; 43:468–475

11. Metts AV, Rubin-Falcone H, Ogden RT, et al: Antidepressant medication exposure and 5-HT_{1A} autoreceptor binding in major depressive disorder. *Synapse* 2019; 73:e22089
12. Gray NA, Milak MS, DeLorenzo C, et al: Antidepressant treatment reduces serotonin-1A autoreceptor binding in major depressive disorder. *Biol Psychiatry* 2013; 74:26–31
13. Lan MJ, Hesselgrave N, Ciarleglio A, et al: Higher pretreatment 5-HT_{1A} receptor binding potential in bipolar disorder depression is associated with treatment remission: a naturalistic treatment pilot PET study. *Synapse* 2013; 67:773–778
14. Wang L, Zhou C, Zhu D, et al: Serotonin-1A receptor alterations in depression: a meta-analysis of molecular imaging studies. *BMC Psychiatry* 2016; 16:319
15. Milak MS, Pantazatos S, Rashid R, et al: Higher 5-HT_{1A} autoreceptor binding as an endophenotype for major depressive disorder identified in high risk offspring. A pilot study. *Psychiatry Res Neuroimaging* 2018; 276:15–23
16. Pillai RLI, Zhang M, Yang J, et al: Will imaging individual raphe nuclei in males with major depressive disorder enhance diagnostic sensitivity and specificity? *Depress Anxiety* 2018; 35: 411–420
17. Sullivan GM, Oquendo MA, Milak M, et al: Positron emission tomography quantification of serotonin(1A) receptor binding in suicide attempters with major depressive disorder. *JAMA Psychiatry* 2015; 72:169–178
18. Oquendo MA, Galfalvy H, Sullivan GM, et al: Positron emission tomographic imaging of the serotonergic system and prediction of risk and lethality of future suicidal behavior. *JAMA Psychiatry* 2016; 73:1048–1055
19. Mann JJ, Waternaux C, Haas GL, et al: Toward a clinical model of suicidal behavior in psychiatric patients. *Am J Psychiatry* 1999; 156:181–189
20. Mann JJ, Currier D, Stanley B, et al: Can biological tests assist prediction of suicide in mood disorders? *Int J Neuropsychopharmacol* 2006; 9:465–474
21. Melhem NM, Keilp JG, Porta G, et al: Blunted HPA axis activity in suicide attempters compared to those at high risk for suicidal behavior. *Neuropsychopharmacology* 2016; 41:1447–1456
22. O'Connor DB, Green JA, Ferguson E, et al: Cortisol reactivity and suicidal behavior: investigating the role of hypothalamic-pituitary-adrenal axis responses to stress in suicide attempters and ideators. *Psychoneuroendocrinology* 2017; 75:183–191
23. Melhem NM, Munroe S, Marsland A, et al: Blunted HPA axis activity prior to suicide attempt and increased inflammation in attempters. *Psychoneuroendocrinology* 2017; 77:284–294
24. Eisenlohr-Moul TA, Miller AB, Giletta M, et al: HPA axis response and psychosocial stress as interactive predictors of suicidal ideation and behavior in adolescent females: a multilevel diathesis-stress framework. *Neuropsychopharmacology* 2018; 43: 2564–2571
25. Hernández-Díaz Y, González-Castro TB, Tovilla-Zárate CA, et al: The role of peripheral cortisol levels in suicide behavior: a systematic review and meta-analysis of 30 studies. *Psychiatry Res* 2020; 293:113448
26. O'Connor DB, Ferguson E, Green JA, et al: Cortisol levels and suicidal behavior: a meta-analysis. *Psychoneuroendocrinology* 2016; 63:370–379
27. Ibrahim P, Almeida D, Nagy C, et al: Molecular impacts of childhood abuse on the human brain. *Neurobiol Stress* 2021; 15: 100343
28. Bendezú JJ, Calhoun CD, Vinograd M, et al: Exploring joint HPA-inflammatory stress response profiles in adolescent girls: implications for developmental models of neuroendocrine dysregulation. *Dev Psychobiol* 2022; 64:e22247
29. King CA, Merchant CR: Social and interpersonal factors relating to adolescent suicidality: a review of the literature. *Arch Suicide Res* 2008; 12:181–196
30. Black C, Miller BJ: Meta-analysis of cytokines and chemokines in suicidality: distinguishing suicidal versus nonsuicidal patients. *Biol Psychiatry* 2015; 78:28–37
