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What physicians can do to prevent suicide

■ ABSTRACT

Many people who attempt suicide or succeed at it visit their physicians shortly before the act; thus, primary care physicians have a key role in preventing suicide. The first step is to suspect that the patient might be at risk, and the second step is to ask about it. Nevertheless, one cannot predict whether any particular person will or will not attempt suicide.

■ KEY POINTS

The most likely person to commit suicide is a white man older than age 85; in this population the rate is 59 per 100,000 persons.

Standardized psychological rating scales cannot accurately predict suicide in individual cases, nor should the results from a screening tool be used to dictate a course of action, such as admission to or discharge from the hospital.

Depression is not the only clinical condition that leads to suicide, and the failure to diagnose depression associated with bipolar disorder instead of unipolar major depression can lead to disastrous outcomes.

Clozapine carries a specific indication for preventing suicide in patients with schizophrenia; lithium reduces the risk of suicide in patients with bipolar disorder.

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This paper discusses therapies that are experimental or are not approved by the US Food and Drug Administration for the use under discussion.

"There is but one truly serious philosophical problem, and that is suicide. Judging whether life is or is not worth living amounts to answering the fundamental question of philosophy."

Albert Camus

DESPITE OUR BEST EFFORTS, no one can say with certainty that any given patient will or will not attempt suicide.¹ We should, however, notice when a patient *might* be at risk—and not be afraid to ask whether he or she is thinking about it.

Of utmost importance is the physician's ability to recognize that the patient is suffering and not allow him or her to be alone to ponder Camus' "philosophical problem" of whether or not life is worth living. It is only at that point that meaningful intervention may begin.

This article explores the epidemiology, neurobiology, and risk factors for suicide, and what primary care physicians can do to prevent it.

■ A NATIONAL HEALTH PROBLEM

Suicide, the 11th leading cause of death in the United States, takes the lives of more than 30,000 Americans every year. The US age-adjusted suicide rate has held fairly steady over decades, with only a slight decrease from 11.5 suicides per 100,000 persons in 1981 to 10.7 in 2000.²

That this figure has remained relatively unchanged is bad enough, since the treatment of psychiatric disorders has advanced markedly in the last quarter century. Worse, the suicide rate has actually increased in some groups such as adolescents and the elderly, leading the US Surgeon General in 1999 to declare suicide a national public health problem.³

**TABLE 1**

Suicide risk factors

Demographic variables

Male
Widowed, divorced, or separated
Age > 45 years
Living alone
White
No children or children older than 18 years
Imprisoned
Rural

Psychosocial variables

Lack or loss of social supports
Recent loss of employment
Decrease in socioeconomic status or poverty
Psychologic turmoil
Aggressive or impulsive traits
History of victimization
Gun ownership
"Imitation" suicide (Werther effect)
Severe relationship conflict
Hopelessness
Occupational risk (physicians, dentists, nurses, pharmacists, veterinarians, farmers)
Writing suicide notes
Substance abuse
Family history of suicide
Previous attempts

Psychiatric conditions

Psychiatric diagnosis of recent onset
Mood disorder, particularly major depression and bipolar disorder
Schizophrenia
Alcohol or other substance abuse or addiction
Personality disorder
Panic attacks or severe psychic anxiety
Insomnia
Poor concentration or confusion
Anhedonia

Medical disorders

Huntington disease
Stroke
Multiple sclerosis
Epilepsy
Head injury
Malignant neoplasms
Systemic lupus erythematosus
Peptic ulcer disease
Spinal cord injuries
Renal disease
Acquired immunodeficiency syndrome
History of head injury
Pain

About 50% of persons who commit suicide saw a health care provider within 1 month before the act

PHYSICIANS HAVE A KEY ROLE

Primary care physicians have a key role in preventing suicide, as they have the most encounters with potentially suicidal patients and therefore the most opportunity to intervene. For example:

- At least half of all patients who receive mental health care obtain it from their primary care physician.⁴
- The suicide rate in patients recently discharged from the general hospital is three times higher than that of the general population, at 32 per 100,000 patient-years.⁵
- Many people who either attempt suicide or succeed at it visit their physicians shortly before the act. An estimated 50% of suicide victims had some interaction with a health care provider within 1 month of the act. Of elderly people who commit suicide, 75% visit a physician in the month before.

