Improving Suicide Prevention Through Evidence-Based Strategies: A Systematic Review

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Objective: The authors sought to identify scalable evidence-based suicide prevention strategies.

Methods: A search of PubMed and Google Scholar identified 20,234 articles published between September 2005 and December 2019, of which 97 were randomized controlled trials with suicidal behavior or ideation as primary outcomes or epidemiological studies of limiting access to lethal means, using educational approaches, and the impact of antidepressant treatment.

Results: Training primary care physicians in depression recognition and treatment prevents suicide. Educating youths on depression and suicidal behavior, as well as active outreach to psychiatric patients after discharge or a suicidal crisis, prevents suicidal behavior. Meta-analyses find that antidepressants prevent suicide attempts, but individual randomized controlled trials appear to be underpowered. Ketamine reduces suicidal ideation in hours but is untested for suicidal behavior prevention. Cognitive-behavioral therapy and dialectical behavior therapy prevent suicidal behavior. Active screening for suicidal ideation or behavior is not proven to be better than just screening for depression. Education of gatekeepers about youth suicidal behavior lacks effectiveness. No randomized trials have been reported for gatekeeper training for prevention of adult suicidal behavior. Algorithm-driven electronic health record screening, Internet-based screening, and smartphone passive monitoring to identify high-risk patients are under-studied. Means restriction, including of firearms, prevents suicide but is sporadically employed in the United States, even though firearms are used in half of all U.S. suicides.

Conclusions: Training general practitioners warrants wider implementation and testing in other nonpsychiatrist physician settings. Active follow-up of patients after discharge or a suicide-related crisis should be routine, and restricting firearm access by at-risk individuals warrants wider use. Combination approaches in health care systems show promise in reducing suicide in several countries, but evaluating the benefit attributable to each component is essential. Further suicide rate reduction requires evaluating newer approaches, such as electronic health record–derived algorithms, Internet-based screening methods, ketamine's potential benefit for preventing attempts, and passive monitoring of acute suicide risk change.

Suicide is the 10th leading cause of death in the United States, with 48,344 suicide deaths in 2018, and it is the second leading cause of death in the 15- to 34-year age range (1). Alarmingly, the age-adjusted suicide rate rose 36.7% between 2000 and 2018 (10.4/100,000 to 14.2/100,00) (2, 3). This situation may be even worse. The 40.7% increase in the unintentional death rate from 2000 to 2017 is almost entirely due to unspecified falls (up 86.5%) and unintentional poisonings (up 98.5%), two causes of death that include misclassified suicides. The first U.S. national suicide prevention plan was proposed in 2000 (4), but from 2000 to 2012, the U.S. slipped from the 72nd to the 31st percentile worldwide in suicide rate (5). In this review we show that the U.S. suicide rate increase relative to the rest of the world has occurred in the context of underutilized proven suicide prevention options.

A critical review of suicide prevention methods is facilitated by an exponential increase in effectiveness data.

The most widely cited review of suicide prevention was published in 2005 (6). From 2005 to 2019, more than four times as many articles on suicide prevention were published compared with the previous 40 years (1966–2005). We reviewed all randomized controlled trials published between 2005 and 2019 that examined suicide, nonfatal suicide attempts, and suicidal ideation. The benefits of reducing access to the most lethal methods used for suicide and the impact of prescribing antidepressants were examined using epidemiological studies, mostly time-series studies, some with contemporaneous geographic controls, identified using the same search engines. We focused on suicidal behavior as an outcome and not suicidal ideation, because there is a closer relationship between nonfatal suicide attempts and suicide deaths than there is between suicidal ideation and suicide deaths (7).

Suicide risk can be understood in terms of a stress-diathesis model (8) (Figure 1) in which stress results