31. Furczyk K, Schutova B, Michel TM, et al: The neurobiology of suicide—a review of post-mortem studies. *J Mol Psychiatry* 2013; 1:2
32. Pandey GN, Zhang H, Sharma A, et al: Innate immunity receptors in depression and suicide: upregulated NOD-like receptors containing pyrin (NLRPs) and hyperactive inflammasomes in the postmortem brains of people who were depressed and died by suicide. *J Psychiatry Neurosci* 2021; 46:E538–E547
33. Zeng D, He S, Ma C, et al: Network-based approach to identify molecular signatures in the brains of depressed suicides. *Psychiatry Res* 2020; 294:113513
34. Piras IS, Huentelman MJ, Pinna F, et al: A review and meta-analysis of gene expression profiles in suicide. *Eur Neuropsychopharmacol* 2022; 56:39–49
35. Pandey GN, Rizavi HS, Ren X, et al: Toll-like receptors in the depressed and suicide brain. *J Psychiatr Res* 2014; 53:62–68
36. Pandey GN, Rizavi HS, Ren X, et al: Proinflammatory cytokines in the prefrontal cortex of teenage suicide victims. *J Psychiatr Res* 2012; 46:57–63
37. Hoyo-Becerra C, Huebener A, Trippler M, et al: Concomitant interferon alpha stimulation and TLR3 activation induces neuronal expression of depression-related genes that are elevated in the brain of suicidal persons. *PLoS One* 2013; 8:e83149
38. Le-Niculescu H, Levey DF, Ayalew M, et al: Discovery and validation of blood biomarkers for suicidality. *Mol Psychiatry* 2013; 18:1249–1264
39. Brundin L, Bryleva EY, Thirtamara Rajamani K: Role of inflammation in suicide: from mechanisms to treatment. *Neuropsychopharmacology* 2017; 42:271–283
40. Pace TWW, Hu F, Miller AH: Cytokine-effects on glucocorticoid receptor function: relevance to glucocorticoid resistance and the pathophysiology and treatment of major depression. *Brain Behav Immun* 2007; 21:9–19
41. Vitkovic L, Bockaert J, Jacque C: “Inflammatory” cytokines: neuromodulators in normal brain? *J Neurochem* 2000; 74: 457–471
42. Marsland AL, Gianaros PJ, Abramowitch SM, et al: Interleukin-6 covaries inversely with hippocampal grey matter volume in middle-aged adults. *Biol Psychiatry* 2008; 64:484–490
43. Schmaal L, van Harmelen AL, Chatzi V, et al: Imaging suicidal thoughts and behaviors: a comprehensive review of 2 decades of neuroimaging studies. *Mol Psychiatry* 2020; 25:408–427
44. Maes M, Leonard BE, Myint AM, et al: The new “5-HT” hypothesis of depression: cell-mediated immune activation induces indoleamine 2, 3-dioxygenase, which leads to lower plasma tryptophan and an increased synthesis of detrimental tryptophan catabolites (TRYCATs), both of which contribute to the onset of depression. *Prog Neuropsychopharmacol Biol Psychiatry* 2011; 35: 702–721
45. Messaoud A, Mensi R, Douki W, et al: Reduced peripheral availability of tryptophan and increased activation of the kynurenine pathway and cortisol correlate with major depression and suicide. *World J Biol Psychiatry* 2019; 20:703–711
46. Serafini G, Adavastro G, Canepa G, et al: Abnormalities in kynurenine pathway metabolism in treatment-resistant depression and suicidality: a systematic review. *CNS Neurol Disord Drug Targets* 2017; 16:440–453
47. Perrain R, Dardennes R, Jollant F: Risky decision-making in suicide attempters, and the choice of a violent suicidal means: an updated meta-analysis. *J Affect Disord* 2021; 280:241–249
48. Yirmiya R, Goshen I: Immune modulation of learning, memory, neural plasticity and neurogenesis. *Brain Behav Immun* 2011; 25:181–213
49. Durkheim E: *Suicide: A Study in Sociology*. New York, Free Press, 1951

50. Abramson LM, Alloy LB, Hogan ME, et al: The hopelessness theory of suicidality; in *Suicide Science: Expanding the Boundaries*. Edited by Joiner T, Rudd MD. Norwell, MA, Kluwer Academic Publishers, 2000
51. Beck AT: *Depression: Clinical, Experimental, and Theoretical Aspects*. New York, Harper and Row, 1967
52. Klonsky ED, May AM: The three-step theory (3ST): a new theory of suicide rooted in the “ideation-to-action” framework. *Int J Cogn Ther* 2015; 8:114–129