WHO ATTEMPTS SUICIDE?

There are a variety of factors and conditions reported to increase the risk of suicide, including demographic variables (such as being male, living alone), psychosocial variables (gun ownership, loss of social support), psychiatric conditions (substance abuse, schizophrenia), and medical disorders (stroke, epilepsy). For a full list, see **TABLE 1**. None is pathognomonic, however. Human suffering appears to be the most common unifying variable among suicide victims, and physicians should try to be alert for it and do something about it, so far as we can.

Demographic variables

Gender. Women are three times more likely to attempt suicide than men. Yet four times as many men as women die of suicide. In general, men choose more-lethal methods of

suicide, such as with a gun, which increases the likelihood of completing suicide.

Age. More than half of people who die of suicide are men between the ages of 25 and 65. It is the third leading cause of death for persons ages 15 to 24, behind only accidents and homicide (homicide ranks 14th). Yet the most likely person to commit suicide is a white man older than age 85, in whom the rate is 59 per 100,000 persons.

In young people who attempted suicide, the Centers for Disease Control and Prevention found the following five risk factors⁶:

- Consumption of alcohol within 3 hours of the attempt
- Change of residence within the last 12 months
- Decision to commit suicide within 5 minutes of the attempt
- Young males with a medical condition (four times higher risk)
- Sought help from family and peers rather than from professionals.

Geographic region. According to the American Association of Suicidology (www.suicidology.org), the suicide rate in western mountain states and rural areas exceeds that of the rest of the nation. The rate is highest in Alaska (22.0 per 100,000 persons) and lowest in Washington, DC (4.4 per 100,000).

Psychosocial variables

History of suicide attempts. People who attempt suicide are more likely to try again; however, more than two thirds of people who die by suicide succeed on their first attempt.⁷

Culture and ethnicity. Although the suicide rate may vary from country to country and culture to culture, the risk factors for suicide are likely universal. A 1999 case-control study in India found widespread suicide risk factors such as major psychiatric disorders, a family history of psychiatric disease, and recent life events.⁸ A case-control study in the United Kingdom noted that suicide victims were more likely to have had contact with medical services in the week and month before their deaths.⁹

Therefore, although the influence of culture and ethnicity on suicide should not be ignored, it does not promote or prohibit indi-

vidual suicides, particularly in the context of human suffering.

Gun ownership. Firearms were the most common method for both men and women, accounting for 57% of all suicides.

Psychiatric conditions

More than 90% of people who commit suicide are judged to have had a psychiatric disorder at the time of suicide, as ascertained retrospectively.⁷

Medical disorders

Physical illnesses that cause great pain, disfigurement, limited function, or fear of dependence may take away a person's will to live and increase the risk of suicide.^{7,10,11} Often these medical disorders coexist with psychiatric disorders, making the determination of independent risk more difficult.

Epilepsy in particular carries a fourfold increase in suicide.¹² In children and adolescents, it is the only medical diagnosis in which an increase in suicide has been documented (TABLE 1).¹³

Factors to assess emergent risk

Hall et al¹⁴ described 100 patients who made severe suicide attempts and concluded that the most useful factors in assessing suicide risk in the emergency department or hospital ward were:

- Living alone
- Age 17 to 35
- Complaints of severe hopelessness, anhedonia, and sleep disorder.

■ SUICIDE IS HARD TO PREDICT

In spite of the many known risk factors for suicide, it is very difficult to predict whether an individual patient will attempt it.

Using a method to predict suicide based on 21 risk factors, Pokorny¹⁵ examined 4,800 patients at a Veterans Administration hospital. Suicide was predicted to be of high likelihood in 803 patients, but only 30 (3.7%) of the 803 actually committed suicide during a 5-year follow-up. Furthermore, 37 suicides occurred that were not predicted, so there were more false-negative predictions than true-positive predictions.