FIGURE 1. Targets and methods of suicide prevention
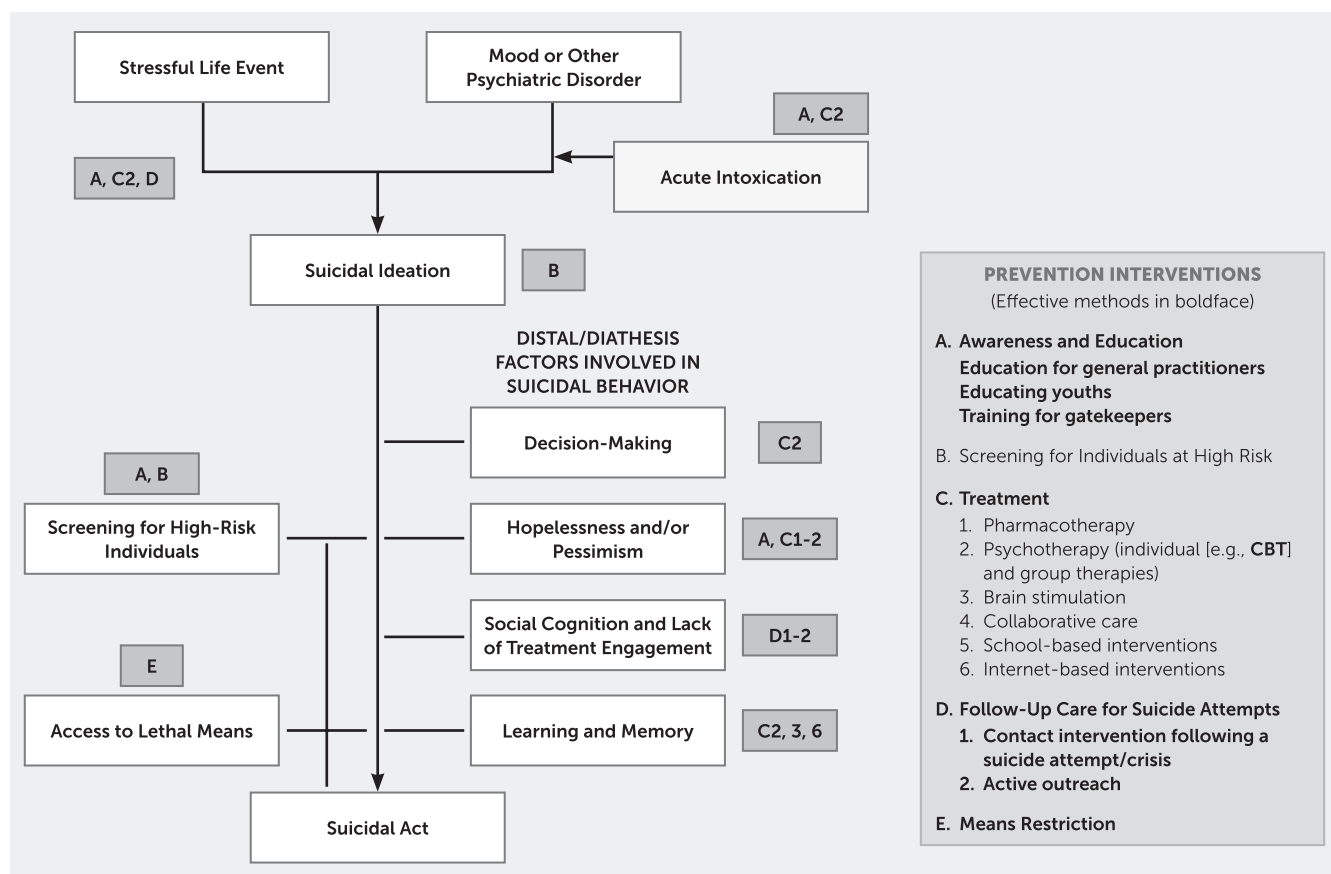
from an internal stressor, usually a psychiatric illness, present in about 90% of all cases of suicide and most commonly major depression, and/or an external stressor involving life events.The diathesis is a combination of heightened perception of emotional distress, a greater propensity for emotion to influence decisions, impaired learning and problem-solving capacity, and distorted social cognition involving a hypersensitivity to negative social signals and diminished sensitivity to positive social signals (8). The diathesis moderates suicide risk, and the risk can be influenced adversely by acute alcohol or drug abuse, via mood or disinhibition (Figure 1). Prevention measures can be aligned with these model components (Figure 1). Each method was judged by two criteria: first, evidence that it prevents suicide attempts and not just suicidal ideation, and second, the possibility that it can be scaled up to city, county, state, and national levels, a requirement for broader suicide prevention.

METHODS

We conducted a literature search in PubMed and Google Scholar for the period 2005 to 2019, in accordance with PRISMA standards for systematic reviews (9). Search identifiers were *suicide, suicide attempt, suicidal behavior,*

and *suicidal ideation* combined separately with each of the following identifiers: *prevention, control, depression, health education, health promotion, public opinion, mass screening, family physicians, medical education, primary health care, antidepressant medications, mood stabilizers, atypical antipsychotics, psychotherapy, schools, adolescents, methods, firearms, overdose, poisoning, gas poisoning, Internet, and mass media.* The search was restricted to articles in English. Randomized controlled trials in which the primary outcome of interest was suicide death, attempted suicide, or suicidal ideation were included because randomized controlled trials provide the strongest evidence of efficacy for a prevention strategy. Because evaluation of restricting access to more lethal methods of suicide, use of electronic health records for screening algorithms, and medication effects on suicide as an outcome require large population studies given the low base rate of suicide, we reviewed epidemiological studies emphasizing time-series designs and studies at the city, county, or general practitioner network level that employed a geographic control or practice control sites. Such studies, together with system-level studies, provide an indication of prevention methods that can be scaled up to a national level (10). These studies were identified using the same search terms and engines as were employed for randomized controlled trials. From the

TABLE 1. Randomized controlled trials of suicidal behavior prevention interventions[a]

Intervention	Studies (N)	Intervention Superior to Control		Intervention Not Superior to Control		Scalability[b]
		N	%	N	%	
General practitioner education[c]	12	10	83	2	17	Yes
Education for youth suicidal behavior (targeting youths for training/education)	3	3	100	0	0	Yes
Education for youth suicidal behavior prevention (targeting adults for training/education)	6	1	17	5	83	Yes
Pharmacotherapy	17	4	24	13	76	Yes
Psychotherapy (CBT, DBT)	18	9	50	9	50	Yes (CBT)
Medication and psychotherapy	3	1	33	2	67	NA
Group psychotherapy	2	1	50	1	50	NA
Contact and/or active outreach	10	7	70	3	30	Yes
Brain stimulation	2	0	0	2	100	NA
Collaborative care	1	1	100	0	0	NA
Firearms restriction[d]	49	48	98	1	2	Yes
Internet based	3	0	0	3	100	NA

[a] Studies were included only if suicide attempts or events or self-injury were outcome measures and not solely suicidal ideation. CBT=cognitive-behavioral therapy; DBT=dialectical behavior therapy.
[b] Scalability was only assessed when findings of efficacy have been replicated.
[c] Contains two randomized controlled trials and 10 quasi-experimental studies.
[d] Contains quasi-experimental and ecological studies.