53. O'Connor RC: Towards an integrated motivational-volitional model of suicidal behaviour; in *International Handbook of Suicide Prevention: Research, Policy and Practice*. Edited by O'Connor RC, Platt S, Gordon J. Hoboken, NJ, Wiley Blackwell, 2011
54. Gijzen MWM, Rasing SPA, Creemers DHM, et al: Effectiveness of school-based preventive programs in suicidal thoughts and behaviors: a meta-analysis. *J Affect Disord* 2022; 298:408–420
55. Franklin JC, Ribeiro JD, Fox KR, et al: Risk factors for suicidal thoughts and behaviors: a meta-analysis of 50 years of research. *Psychol Bull* 2017; 143:187–232
56. King CA, Grupp-Phelan J, Brent D, et al: Predicting 3-month risk for adolescent suicide attempts among pediatric emergency department patients. *J Child Psychol Psychiatry* 2019; 60:1055–1064
57. Melhem NM, Porta G, Oquendo MA, et al: Severity and variability of depression symptoms predicting suicide attempt in high-risk individuals. *JAMA Psychiatry* 2019; 76:603–613
58. Corke M, Mullin K, Angel-Scott H, et al: Meta-analysis of the strength of exploratory suicide prediction models; from clinicians to computers. *BJPsych Open* 2021; 7:e26
59. Belsher BE, Smolenski DJ, Pruitt LD, et al: Prediction models for suicide attempts and deaths: a systematic review and simulation. *JAMA Psychiatry* 2019; 76:642–651
60. Tsui FR, Shi L, Ruiz V, et al: Natural language processing and machine learning of electronic health records for prediction of first-time suicide attempts. *JAMIA Open* 2021; 4:00ab011
61. Aguinaldo LD, Sullivant S, Lanzillo EC, et al: Validation of the Ask Suicide-Screening Questions (ASQ) with youth in outpatient specialty and primary care clinics. *Gen Hosp Psychiatry* 2021; 68:52–58
62. Simon GE, Coleman KJ, Rossom RC, et al: Risk of suicide attempt and suicide death following completion of the Patient Health Questionnaire depression module in community practice. *J Clin Psychiatry* 2016; 77:221–227
63. Lee CS, Wong YJ: Racial/ethnic and gender differences in the antecedents of youth suicide. *Cultur Divers Ethnic Minor Psychol* 2020; 26:532–543
64. Osman A, Bagge CL, Gutierrez PM, et al: The Suicidal Behaviors Questionnaire-Revised (SBQ-R): validation with clinical and nonclinical samples. *Assessment* 2001; 8:443–454
65. Posner K, Brown GK, Stanley B, et al: The Columbia–Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. *Am J Psychiatry* 2011; 168:1266–1277
66. King CA, Brent D, Grupp-Phelan J, et al: Prospective development and validation of the computerized adaptive screen for suicidal youth. *JAMA Psychiatry* 2021; 78:540–549
67. Gibbons RD, Kupfer D, Frank E, et al: Development of a Computerized Adaptive Test Suicide Scale—the CAT-SS. *J Clin Psychiatry* 2017; 78:1376–1382
68. Wasserman D, Hoven CW, Wasserman C, et al: School-based suicide prevention programmes: the SEYLE cluster-randomised, controlled trial. *Lancet* 2015; 385:1536–1544
69. Pistone I, Beckman U, Eriksson E, et al: The effects of educational interventions on suicide: a systematic review and meta-analysis. *Int J Soc Psychiatry* 2019; 65:399–412
70. Diamond G, Ogunkua L, Atte T, et al: The effectiveness of the More Than Sad school-based gatekeeper training program. *School Mental Health* 2021; 13:655–666
71. Godoy Garraza L, Kuiper N, Goldston D, et al: Long-term impact of the Garrett Lee Smith Youth Suicide Prevention Program on youth suicide mortality, 2006–2015. *J Child Psychol Psychiatry* 2019; 60:1142–1147
72. Doupnik SK, Rudd B, Schmutte T, et al: Association of suicide prevention interventions with subsequent suicide attempts, linkage to follow-up care, and depression symptoms for acute care settings: a systematic review and meta-analysis. *JAMA Psychiatry* 2020; 77:1021–1030
73. Stanley B, Brown G: Stanley-Brown Safety Planning Intervention. <https://suicidesafetyplan.com>. Accessed Jan 4, 2023