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■ TOWARD A NEUROBIOLOGY OF SUICIDE

A disorder of serotonin?

In a review of studies that looked at serotonin function, depressed patients who attempted suicide had lower levels of the major metabolite of serotonin (5-hydroxyindoleacetic acid, 5-HIAA) in their cerebrospinal fluid compared with patients who did not attempt suicide.¹⁷ Patients who made more-lethal attempts (eg, by shooting themselves, hanging, or jumping from a high place) had lower 5-HIAA levels than those who made less-lethal attempts (eg, by taking an overdose of drugs or cutting their wrists).¹⁸

Postmortem examinations of suicide victims reveal anatomic and chemical alterations in two brain regions: the orbital prefrontal cortex (an area associated with behavioral inhibition) and the dorsal raphe nucleus of the brain stem.^{19,20} The dorsal raphe nucleus produces serotonin, which is projected to the orbital prefrontal cortex.

These changes are evidence that the brains of suicide victims are less able to make and use serotonin, a key neurotransmitter known to be lacking in the brains of impulsive people and in those with depression. Furthermore, serotonin receptors are altered in the brains of suicide victims, and an increase in the number of serotonin type 1A postsynaptic receptors has been reported.^{21,22}

Could decreased serotonergic transmission to the prefrontal cortex be the common denominator in the gamut of conditions in which suicide risk is heightened? The ventral prefrontal cortex may act as a behavioral regulatory center that does not function correctly in suicidal patients, resulting in greater difficulty resisting powerful impulses or feelings, such as suicidal ideation or anger. This biochemical finding seems to be independent of psychiatric diagnosis, and is found in suicide victims with major depression and other psychiatric conditions such as schizophrenia.²³

Fenfluramine challenge: A test of serotonin function

Another way to measure serotonin function is to measure the serum prolactin level after giving a dose of fenfluramine, which stimulates prolactin release via serotonergic pathways. People who are depressed and who attempted suicide have low prolactin levels after fenfluramine challenge, and people who made serious (“high-lethality”) suicide attempts have lower levels than people who made less-lethal attempts.²⁴ This suggests that hypoactivity in the serotonergic pathways is associated with depression and increasing risk of suicide, particularly by more-lethal methods.

Can PET scans reveal suicide risk?

Yet another way to measure serotonin function is with positron emission tomography (PET).

Raine et al²⁵ found significantly lower rates of resting glucose metabolism in the prefrontal cortical areas of murderers than in nonmurderers on PET scanning. Violent acts, such as murder and suicide, may share a common biologic tendency for serotonin deficiency.

Oquendo et al²⁶ obtained PET scans of the brain after fenfluramine challenge in depressed patients who had attempted suicide by either highly lethal or less-lethal means. They concluded that “prefrontal localized hypofunction and impaired serotonergic response are proportional to the lethality of the suicide attempt and may mediate the effects of suicide intent and impulsiveness on lethality.”

Further studies may determine the utility of PET scans in detecting suicidal risk in living patients on the basis of abnormal ventral prefrontal cortical activity or response to fenfluramine.

Low cholesterol levels?

Low cholesterol levels have been associated with higher suicide rates in some reports. A study of 6,393 French men found that the risk of suicide was more than three times higher (age-adjusted relative risk 3.28) in those with cholesterol concentrations lower than 185 mg/dL (4.78 mmol/L).²⁷ Studies have documented lower brain serotonin activity in ani-

**Low serotonin,
not cholesterol,
may predict
suicide risk**

TABLE 2

Questions that explore suicidal thinking

Have you felt so sad or depressed that you have thought life is not worth living?

Have you thought about hurting yourself or even taking your own life?

Have you thought about a way or plan to kill yourself?

Do you have the means to complete the plan? (eg, do you have access to weapons or pills?)

What has stopped you from following through with the plan?

Have you ever attempted suicide?