20,234 articles identified or their bibliographies, 97 randomized controlled trials and 30 epidemiological studies with suicide, attempted suicide, or suicidal ideation as primary outcomes of interest were selected to evaluate prevention strategies (Table 1, Figure 2). Abstracts were reviewed to select studies for inclusion, and methods and results were obtained from the full text. Results are summarized in Table 1 for the main suicide prevention approaches in terms of proportion of positive outcome studies, and where there were replicated positive findings for reducing suicide attempts, we made a judgment as to whether that method is scalable, based on complexity in terms of training and delivery as well as cost in terms of time and personnel. This approach is consistent with what others have recommended (10), as it builds from individual randomized controlled trials, preferably carried out in different localities or countries, in determining whether a prevention method can potentially be deployed more widely.

RESULTS

Education

We examined education directed at health care professionals, students, the general public, or gatekeepers (military, first responders, school staff, clergy, college campus counselors, human resource departments).

General practitioner and nonpsychiatrist physician education. Doctors in primary care and other nonpsychiatric care settings see 45% of future suicide decedents in the 30 days prior to suicide, and 77% within 12 months of suicide (11), about double the rate of mental health professionals. Therefore, educating nonpsychiatrist physicians may prevent more suicides than further training for psychiatrists. Training primary care doctors and nurses at the local and state levels to better screen and treat depression, with supplemental help available from psychiatrists, lowered suicide rates (12–19), nonfatal suicide attempts (20, 21), and suicidal ideation (22) (Table 2). These findings support results from earlier studies (23–25) and studies of self-harm (26). Repeating the education sessions was found to reduce suicide rates progressively for years (12, 21). In contrast, a single-day training session was found to produce no benefit for suicide deaths over 3 years (27). Studies in areas with suicide rates 3–10 times higher than the U.S. rate have shown that screening for depression combined with referral for depression treatment by a primary care doctor or psychiatrist lowered suicide rates relative to a contemporaneous geographic control (12, 15–17). Conversely, a study of 40 primary care medical practices in the Netherlands found that a decline in depression detection rate from 65% to 44% was associated with higher suicide attempt rates in men (28).

Education for youth suicidal behavior prevention. Four of nine prevention studies in youths reported that mental health education resulted in less suicidal behavior (see Table

S1 in the online supplement), and seven of nine studies found less ideation. A key factor appears to be the population targeted for education. Targeting high school students was found to prevent student suicide attempts (29, 30), whereas studies targeting teachers (29) and all but one parent study (see Table S1) did not find benefit. Of the two successful educational programming studies in high schools, the first (29), involving 168 high schools and 11,110 students, randomized high schools to a teacher/staff gatekeeper education program, a professional screening program with referral of identified at-risk students, student education about mental health (the Youth Aware of Mental Health program), or a control group. The Youth Aware of Mental Health program prevented suicidal behavior relative to the control condition, but the screening intervention and the teacher/staff gatekeeper education program did not. In the second study (30), 4,133 high students were randomized to a mental health and suicide education program or to a control condition. Less suicidal behavior was observed in the active intervention group relative to the control group over the following year.

There have been no controlled trials targeting gatekeeper education in adults. Depression-management education of doctors has been shown to lower adult suicide rates (Table 2), but extending the education to other gatekeepers and to the general public is not proven to further reduce nonfatal and fatal suicide attempt rates (31).

System-level education. A system-level approach, involving the application of a combination of education, training, and screening, shows promise in lowering suicide risk. Unfortunately, when such approaches have been implemented, they have not measured the separate effect of each intervention component. One study (32), funded by the 2004 Garrett Lee Smith Memorial Act, examined the impact of interventions directed at young persons (ages 10–24) on suicide rates in 1,126 U.S. counties. The legislation funded a range of intervention, including gatekeeper training (N=125,000) and screening programs to identify at-risk youths (29,000 were screened). Of note, 73% of education recipients were students, and, as suggested by the high school study mentioned above (29), emphasizing student education may have been crucial for gatekeeper education being effective. Education also included mental health professionals and emergency department staff. The intervention counties exhibited a decline in youth suicide rates that did not extend to other causes of death in youths or to adult suicide rates, compared with 969 demographic and sociologically comparable counties where the program was not implemented. These findings indicate that the benefit for suicide was found in the intervention counties and was confined to the demographic group targeted by the intervention. Moreover, this benefit lasted for 2 years beyond the intervention and was proportional to the number of years the program