74. Skopp NA, Smolenski DJ, Bush NE, et al: Caring contacts for suicide prevention: a systematic review and meta-analysis. *Psychol Serv*. Epub ahead of print Apr 14, 2022
75. Swift JK, Trusty WT, Penix EA: The effectiveness of the Collaborative Assessment and Management of Suicidality (CAMS) compared to alternative treatment conditions: a meta-analysis. *Suicide Life Threat Behav* 2021; 51:882–896
76. Witt KG, Hetrick SE, Rajaram G, et al: Interventions for self-harm in children and adolescents. *Cochrane Database Syst Rev* 2021; 3: CD013667
77. Briggs S, Netuveli G, Gould N, et al: The effectiveness of psychoanalytic/psychodynamic psychotherapy for reducing suicide attempts and self-harm: systematic review and meta-analysis. *Br J Psychiatry* 2019; 214:320–328
78. Mewton L, Andrews G: Cognitive behavioral therapy for suicidal behaviors: improving patient outcomes. *Psychol Res Behav Manag* 2016; 9:21–29
79. Witt KG, Hetrick SE, Rajaram G, et al: Psychosocial interventions for self-harm in adults. *Cochrane Database Syst Rev* 2021; 4: CD013668
80. Witt K, Chitty KM, Wardhani R, et al: Effect of alcohol interventions on suicidal ideation and behaviour: a systematic review and meta-analysis. *Drug Alcohol Depend* 2021; 226:108885
81. Richards JE, Shortreed SM, Simon GE, et al: Association between patterns of alcohol use and short-term risk of suicide attempt among patients with and without reported suicidal ideation. *J Addict Med* 2020; 14:e160–e169
82. Kapur N, Ibrahim S, While D, et al: Mental health service changes, organisational factors, and patient suicide in England in 1997–2012: a before-and-after study. *Lancet Psychiatry* 2016; 3: 526–534
83. Waraan L, Rognli EW, Czajkowski NO, et al: Efficacy of attachment-based family therapy compared to treatment as usual for suicidal ideation in adolescents with MDD. *Clin Child Psychol Psychiatry* 2021; 26:464–474
84. Waraan L, Rognli EW, Czajkowski NO, et al: Effectiveness of attachment-based family therapy compared to treatment as usual for depressed adolescents in community mental health clinics. *Child Adolesc Psychiatry Ment Health* 2021; 15:8
85. Diamond GS, Wintersteen MB, Brown GK, et al: Attachment-based family therapy for adolescents with suicidal ideation: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry* 2010; 49:122–131
86. Diamond GS, Kobak RR, Krauthamer Ewing ES, et al: A randomized controlled trial: attachment-based family and nondirective supportive treatments for youth who are suicidal. *J Am Acad Child Adolesc Psychiatry* 2019; 58:721–731
87. Büscher R, Torok M, Terhorst Y, et al: Internet-based cognitive behavioral therapy to reduce suicidal ideation: a systematic review and meta-analysis. *JAMA Netw Open* 2020; 3:e203933
88. Attridge MD, Morfitt RC, Roseborough DJ, et al: Internet-based cognitive-behavioral therapy for college students with anxiety, depression, social anxiety, or insomnia: four single-group longitudinal studies of archival commercial data and replication of employee user study. *JMIR Form Res* 2020; 4:e17712

89. Melia R, Francis K, Hickey E, et al: Mobile health technology interventions for suicide prevention: systematic review. *JMIR Mhealth Uhealth* 2020; 8:e12516
90. Torok M, Han J, McGillivray L, et al: The effect of a therapeutic smartphone application on suicidal ideation in young adults: findings from a randomized controlled trial in Australia. *PLoS Med* 2022; 19:e1003978
91. Franklin JC, Fox KR, Franklin CR, et al: A brief mobile app reduces nonsuicidal and suicidal self-injury: evidence from three randomized controlled trials. *J Consult Clin Psychol* 2016; 84: 544–557
92. Millner AJ, Coppersmith DDL, Teachman BA, et al: The Brief Death Implicit Association Test: scoring recommendations, reliability, validity, and comparisons with the Death Implicit Association Test. *Psychol Assess* 2018; 30:1356–1366