Has anyone in your family ever attempted or committed suicide?

mals with low cholesterol levels, although this effect has yet to be shown in humans.²⁸

Since the effect of the cholesterol level on the risk of suicide is not definitively known, it likely offers little use as a predictive variable.

Is there a genetic component?

Psychiatric patients have a higher risk of suicidal behavior if they have a family history of suicide.²⁹ Studies have shown a higher concordance rate for completed and attempted suicides in monozygotic vs dizygotic twins.^{29,30} Familial transmission studies further indicate that suicidal behavior might be transmitted independently of psychiatric disease.^{29,31}

If suicidal behavior is inherited, multiple genes are probably involved.³² Nielsen et al³³ reported an association between suicidal behavior and the L allele on the short arm of chromosome 11, which is associated with production of a less-active variant of tryptophan hydroxylase, an enzyme involved in serotonin synthesis.

■ A STEPWISE APPROACH

Jacobs et al³⁴ propose a stepwise approach to the clinical problem of suicide.

Suspect that a patient might be at risk

The first step is to suspect that a patient might be at risk of suicide. Recall that many factors can predispose to suicide, including many psychiatric and medical conditions (TABLE 1).

Particular attention should be focused on the major psychiatric syndromes of depression, manic-depression (bipolar disorder),

schizophrenia, substance abuse, and personality disorders, given the strong association between these disorders and suicide.

Specific risk factors may exist for each of the diagnoses mentioned above. For example, in both depression and bipolar disorder, patients are more likely to attempt suicide early in the course of the illness, often before it is diagnosed or effective treatment is offered. The recovery period and the immediate postdischarge period are also times of heightened risk.

Ask about it

If you suspect that a patient is at risk, gently ask about suicidal thoughts, plans, and behaviors (TABLE 2). Asking allows the patient to discuss his or her feelings and helps you think about what to do next: the clinician gains the opportunity to explore the extent and seriousness of the suicidal thoughts and associated risk factors or conditions, such as depression.

The highest risk is with suicidal thoughts accompanied by a specific, lethal method with few identified deterrents. Nonsuicidal thoughts of death carry a lower risk.

Patients who reveal passive suicidal ideation (eg, "I sometimes wish I would just die in my sleep") and significant deterrents to action (eg, "My children need me" or "It's against my religion") should be referred for psychiatric consultation. Those without deterrents or who discuss active and imminent thoughts and recent actions, such as writing suicide notes, purchasing a weapon, or stockpiling pills, should be emergently evaluated for psychiatric admission.

**Don't worry
that asking
patients about
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to try it**



Don't worry that asking your patients about suicide will give them the idea to try it. Patients are often relieved to open a direct and concerned dialogue about suicide. Patients who seek help from a physician want to feel that there is hope for them to feel better. Patients with suicidal thoughts are almost always ambivalent about suicide to some extent—conflicted by simultaneous desires to live and to die—and the clinician can intervene by allying with that part of the patient that wants to live. Creation of this therapeutic connection with the patient will assist in the next step.

Merely asking about suicidal thoughts and accepting negative replies does not constitute a thorough assessment of suicide risk, however. Despite our relative inability to predict an individual suicide, it is invaluable to go through the process of attempting to evaluate an individual patient's risk for suicide through direct questioning of suicidal thinking, review of risk factors, or clinical rating scales.

In the general practitioner's office or emergency department, the risk assessment process helps to inform the physician as to the next appropriate course of action (discharge home, medication, psychiatric referral, consultation, hospitalization). The purpose of a suicide assessment is to better understand the reasons for the suicidality and allow for a more informed intervention, not to predict suicide.

Determine the level of intervention required

To determine the appropriate level of intervention, one needs to understand the basis for the suicidality and to estimate its acuteness or chronicity.

Suicidality that is judged to be related to axis I psychiatric disorders (ie, major depression, bipolar disorder, schizophrenia) tends to be more acute, with prominent feelings of anguish, pain, and a wish to escape. Patients may describe a more driven quality to the suicidality, which mandates a treatment plan that includes an attempt to keep the patient safe until the suicidal feelings remit. Hospitalization is often needed as well as focused treatments such as medication, psychotherapy, or electroconvulsive therapy.

