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# Suicidal behavior: Risk and protective factors.

**Conducta suicida: factores de riesgo y protección.**

**Ricardo Cáceda** <sup>1,a,b</sup>

## RESUMEN

Aproximadamente un millón de personas mueren cada año debido a suicidio. Poblaciones de alto riesgo de suicidio incluyen militares, adolescentes, ancianos, y pacientes con enfermedades crónicas mentales o médicas. Más de 90% de suicidios ocurren en personas que sufren de alguna enfermedad psiquiátrica. Prácticamente todas las enfermedades psiquiátricas aumentan el riesgo de suicidio, sin embargo la depresión está asociada a más de la mitad de los casos de suicidio. Hallazgos clínicos, epidemiológicos, autopsias psicológicas, en genética, neuroquímica, y neuroimágenes han incrementado significativamente nuestro conocimiento sobre el suicidio. El factor biológico más consistentemente asociado a suicidio es la disminución en la neurotransmisión serotoninérgica, particularmente en la zona ventral de la corteza prefrontal. Déficits en la función de la zona ventral de la corteza prefrontal están asociadas a impulsividad y a subóptima toma de decisiones. Las otras aminas biogénicas y el eje hipotalámico-pituitaria-adrenal (HPA) también parecen estar involucrados en la proclividad al suicidio. Los factores cognitivos y psicológicos involucrados en suicidio incluyen desesperanza, dolor psicológico o mental, impulsividad, pobre habilidad para solucionar problemas, perfeccionismo y pobre autoestima. Los factores de protección contra el suicidio más estudiados son: acceso y utilización de servicios de salud, conexión significativa con familia y la comunidad, y creencias religiosas y culturales que se oponen al suicidio. A pesar de la abundancia de estudios realizados, aun carecemos de factores fidedignos de predicción de riesgo de suicidio y debemos basarnos en el reporte del individuo y emplear el juicio clínico. Por eso continúa siendo tremendamente difícil predecir quién morirá por suicidio. Dada esta dramática carencia, continúa siendo una alta prioridad el desarrollo de estrategias de detección y prevención de suicidio, especialmente en poblaciones de alto riesgo.

**PALABRAS CLAVE:** Suicidio, depresión, neuroimágenes, genética, neurotransmisores.

## SUMMARY

Approximately one million people worldwide die from suicide every year. High risk populations include active military, adolescents, the elderly and the chronically mentally and physically ill. More than 90% of suicides are in individuals with a diagnosable psychiatric disorder. Practically all of the major psychiatric disorders are associated with an increased risk for suicide, but depression accounts for more than half of the cases. Clinical observation, epidemiological studies, psychological autopsies, genetics, neurochemistry and brain imaging have yielded important findings that have contributed to our increased understanding of suicide. The strongest biological factor associated with suicide is decreased serotonergic neurotransmission, particularly in the ventral prefrontal cortex. Deficits in ventromedial prefrontal cortex function are associated with impulsivity and impaired decision making. Additionally, a burgeoning body of evidence supports a central role of other biogenic amines and the hypothalamic-pituitary-adrenal (HPA) axis in suicide diathesis. Cognitive and psychological factors for high suicide risk include hopelessness, psychological or mental pain, impulsivity, poor problem solving skills, perfectionism, and self-dislike. Strong protective factors against suicide include access and utilization of healthcare resources, connectedness to family and community, and culture and religious beliefs that discourage suicide. Despite this plethora of research,

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we still lack reliable predictors of suicide risk and must rely heavily upon self-report and clinical judgment. Thus, it remains singularly difficult to predict who is going to commit suicide. Therefore, there is an urgent unmet need to develop effective early detection methods and treatments, particularly for high-risk populations.

**KEYWORDS:** Suicide, depression, decision making, brain imaging, genetics, neurotransmitters.

## INTRODUCTION

Each year approximately one million people worldwide die by suicide (1). In the US, suicide ranked the tenth highest among causes of death in 2010, claiming more than 38,000 lives (2). Estimates of the ratio of suicide attempts to completion range from 10:1 to 20:1. Moreover, more than 13% of the general US population experience suicidal ideation at some point in their lives. Approximately, 4% elaborate suicidal plans and a slightly higher number attempts suicide at some point (3,4). These statistics are believed to be underestimates, because a considerable number of suicides are likely underreported or misclassified as single person car accidents, accidental poisonings, etc. Of paramount importance to preventive efforts is the ability to predict who is at immediate risk for suicide, an assessment that currently is mostly done empirically. A critical element in this process of determining the likelihood of suicide is the evaluation of risk and protective factors, including behaviors. Identified risk factors for suicide can be classified as demographic, clinical, biological, psychological, cognitive, and family/social variables. Here, we discuss the suicide-associated risk and protective factors considered during the clinical decision-making processes of determining suicide risk and choosing therapeutic interventions.