93. Sohn MN, McMorris CA, Bray S, et al: The death-implicit association test and suicide attempts: a systematic review and meta-analysis of discriminative and prospective utility. *Psychol Med* 2021; 51:1789–1798
94. Stone M, Laughren T, Jones ML, et al: Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US Food and Drug Administration. *BMJ* 2009; 339:b2880
95. Cipriani A, Zhou X, Del Giovane C, et al: Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis. *Lancet* 2016; 388:881–890
96. Bridge JA, Iyengar S, Salary CB, et al: Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. *JAMA* 2007; 297:1683–1696
97. Gusmão R, Quintão S, McDaid D, et al: Antidepressant utilization and suicide in Europe: an ecological multi-national study. *PLoS One* 2013; 8: e66455
98. Gibbons RD, Hur K, Bhaumik DK, et al: The relationship between antidepressant medication use and rate of suicide. *Arch Gen Psychiatry* 2005; 62:165–172
99. Simon GE, Savarino J: Suicide attempts among patients starting depression treatment with medications or psychotherapy. *Am J Psychiatry* 2007; 164:1029–1034
100. Wilkinson ST, Trujillo Diaz D, Rupp ZW, et al: Pharmacological and somatic treatment effects on suicide in adults: a systematic review and meta-analysis. *Depress Anxiety* 2022; 39:100–112
101. Zisook S, Lesser IM, Lebowitz B, et al: Effect of antidepressant medication treatment on suicidal ideation and behavior in a randomized trial: an exploratory report from the Combining Medications to Enhance Depression Outcomes Study. *J Clin Psychiatry* 2011; 72:1322–1332
102. Hawkins EM, Coryell W, Leung S, et al: Effects of somatic treatments on suicidal ideation and completed suicides. *Brain Behav* 2021; 11:e2381
103. McDowell AK, Lineberry TW, Bostwick JM: Practical suicide-risk management for the busy primary care physician. *Mayo Clin Proc* 2011; 86:792–800
104. Hampton T: Depression care effort brings dramatic drop in large HMO population's suicide rate. *JAMA* 2010; 303:1903–1905
105. Coffey MJ, Coffey CE, Ahmedani BK: Suicide in a health maintenance organization population. *JAMA Psychiatry* 2015; 72: 294–296
106. Sakashita T, Oyama H: Suicide prevention interventions and their linkages in multilayered approaches for older adults: a review and comparison. *Front Public Health* 2022; 10:842193
107. Lim JS, Buckley NA, Chitty KM, et al: Association between means restriction of poison and method-specific suicide rates: a systematic review. *JAMA Health Forum* 2021; 2:e213042
108. McCourt AD, Crifasi CK, Stuart EA, et al: Purchaser licensing, point-of-sale background check laws, and firearm homicide and suicide in 4 US states, 1985–2017. *Am J Public Health* 2020; 110: 1546–1552
109. Kivisto AJ, Kivisto KL, Gurnell E, et al: Adolescent suicide, household firearm ownership, and the effects of child access prevention laws. *J Am Acad Child Adolesc Psychiatry* 2021; 60: 1096–1104
110. Brodsky BS, Spruch-Feiner A, Stanley B: The Zero Suicide Model: applying evidence-based suicide prevention practices to clinical care. *Front Psychiatry* 2018; 9:33
111. Labouliere CD, Vasan P, Kramer A, et al: “Zero Suicide”—a model for reducing suicide in United States behavioral healthcare. *Suicidologi* 2018; 23:22–30
112. Fontanella CA, Warner LA, Steelesmith DL, et al: Association of timely outpatient mental health services for youths after psychiatric hospitalization with risk of death by suicide. *JAMA Netw Open* 2020; 3:e2012887
113. Brent DA, Porta G, Rozenman MS, et al: Brief behavioral therapy for pediatric anxiety and depression in primary care: a follow-up. *J Am Acad Child Adolesc Psychiatry* 2020; 59:856–867
114. O'Keefe VM, Fish J, Maudrie TL, et al: Centering indigenous knowledges and worldviews: applying the Indigenist Ecological Systems Model to youth mental health and wellness research and programs. *Int J Environ Res Public Health* 2022; 19:6271