In patients with suicidal thoughts related to personality disorders and environmental factors, suicide risk tends to be more chronic and has an impulsive quality. Personality-disordered patients may report more feelings of anger, rage, or vengeance associated with their suicidal thoughts. Hospitalization may become necessary, although repeated or multiple hospitalizations may be countertherapeutic. Instead, attempts should be made to teach the patient to work within therapy to keep himself or herself safe using psychiatric or psychological consultation, limit-setting, and behavioral techniques.

To effectively manage suicide risk, the clinician must maintain a therapeutic connection with the patient, and the patient has to be able to understand and follow the agreed-upon safety plan and treatment.

Document the assessment and treatment plan

Documenting the assessment and decision-making process helps one to clarify the treatment plan and to communicate better with other care givers. A brief, timely summary is also suggested for medicolegal risk management; it should be legible and communicate the estimated degree of risk, known data, diagnosis, and planned interventions (medications, tests, consultations, follow-up reassessments planned).

■ IN A CRISIS

A clinician who has a potentially suicidal patient in the office should perform a careful suicide risk assessment as outlined above. If the patient does not cooperate with the assessment or if the clinician believes that the patient is at imminent risk, then the patient should be referred for immediate psychiatric hospitalization. In fact, the physician has an obligation to hospitalize any patient thought to pose an imminent danger to self or others due to mental illness, even if the patient or family objects to it at the time.

Patients reporting suicidal ideation to their physicians by telephone should be reported to the local authorities immediately so that they may be brought to the nearest emergency department for assessment.

**National suicide
hotline:
1-800-SUICIDE**

Most communities have 24-hour suicide prevention hotlines. The National Hotline crisis number is 1-800-SUICIDE, and it will refer patients to local resources. Various Internet resources include www.yellowribbon.org and www.mentalhealth.org, which offer services and advice for patients, families, and providers.

■ DRUG THERAPY

In theory, recognizing suicide risk will lead to suicide prevention. In practice, the idea is to promptly identify and treat mental disorders that are associated with an increased risk of suicide.

One should always consider immediate drug therapy and possibly psychiatric hospitalization if the patient is experiencing emotional suffering due to command hallucinations (ie, voices telling the patient to kill himself), paranoid delusions, severe or psychotic depression, acute agitation or panic, mood swings, or manic episodes.

Appropriate antipsychotic medications or benzodiazepines may eliminate psychotic symptoms and thus may reduce the risk of suicide by reducing anxiety.³⁵ Relief of depression with antidepressant medications can have considerable impact on a patient's outlook on life, supporting the part of himself or herself that wants to live but is clouded by melancholia.

Expect good days and bad days

It is of utmost importance to discuss the risks and benefits of all medications with patients and their families, and particularly to outline the possible course of improvement. Even if the patient responds to medications, recovery is often not smooth or predictable. For example, patients recovering from a depressive episode may continue to have "bad days" interspersed with "good days."

The feeling of slipping back into depression after improving somewhat can be deflating to many patients and may invoke a sense of hopelessness or suicidal thinking again. Early in treatment, some patients may continue to feel depressed but may have more energy or initiative, and the combination may make them more likely to act on suicidal

thoughts or plans. Educating patients and their families about the potentially rocky course of recovery may significantly reduce the risk of suicide.

In addition to a disease-specific benefit, some agents may possess direct antisuicidal effects independent of the disorder being treated. Most evidence in this area supports the roles of clozapine and lithium in preventing suicide.

Clozapine

The US Food and Drug Administration recently approved an indication for clozapine (Clozaril) specifically for preventing suicide in patients with schizophrenia. This drug had previously demonstrated efficacy in controlling psychosis and stabilizing mood in patients with severe mental illness (schizophrenia and bipolar disorder).