### Risk behaviors

Certain risk behaviors are the product of multiple factors and are known to precede suicide. The behaviors most associated with suicide are substance abuse (primarily alcohol), violence, impulsivity, self-harm, and irregular sleep.

#### *Substance Abuse*

Most studies that attempt to determine the correlation between chronic substance abuse and suicide risk have focused on alcohol. Current evidence points to a causal role of chronic alcohol use disorders in suicide, with odds ratios for ideation ranging from 2.0–2.5, and for attempts at 2.6–3.7 (5). Prior acute intoxication is not uncommon in completed suicides (6), and up to one-third of suicide completers had elevated blood alcohol levels (7,8). Powell et al.

(9) estimated an odds ratio of 6.2 (CI 3.2–11.8) for suicidal attempts associated with alcohol use three hours prior; and Borges and Rosovsky (10) reported a positive correlation between the amount of alcohol consumed and suicide attempts. Increased acute risk for suicide is also associated with cannabis-, inhalant-, and cocaine-intoxication (11). Use of multiple substances may escalate up to threefold the likelihood of suicide. Individuals with opioid use disorders and mixed intravenous drug use have an even higher risk for suicide than those with alcohol use disorders (12).

#### *Violence*

Violence directed toward self and/or others—even just witnessing violence—significantly increase the risk for suicide. Exposure to violence as a suicide risk factor can be represented on a continuum from predisposing (e.g., childhood trauma) to proximate (e.g., rape or self-injury) (13). Both suicidal and non-suicidal self-injury have been shown to increase the risk of suicide in different populations. History of suicidal attempts is considered one of the strongest predictors for suicide completion, although suicide risk declines over time. Prospective studies have shown that 4–13% of suicide attempters eventually complete suicide (14–18). On the other hand, non-suicidal self-injury, such as cutting and burning, also increases the risk of suicide at least twofold, particularly in populations suffering from psychiatric disorders (19).

History of childhood trauma increases two- to fivefold the risk of suicidal behavior (20). Childhood abuse can greatly disturb the development of the victim's self and of his/her interpersonal relationships, predisposing the individual to psychopathology and dysfunctional personality traits, which in turn increase the risk of suicide (21,22). Additionally, adolescent victims of dating violence are at higher risk for planning and attempting suicide (23). Frequent fighting among high school students is associated with a sixfold increase in risk of suicide (24).

The association between violence and suicide is also described in adults. Assaultive behavior and impulsivity are associated with suicidal ideation in

veterans (25). The Institute of Medicine reported in 2006, overwhelming evidence of an association between deployment to a war zone and elevation of suicide risk subsequent to that deployment (26). Exposure to combat can cause psychological and physical consequences such as post-traumatic stress disorder (PTSD), traumatic brain injury, chronic pain or physical impairments, which may explain the significantly higher suicide rates reported in veterans compared with the general population (27-29). For instance, 20% of the US veterans of the Iraq war require treatment for mental illness (30).

### **Risk factors (Table 1)**

#### *Demographic risk factors*

Suicide is unevenly distributed among the population. For instance, despite suicidal ideation occurring more frequently among females, males commit suicide four times more frequently than females. The most common method for men in the US is use of firearms and for women is by poison, although gender-specificity of lethal method may vary across countries. Suicide is the third leading cause of death in people younger than 25 years worldwide (31). In several countries, ethnic or cultural minorities are at much greater risk for suicide. Young American Indians and Alaska natives commit suicide 2.5 times more frequently than the general population. The suicide rate among Hispanic female adolescents in the US is almost twice that of adolescent females in other ethnic groups. Such disparities in suicide risk among minorities may be associated with less access to healthcare services.