FIGURE 2. Selection of articles on suicidal behavior prevention for review[a]
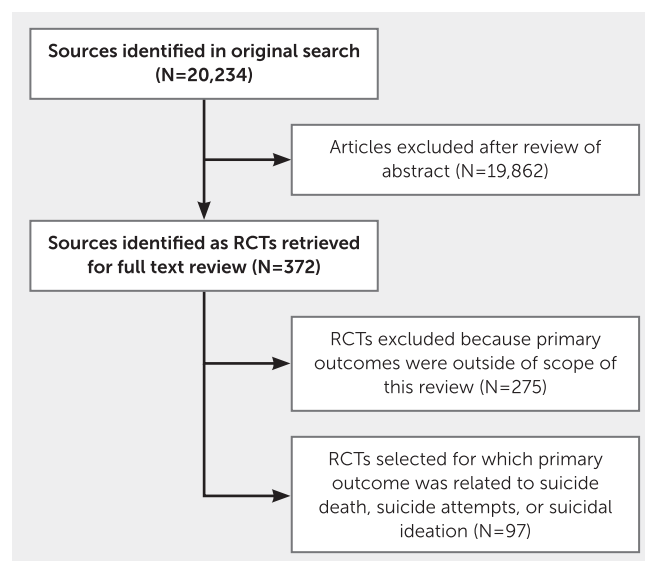
[a] RCT=randomized controlled trial.

ran (32). Follow-up found that the benefit faded once programming stopped, regardless of the number of years it had been operating.

System-wide health care changes have not been tested in a randomized study, but promising results have emerged from opportunistic before-and-after studies (33). One retrospective study in the United Kingdom (34) found benefit for an array of clinical service changes—including improved depression management, continuity of care from adolescent patient services to adult patient services, improved community services, and lower staff turnover—with reduced suicide rates producing incident rate ratios of 0.71–0.79. A decline in suicide rates was temporally and geographically linked to the implementation of the improvements to mental health services between 1997 and 2012. Although the study did not control for changes in the secular suicide rate and there was no randomization of the intervention, interestingly, the poorest or most underresourced districts where interventions were deployed showed the greatest declines in suicide rates (35).

Denmark formerly had one of the highest suicide rates in the world. In 1980, the annual suicide rate was 38/100,000 for persons over age 15. Since 2007, the rate has stabilized at 11.4/100,000. The Danish suicide prevention effort has many components, one of the most important of which was means restriction, but other elements included a 66% increase in psychiatric services since 2000, establishment of suicide prevention clinics, psychiatric emergency outreach teams, and a postdischarge program called Strengthening Outpatient Care After Discharge (36).

A U.S. study examined the effect of staff education and frequent screening of suicide risk in all psychiatric patients in the Henry Ford Health System, which resulted in nine

TABLE 2. Studies of general practitioner and nonpsychiatric physician education for suicidal behavior prevention[a]

Source	Prevention Strategy	Length of Intervention	Population	Study Type	Location	Outcome
Oyama et al., 2005 (15)	Educational intervention for nurse depression screening and GP management	8 years, screening and depression management	Older adults	Quasi-experimental[b]	Japan	Greater reduction in female suicide in intervention region compared with control region (IRR=0.35). No regional difference in male suicides.
Oyama et al., 2006 (17)	Educational intervention for nurse depression screening and GP management	10 years, screening and depression management	Older adults	Quasi-experimental[b]	Japan	Reduction of 64% in female suicide rate in the intervention region (IRR=0.36), but no change in the control region. No change in male suicide rate.
Oyama et al., 2006 (16)	Educational intervention for nurse depression screening and GP management	10 years, screening and depression management	Older adults	Quasi-experimental[b]	Japan	Greater reduction in female suicide rates in intervention region compared with control region (IRR=0.43). No regional differences in male suicides.
Oyama et al., 2006 (14)	Educational intervention for nurse depression screening and GP management	5 years, screening and depression management	Older adults	Quasi-experimental[b]	Japan	Reduction of 74% in female suicide rate in the intervention region (IRR=0.26), significant using a one-tailed test, and no change in the control region. No change in male suicide rate.
Henriksson and Isacsson, 2006 (18)	Yearly 2-day GP training sessions	8 years, GP screening and depression treatment	Adults	Quasi-experimental[b]	Sweden	Preintervention (1970–1994) suicide rate was higher in Jämtland County (Sweden) than nationwide (p<0.05), but during intervention period (1995–2002) it dropped in intervention region, so the two rates no longer differed.
Szanto et al., 2007 (12)	Annual educational program for GPs and their nurses	5 years, GP supervised depression management	Adults	Quasi-experimental[b]	Hungary	Decrease in suicide rate in intervention region greater than the larger county (p<0.001) and Hungary (p<0.001).
Alexopoulos et al., 2009 (22)	GP training and case managers	2 years, algorithm-based treatment advice	Older adults	Randomized controlled trial[c]	United States	Intervention group more likely to receive antidepressants or psychotherapy (p<0.001), and those with major depression had lower rates of suicidal ideation at 4, 8, and 24 months (p=0.04). No difference in suicidal behavior.

continued

TABLE 2., *continued*

Source	Prevention Strategy	Length of Intervention	Population	Study Type	Location	Outcome
Hegerl et al., 2010 (21)	Four-level intervention program including GP education	2 years, GP depression management	Adults	Quasi-experimental[b]	Germany	Intervention region had greater reduction in suicidal acts (suicides and suicide attempts) (p<0.0065) and attempts (p<0.0005) versus control from baseline to 1-year follow-up of the 2-year intervention (2000–2003).The reduction in attempts was more pronounced for high-lethality than low-lethality methods and persisted for 4 years.
Hübner-Liebermann et al., 2010 (19)	Four-level intervention program including GP education in depression management	5 years, GP depression management	Adults	Quasi-experimental[b]	Germany	Suicide rate declined in the intervention region (p=0.02) but not in the control region.
Roškar et al., 2010 (27)	One-day GP educational program	3 years, GP depression management	Adults	Quasi-experimental[d]	Slovenia	Intervention group had greater increase in antidepressant prescriptions (p<0.05) compared with control group, but no group differences in suicide rate.
Almeida et al., 2012 (26)	GP practice audit with feedback on depression and self-harm, educational materials, and control education GP group	2 years, GP depression management	Older adults	Randomized controlled trial[e]	Australia	Intervention group had less self-harm behaviors (odds ratio=0.80, p<0.05) over 2 years.
Hegerl et al., 2019 (20)	Four-level intervention program including GP training, GP consultation hotline	2 years, GP depression treatment	Adults	Quasi-experimental[b]	Germany, Hungary, Ireland, Portugal	In Portugal, the intervention region saw a greater reduction in suicidal acts (suicides and suicide attempts) (p=0.05) and attempts (p=0.02) compared with control region. No group differences found in the other countries.