Early retrospective studies reported that patients with schizophrenic or schizoaffective disorders were less likely to commit suicide if they were receiving clozapine.^{36,37}

In a 2-year prospective controlled study, 980 patients treated for schizophrenia or schizoaffective disorder at high risk for suicide due to past suicidal behavior received either clozapine or olanzapine, a newer antipsychotic medication. At 2 years, the incidence of suicide attempts and hospitalizations to prevent suicide was 26% lower in the clozapine group than in the olanzapine group.³⁸

Although the protective effects of clozapine against suicide were independent of effects on psychotic symptoms, additional study is needed to determine whether this preventive effect exists for suicidal patients treated with clozapine for other disorders.

Mechanism of action. It is not known how clozapine exerts its antisuicidal effects. Interestingly, clozapine has prominent anti-serotonin activity, particularly at 5-HT_{2A} receptors, suggesting that other mechanisms are involved. This contrasts with most observations that have suggested that low serotonin levels can predispose to suicidal behavior.

Side effects. Clozapine use has been associated with a 1% to 2% incidence of agranulocytosis, which requires white blood cell monitoring every week for the first 6 months of treatment and every 2 weeks thereafter.

**Hospitalize
any patient
at imminent
danger due to
mental illness**



A dose-related increased risk for seizure exists with clozapine, from 1% at doses below 300 mg/day to 5% at doses above 600 mg/day.

Other serious potential side effects include myocarditis and orthostatic hypotension.³⁹

Lithium

Bipolar disorder poses a high risk of suicide; an estimated 25% to 50% of bipolar patients attempt suicide at least once.⁴⁰

Lithium has consistently been reported to reduce the risk of suicide in patients with bipolar disorder. Tondo et al⁴¹ performed a meta-analysis of 22 studies with a total of 5,647 patients and estimated that suicide was 82% less frequent during lithium treatment. This benefit has not been observed for other mood stabilizers other than clozapine, suggesting that lithium's antisuicide effect is not solely due to its mood-stabilizing effects.

In addition, many studies observed an increased incidence of suicides and suicide attempts in bipolar patients after they stopped taking lithium.^{41,42} Within the first year of lithium discontinuation, affective illness recurred in two thirds of patients, and suicidal behavior increased by a factor of 20.⁴² In nearly 90% of these cases, the suicides or near-suicides occurred during the depressive or mixed states of bipolar disorder, not during the manic phase.

Mechanism of action. Lithium's antisuicidal effects may arise from its serotonin-enhancing effects in the limbic forebrain.⁴³ Although unproven, this theory is consistent with observations that have associated central serotonergic deficiency with suicidal and aggressive behaviors.

Side effects. Lithium therapy may mandate blood testing to monitor for lithium-induced hypothyroidism or renal insufficiency.

At therapeutic levels, lithium can cause tremor, polydipsia, polyuria, confusion, and gastrointestinal disturbances. Lithium toxicity from any cause can lead to delirium, convulsions, coma, and death.

Is it depression—or bipolar disorder?

Bipolar disorder needs to be recognized and treated earlier than it generally is now. An average of 8.3 years has been reported to elapse between the onset of bipolar disorder to the start of lithium treatment; in contrast, an average of 7.5 years elapses between the onset of bipolar disorder and the first suicide attempt.⁴² Failure to diagnose and treat bipolar disorder contributes to prolonged suffering and perhaps suicide.

If you recognize clinical depression in a patient, you should not reflexively prescribe antidepressant medications; rather, you should investigate the potential diagnosis of bipolar disorder through further interview or psychiatric consultation.

Contrary to popular misconception, patients with bipolar disorder spend much more time in depression than in the manic or elevated phases of the illness.⁴⁴ Giving antidepressant drugs to a patient with bipolar disorder can tip him or her from the depressed phase to a manic, agitated, or psychotic state or to frequent mood cycling (rapid cycling bipolar disorder). The use of lithium or other mood stabilizers must be considered prior to or coincident with the use of traditional antidepressants in patients with bipolar depression.

An upcoming paper on the recognition of bipolar disorder in primary care will also review the phenomenon of antidepressant-induced mood cycling, particularly given the increased incidence of suicide in bipolar depression. 

Failure to diagnose bipolar instead of unipolar depression can be disastrous

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