Interestingly, suicide rates by season have been reported to peak in the spring in several countries, regardless of geographic location. This seasonal association seems to be stronger for suicide by violent methods and greater in rural areas (for review see (32)). This phenomenon might be related to intensity of seasonal activities such as agricultural work in the rural areas, or ambient pollen concentration (33). Although the adolescent suicide rate is lower than the rate in the general population, it receives strong attention from the public and the media. Approximately 3% of adolescents worldwide make medically serious suicide attempts. After puberty, suicide rates increase until they stabilize in young adulthood. The 2003 Youth Risk Behavior Surveillance System (YBRSS) reported that 17% of US high school students seriously considered suicide, 16.9% had a plan, and 8.5%

had attempted suicide previously (34). Risk factors associated with suicide in adolescents are very similar to those in the general population and include: prior attempts, depressed mood, anger, impulsive aggressive behavior, substance abuse, hopelessness, problem-solving deficits, low family cohesion, high conflict, unsatisfactory parent-adolescent relationships, and physical or sexual abuse (35). Interpersonal factors associated with adolescent suicide include poor family and friends support, social isolation, peer victimization, and emotional neglect (36).

Worldwide, suicide is more common in the elderly than in any other age group (37). The highest suicide rate in the US is among men over 75; 36 per 100,000, about three times higher than in the general population (2). Non-Hispanic white men, age 85 and older, are the most likely demographic group in the US to die by suicide, with a rate more than fourfold higher than the general population (38). Suicide attempts in late life are more lethal than in mid-life (39), with up to one-half ending in death (40). In developed countries, elderly suicide is strongly linked to psychiatric illness, mainly depression and alcohol use disorders (41). Cognitive rigidity and obsessional traits increase suicide risk (42, 43), probably because they undermine the ability to make substantial adaptations often needed to cope with the challenges of aging. Physical illness, bereavement, and loss of independence are also important factors (44, 45).

#### *Biological risk factors*

There is a clear transmission of suicide within families (46). Much of the family history of suicidal behavior may be explained by the presence of mental illness (47). However, family, twin, and adoption studies have provided evidence for familial transmission of suicidal behavior even after controlling for mood and psychotic disorders (48). The strongest biological finding in suicide research is the association with reduced serotonergic neurotransmission. However, other monoamines and neuropeptides have also been intensely studied. For instance, the strongest predictors for completion of suicide in patients with mood disorders are biological (low levels of serotonin metabolites in cerebrospinal fluid [CSF], blunted serotonergic response to fenfluramine challenge, hyperactivity of the HPA axis, and low cholesterol) (49,50). Supporting evidence has been accrued from examination of CSF, postmortem brain tissue, genetics, and brain imaging (Table 1).

**Table 1. Risk factors for suicide*****Predisposing factors****Biological factors*

Serotonergic dysfunction  
 Noradrenergic dysfunction  
 Dopaminergic dysfunction  
 Hypothalamic-pituitary-adrenal axis hyperactivity  
 Chronic hypoxia  
 Infections (i.e., HIV, *Toxoplasma gondii*)

*Psychological factors*

Aggression, hostility, or impulsivity tendencies  
 Suicidal thoughts  
 Presence of hopelessness  
 Low self-esteem, feelings of failure  
 Lack of religious or moral constraints against suicide

*Clinical factors*

Severe depressive symptoms  
 Being in the first 3 months after the onset of the depressive episode  
 Early onset of depression, being younger at first hospitalization, more previous hospitalizations  
 Axis I comorbidities (e.g., mood, anxiety, psychotic, and substance use disorders)  
 Comorbid personality disorders or traits (e.g., borderline, antisocial)  
 Chronic medical illness  
 Past personal history of suicide attempt  
 Past history of taking precautions against being discovered after an attempt  
 Presence of a family history of suicide

*Demographic/social factors*

Demographic factors (gender, race, age)  
 Social isolation  
 Not living with a child younger than 18  
 Childhood history of physical or sexual abuse  
 Parental loss through death before the age of 11  
 Corporal punishment in adolescence  
 Family history of child maltreatment

***Triggering factors***

Recent bereavement  
 Social, financial, or family crisis or loss (negative life events)  
 Unemployment or financial problems  
 Access to means with greater lethality  
 Contagion or recent exposure to suicide  
 Acute substance intoxication  
 Being recently widowed/separated/divorced