[a] GP=general practitioner; IRR=incidence rate ratio.

[b] Studies used a control region as a comparison and examined time periods before and after intervention onset. For such community-level intervention studies, no inclusion or exclusion criteria were employed.

[c] Patient inclusion criteria were treatment at one of the 20 primary care practices participating in the study, age at least 60 years, and meeting DSM-IV criteria for major depression or having minor depression (defined as three to four depressive symptoms, a score ≥10 on the 24-item Hamilton Depression Rating Scale, and a duration of at least 1 month); intervention group, N=320; control group, N=279.

[d] The study used physicians who did not attend GP training as a control group for two regions and had one region as an additional control; pre- and postintervention time periods were examined.

[e] General practitioner inclusion criteria included being on a list provided by the Australasian Medical Publishing Company, working at least 2 days per week, having at least 50 patients at least 60 years old who spoke English, and not planning to retire or move practice within the next 2 years; intervention GP group, N=188 (11,402 patients age ≥60); GP control group, N=185 (10,360 patients age ≥60).

consecutive quarters without a suicide, compared with a suicide rate of 80/100,000 in 2000. The program ran from 2001 to 2007, and the rate declined to zero in the period 2008–2010, inspiring the notion of zero suicide as a goal for health care systems. Implementing and sustaining such results is aspirational and is worthy of further evaluation (33).

Screening
Screening for suicide risk to identify otherwise undetected at-risk individuals (30, 37), if coupled with effective referral for evaluation and treatment, was found in some studies to prevent suicidal behavior (15–17, 37, 38). However, other studies did not find screening and referral of at-risk high school students to be effective (29). Brief screening tools such as the P4, which assesses the four p's (past suicide attempt, suicide plan, probability of completing suicide, and preventive factors), and the Columbia-Suicide Severity Rating Scale (C-SSRS), which assesses severity of previous suicidal behavior and current suicidal ideation, may improve triage (37, 39). The 2014 U.S. Preventive Services Task Force report concluded that there is insufficient evidence that screening, specifically for suicide risk in primary care, identifies new cases beyond screening for a psychiatric disorder, distress, or a past suicide attempt (40). The C-SSRS predicted suicide attempts with an odds ratio of 4.8 (95% CI=2.23, 10.32, p<0.001) in adolescents and young adults following an emergency psychiatric evaluation (41). Screening in the U.S. military (42) indicated that current ideation added predictive power to a history of a previous suicide attempt. More complex electronic health record–based screening may improve identification of higher-risk patients (43–47).

Treatment Interventions
Pharmacotherapy. Seventeen pharmacotherapy trials with suicidal behavior as an outcome (see Table S2A in the online supplement), including 12 studies in adults, five pediatric studies, and seven randomized controlled trial meta-analyses (48–54), have appeared since the U.S. Food and Drug Administration (FDA) (51) adopted black box warnings in 2004 and 2006 regarding psychotropic medication–related suicide risk in children and young adults, respectively. Medications reduced suicidal behavior in four of the 12 adult studies (55–58), but those effective medications belonged to pharmacologically diverse classes. More promisingly, antidepressants reduced suicidal ideation in nine of 12 studies that reported effects on suicidal ideation (55, 57, 59–65). Meta-analyses of both randomized controlled trials and pharmacoepidemiological studies often found stronger benefits than single randomized controlled trials, perhaps because they included larger samples. Pharmacoepidemiological studies often involve much larger samples, follow outcomes over a longer time frame, and apply less stringent participant exclusion criteria, resulting in the inclusion of a more clinically representative patient population, including dual-diagnosis patients and patients with more severe presentations. A

meta-analysis of all FDA-registered randomized placebo-controlled studies of fluoxetine and venlafaxine found that these medications decreased suicidal ideation and behavior (49, 52). An FDA meta-analysis found that antidepressants lowered risk of suicidal behavior in older age groups, but subsequent pharmacoepidemiological studies found that selective serotonin reuptake inhibitors (SSRIs) reduced suicidal behavior more broadly, including in young adults (66, 67).

There may be advantages for specific types of antidepressants. SSRIs appeared to be more effective than noradrenergic drugs for suicidal ideation (59, 61). Contrary to earlier FDA findings, SSRIs may work without increasing risk of treatment-emergent suicidal ideation or behavior, even in youths (67–69). Longitudinal pharmacoepidemiological studies in adolescents, young adults, and older adults have found that the greatest risk for a suicide attempt was in the month before antidepressant medication began; after the medication was initiated, the risk declined progressively over months (66, 67, 70). Ketamine, an NMDA glutamate receptor antagonist, has been found to reduce suicidal ideation within 1–4 hours in patients with major depression (71–75) or bipolar disorder (76, 77). One randomized controlled trial found that ketamine, used adjunctively with other psychotropic medications, provided benefit for suicidal ideation that persisted for weeks (72), but its effect on suicidal behavior has never been evaluated. The FDA approved intranasal esketamine for the treatment of depression with suicidal ideation, but not for the treatment of suicidal ideation. A meta-analysis found that intravenous ketamine improved suicidal ideation but that other routes of administration lacked proof of efficacy (78). The intranasal route may be less effective because of more erratic absorption and more side effects than the more slowly administered intravenous route (78).

Two of four randomized controlled trials showed benefit for suicidal behavior with lithium compared with various other medications (55, 58, 79, 80). A meta-analysis of randomized controlled trials in bipolar disorder found no evidence of lithium preventing suicide (81); however, a meta-analysis of nonrandomized studies suggested that the risk of attempts and suicide was five times less with lithium treatment (82). Although one study found no correlation between lithium levels in drinking water and bipolar disorder and many other psychiatric disorders (83), 11 of 16 ecological studies reported that these levels were linked to lower suicide rates (84).

Three randomized controlled trials in adolescents and young adults found that antidepressants reduced suicidal ideation (62, 64, 65), one study did not (85), and none found a reduction in suicidal behavior. A systematic review of antidepressants in pediatric populations found that SSRIs were associated with increased odds of a suicide attempt (53), but most subsequent meta-analyses and epidemiological studies in both pediatric (48, 50) and adult populations (49, 52, 66, 67, 86) reported a more favorable risk-benefit ratio than the

FDA analyses (51, 87), including benefits for suicidal behavior. The FDA meta-analysis of pediatric randomized controlled trials did not find a difference in suicidal behavior between placebo and active drugs (88), and even in the adolescent studies that reported more suicidal events compared with placebo, the number needed to harm (suicide-related event or ideation) was much greater than the number needed to benefit (89).

Psychotherapy. Randomized controlled trials of psychotherapy are summarized in Table S3A in the online supplement. Cognitive-behavioral therapy (CBT) decreases suicidal behavior risk in adults and adolescents with depression and in adults with borderline personality disorder, and it halved suicide reattempt rates in patients presenting to an emergency department after a recent suicide attempt compared with treatment as usual (90). CBT for suicidal individuals is designed to help high-risk individuals apply more effective coping strategies (e.g., cognitive restructuring) in the context of stressors and problems that trigger suicidal behaviors. Therapists also are trained to identify patient-specific factors that promote suicidal behaviors (90, 91). In substance use disorders, CBT has been reported to reduce attempt frequency compared with treatment as usual in adolescents (92) but not in adults (93). CBT may work by improving negative problem orientation and emotion regulation (94), reducing impulsiveness (95), and attenuating suicidal ideation (96).

Dialectical behavior therapy (DBT) for borderline personality disorder in adolescents, college students, and adults prevents suicide attempts and hospitalization for suicidal ideation and lessens medical consequences of self-harm behaviors compared with treatment as usual (see Table S3A in the online supplement). Treatment dose may be a factor because a single session of DBT was not found to reduce suicidal ideation (97), whereas most effective studies employed a 20-week DBT intervention (98, 99).

Psychodynamic psychotherapies for borderline personality disorder have been found to prevent suicidal or self-harm behavior in most controlled studies (see Table S3A). There are no replicated studies of other types of psychotherapeutic interventions showing prevention of suicidal behavior. Even if psychotherapies were effective, only CBT appears to be scalable (Table 2).

Comparison of pharmacotherapy and psychotherapy. Despite efficacy evidence for pharmacotherapy and psychotherapy separately, combinations of both showed no advantage for suicidal behavior (see Table S3B in the online supplement).

Group psychotherapy. Group psychotherapies reduced suicidal ideation in five of 10 studies (100–109) and suicide in one (100), but none of the studies reported reductions in nonfatal suicide attempts (see Table S3C in the online supplement). Cost-effectiveness and potential for scaling are moot without replicated efficacy for suicidal behavior.

Contact and/or active outreach following a suicide attempt or suicidal ideation crisis. The period of greatest risk of suicidal behavior is after discharge from the emergency department or from an inpatient hospital unit (110–112). Eighty percent of suicide deaths following a nonfatal suicide attempt happen within 1 year. Follow-up contact interventions as simple as sending postcards prevented suicide attempt in two of four studies (see Table S4 in the online supplement), consistent with earlier studies that found a robust benefit for reducing suicidal behaviors (110). Enhancing treatment engagement and adherence after an emergency department visit or hospital stay through follow-up contact calls reduced attempts or ideation in four of five studies (see Table S4). These interventions are scalable, as shown by a multinational study reporting that psychoeducation paired with telephone or in-person contact reduced the suicide rate over 18 months among suicide attempters (113). Another study used a similar approach by sending caring text messages over 1 year to active military personnel who had reported a suicide attempt (half the sample) or suicidal ideation, but not in the context of discharge from the hospital or emergency department. The intervention lowered subsequent suicide attempts by almost half (114). A cohort comparison study of safety planning interventions, administered in the emergency department with follow-up telephone contact, produced a 45% reduction in suicidal behaviors compared with treatment as usual (115).

Brain stimulation. Repetitive transcranial magnetic stimulation and electroconvulsive therapy have been reported to reduce suicidal ideation, but the study samples were too small for evaluation of effects on suicide attempts (see Table S2B in the online supplement). Deep brain stimulation has also not been shown to prevent suicide attempts (see Table S2B).

Collaborative care. Collaborative care involves embedding psychiatric expertise within a primary care setting, army units, and schools to enhance mental health care. This approach was found to benefit suicidal ideation, but mostly it did not prevent suicidal behavior. The exceptions are a collaborative care program involving lay health workers in both primary and private care settings (116) and depression screening studies in which psychiatrists oversaw the antidepressant treatment, resulting in reduced suicide rates in both men and women (Table 2). By contrast, when general practitioners delivered this treatment, it was found to work in women but not in men (Table 2).

Internet-based interventions. Internet-based interventions have not been shown to prevent suicidal behavior (see Table S5 in the online supplement) but are highly scalable. Only three of 10 studies reported benefit for suicidal ideation (117–123). Internet-based interventions can reach most untreated at-risk individuals and provide low-cost screening,

psychoeducation, and web-based psychotherapeutic treatment interventions. A Dutch study found that adolescents disclosed comparable information about their mental health via web-based and paper-and-pencil screening forms (123). Online interventions have been found to increase suicide-prevention-related knowledge (124), but not all improved suicide literacy or reduced suicide stigma (122). Internet CBT, with or without telephone follow-up, was not more effective compared with waiting list control conditions for reducing suicidal ideation (121, 125). A game-like mobile app showed promise in reducing self-injury and suicide plans, but not suicidal ideation (126).

Means Restriction

Restricting access to the most available and lethal means for suicide, such as firearms, has been found to lower suicide rates (127–137). Pesticide ingestion was employed in approximately one-third of suicides worldwide, mostly in rural Asia and Latin America (138). Centralized locked or guarded storage facilities combined with use of less toxic chemicals have contributed to a worldwide decline in pesticide suicides (129). Restricting access to pesticides in Sri Lanka reduced pesticide-related suicide rates without a concurrent increase in non-pesticide-related suicide deaths (139). Firearm suicide rate is closely related to firearm ownership rate (140). Firearms are used in half of all U.S. suicides (130, 131). Gun access restriction and gun safety education programs reduced firearm suicides, with only modest method substitution (127, 132–135). Firearm buyback programs have reduced firearm-related suicides (141), but legal precedents and public opinion can undermine gun control and buyback programs and have prevented the United States from emulating the reduction in firearm suicides seen in other countries. Improved gun safety through education is more feasible than reducing gun ownership in the United States because of legal impediments to national gun control, and most guns used for suicide were purchased years before the suicide (132). Other proven means restriction approaches include better catalytic converters in automotive exhaust systems that reduce carbon monoxide content (136, 142), switching from coal gas to natural gas, which has a low carbon monoxide content (128), and barriers at suicide hot spots such as bridges and railway stations (137).

DISCUSSION

Applying the criteria of replicated efficacy for preventing suicidal behavior and scalability (Table 1) means that the best options for suicide prevention and for extending these approaches are 1) educating primary care physicians in depression management and evaluating the expansion of such programs to other nonpsychiatric medical specialists, such as internists and obstetrician-gynecologists; 2) educating high school students about mental health and evaluating extension of this approach to college students; 3) means restriction; and 4) predischarge education and follow-up

contact and outreach for psychiatric patients discharged from the emergency department or hospital and for patients after a suicide crisis. Effective but less scalable options include specific psychotherapies (CBT, DBT). Finally, unproven options that are scalable and promising include fast-acting medications such as ketamine and Internet-based screening and treatment delivery and continuous passive monitoring of risk.

Educating nonpsychiatrist primary care physicians to better diagnose and treat major depression prevents suicide and nonfatal suicide attempts (Table 2). Several related observations explain why. Approximately 90% of suicide decedents had a current diagnosable psychiatric disorder, most commonly major depression, that was untreated at time of death (111, 143, 144). Suicidal ideation is common. In 2015, 9.8 million persons (4% of all persons age 18 and older) in the United States had serious thoughts about attempting suicide, and yet more than half had received no mental health services in the previous year. The result: 1.47 million persons (0.6% of all persons age 18 and older) made a suicide attempt (145). Despite a large increase in antidepressant prescription rates (49, 52, 59, 66, 86, 146), when suicide decedents seek help, they tend to go to nonpsychiatrist physicians and end up untreated for their depression.

The debate about the safety of antidepressant treatment in adolescents and young adults needs to be informed by the 17 randomized controlled trials (see Table S2A in the online supplement) as well as meta-analytic and pharmacoepidemiological studies (48–50, 52–54, 66, 67, 86) published since the FDA issued black box warnings for many classes of psychotropic medications. Both pediatric and adult studies of antidepressant effects on suicidal behavior show reductions in suicidal behavior in meta-analyses, more robustly than in individual randomized controlled trials, probably because the low base rate of suicide attempts requires larger sample sizes. Ketamine reduces suicidal ideation within 1–4 hours, instead of weeks like other antidepressants, in major depression (71–73) and bipolar disorder (76, 77). Rapid, robust reduction of suicidal ideation may dramatically increase patient safety, but ketamine's effect on suicidal behavior is unknown and is therefore a priority for suicide prevention research. More information is needed on the relative efficacy of intranasal and intravenous ketamine.

Educating other gatekeepers about the signs of suicide risk and the need to refer patients for help raises questions about whom to focus on for the best results (see Table S1 in the online supplement). Two studies in high schools found that pupil education prevented suicide attempts (29, 30), with one finding it more effective than teacher/gatekeeper training and that the latter was no better than the control arm of the study (29). In the absence of data from randomized controlled trials on whether training adult gatekeepers prevents adult suicidal behavior, it is unknown whether colleges, universities, military, and police should try to educate everyone in their system or just focus on their student body or workforce.

Screening for suicidal ideation in school, college, military, and medical clinic populations seeks to identify otherwise undetected at-risk individuals. Although it does not induce subsequent suicidal ideation (38, 147), screening a non-help-seeking population for suicidal ideation and nonfatal suicide attempts, beyond screening for major depression, remains a debated approach (40). Newer promising approaches may involve using smartphone technology to detect risk (148, 149) and algorithm-guided electronic health record screening (43, 44, 46, 150).

CBT, DBT, and individual psychodynamic psychotherapies prevent suicide attempts, but aside from CBT, scalability limits their value in suicide prevention. Combining medication with individual psychotherapy does not offer any measurable advantage. No brain stimulation therapies have demonstrated suicidal behavior prevention. Sleep disturbance (151) and effects on mood and decision making by acute alcohol intake (152) are risk factors for suicidal behavior that warrant further evaluation as potential prevention targets.

The period of greatest risk for repeating a suicide attempt is in the month or year following an index attempt, and particularly after discharge from a psychiatric visit to an emergency department or a stay in an inpatient hospital unit (110–112).Predischarge education and assertive outreach after discharge or a suicide-related crisis prevent suicide attempts (Table 2; see also Table S1 in the online supplement). Surprisingly, this approach has not been widely adopted in the United States, which may reflect gaps in continuity of care between inpatient and outpatient systems and between emergency departments and outpatient care. Calibrating suicide prevention efforts to times of greater risk as well as to patients showing higher risk clinical profiles would be more efficient and potentially effective.

The Internet has great potential for suicide prevention by screening, education, outreach, referral, and monitoring of ongoing risk and treatment, but applications are new, and testing of their efficacy is still in progress (120–122, 153). Internet-based interventions are economical and scalable, reaching untreated at-risk individuals and offering help to anyone with a telephone and Wi-Fi access. Passive monitoring via a smartphone is an inexpensive but untested method for tracking risk.

Most suicide attempt survivors do not ultimately die by suicide, which is why means restriction, which targets the most lethal methods, saves many lives (154, 155). Surprisingly, faced with no access to their chosen method, most individuals do not turn to alternative means for suicide, as shown for coal and gas (156) and firearm restriction (127). Means restriction needs to target the main means used in a given region. Firearms are used in half of all suicides in the United States (1), yet restricting access of at-risk individuals to firearms is underutilized in this country (132). Gun buyback programs have worked in other countries (141), but safer gun storage education and state-regulated requirements may be more effective in the United States because

most firearms used for suicide were purchased years earlier (157). Pesticides are highly lethal and are the leading suicide method worldwide, and the decline in suicide deaths worldwide is largely due to restriction of access to pesticides where those deaths occur most, namely, in rural China (138, 158), India (129), and Sri Lanka (159).

The major limitation of this review is the uneven quality and quantity of data available for different suicide prevention strategies. Within strategies, there is heterogeneity of study populations in terms of psychiatric illness, proportion of higher-risk patients (such as those with a history of a past suicide attempt), age, ethnicity, and proportion of males (because males have 3–4 times the suicide rate of females). Higher-risk groups (e.g., Native Americans, First Nations), demographic groups such as children and the elderly, and psychiatric disorders such as schizophrenia, eating disorders, and substance use disorders are understudied. Small sample sizes, too few studies, and lack of replication studies diminish the ability to draw firm conclusions about many approaches. Suicidal ideation is an unsatisfactory alternative outcome measure because it is not as closely related to suicide deaths as nonfatal suicide attempts. Evaluating complex interventions with multiple components makes it hard to determine the effective elements. Finally, there is a need for objective criteria for determining which interventions are capable of being scaled up from local studies to national-level deployment.

CONCLUSIONS

Education of primary care physicians, and potentially of internists and obstetrician-gynecologists, in the diagnosis and treatment of depression is a robust suicide prevention approach. Other proven scalable strategies (Table 1) are 1) follow-up of discharged and other acutely suicidal patients with active outreach, 2) treatment with CBT, and 3) implementation of means restriction. Education directed at youths prevents suicidal behavior, but education directed at teachers does not; no randomized controlled trial data are available for prevention of adult suicide by educational programming. Any prevention program requires outcome assessment that must include suicidal behavior, and preferably also mediating effects such as help-seeking behavior, treatment provision, and treatment adherence. The biggest challenge in suicide prevention lies in improving the identification of who is at high risk and when. Determination of imminent risk is needed for calibration of prevention efforts to high-risk periods by employment of rapid reduction of suicidal ideation and means restriction. Fast-acting medications like ketamine may have a role during acute suicide risk but are untested for prevention of suicide attempts. Determination of imminent risk has evolved toward continuous monitoring via mobile devices (148, 149). Further research is needed to evaluate such approaches and how to integrate them into prevention responses.

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