*Serotonin (5-HT)*

Numerous studies over the past three decades have linked functional abnormalities in the central serotonergic system with the pathogenesis of suicidal behavior (51). Several lines of evidence have revealed reduced serotonergic activity in individuals who have history of suicidal behavior, including reduced CSF concentrations of the major serotonin metabolite 5-hydroxyindolacetic acid (5-HIAA) in suicide attempters with diagnoses of depression, schizophrenia, and/or personality disorders (52-54). Decreased CSF 5-HIAA concentrations also predict future suicide attempts and completions (55,56). Suicidal patients also exhibit a blunted prolactin

response to fenfluramine challenge (used as a tool to assess serotonin neurotransmission in vivo by inducing release of serotonin from synaptic vesicles) (57,58). The lethality of suicidal behavior is also associated with lower plasma serotonin concentrations (59) and reduction in serotonin binding density (60, 61). Postmortem studies of suicide attempters have shown decreased presynaptic 5-HT<sub>2</sub> receptor binding in ventromedial prefrontal cortex (VMPFC) (60). Polymorphisms in different genes of the serotonin system have been associated with suicide including serotonin, serotonin transporter (5-HTTLPR), serotonin receptors, and tryptophan hydroxylase (TPH2) (62,63). Many of these findings led to the view that serotonergic input to the VMPFC may modulate

vulnerability to suicide behavior, independent of psychiatric diagnosis (61). Lastly, low serotonergic tone has also been associated with cognitive factors predisposing to suicide (64,65).

#### *Noradrenergic and dopaminergic systems*

Striatal dopamine (DA) activity is directly associated with impulsivity (66). Norepinephrine (NE) and DA systems are much less explored in suicide than serotonin. Overall, decreased NE neurotransmission is associated with completed suicide and suicide attempts across different psychiatric conditions (67, 68). Decreased DA metabolites are found in the CSF of suicide attempters suffering from depression (54). Reduced DA transporter and increased DA<sub>2/3</sub> receptor binding in the amygdala are described in depressed patients who committed suicide (69). Corresponding up-regulation in the density of the  $\alpha_{2A}$  adrenergic receptor binding sites was found in the brains of depressed suicide victims. Moreover, patients with a history of suicidal behavior exhibited lower growth hormone response to apomorphine (70).

Also, abnormalities in the enzymes regulating the synthesis and catabolism of biogenic amines have been implicated in suicide. Monoamine oxidase A (MAOA) is a mitochondrial membrane enzyme that plays a key role in the metabolism of biogenic amines, including NE, DA and serotonin. High MAOA activity, resulting in reduced levels of these neurotransmitters, is found in mood disorders and aggressive behavior. Low platelet MAOA activity has been connected with personality traits such as impulsivity, sensation seeking, and aggression. A functional polymorphism of the MAOA gene has been linked to violent suicide methods (71). Catechol-O-methyltransferase (COMT), the major DA-degrading enzyme in the PFC, is of potential interest as a candidate gene for suicidal behavior. Modestly significant associations between the COMT and tyrosine hydroxylase polymorphisms and suicide have been reported (62,72). The DA receptor variant DRD2 has been similarly linked to suicide attempts (62). A single nucleotide polymorphism (SNP) within a coding region of the  $\alpha_{2A}$ -adrenergic receptor gene (ADRA2A) may confer susceptibility to suicide, but this finding has not been replicated (63).

#### *Other neurotransmitter systems*

A vast body of literature supports increased HPA axis activity as a major risk factor for suicide (73). Increases in CSF concentrations of corticotropin-

releasing factor (CRF), reductions in CRF<sub>1</sub> receptor prefrontal binding sites, and reductions in CRF<sub>1</sub> receptor mRNA expression (74) are found in suicide victims. Further, a positive dexamethasone suppression test (defined as nonsuppression of cortisol) has consistently been associated with an increased risk for suicide (75). Variation of the CRF<sub>2</sub> receptor gene has been correlated with the severity of suicide attempts in schizophrenia (76).

Brain-derived neurotrophic factor (BDNF), the most prevalent neurotrophin in the brain, is reduced in plasma of schizophrenic and depressed suicidal patients. Conflicting findings regarding the implications of functional BDNF polymorphisms (i.e., BDNF Val66Met) and suicide remain.

#### *Brain imaging studies*

Both structural and functional studies have explored the underlying neural mechanisms of suicidal behavior. Deep white matter lesions particularly in the frontal cortex, reported in patients with mood disorders, have been associated with suicidal ideation (77). Depressed individuals who attempt suicide using a highly lethal method show decreased metabolic activity in the ventral PFC (78). Individuals who had a recent suicide attempt exhibited bilateral prefrontal hypoperfusion and increased left-sided thalamic neural activity (79). Amen, et al. (80) showed that patients who subsequently committed suicide displayed hypoperfusion of the ventrolateral prefrontal cortex (VLPFC) and nucleus accumbens.

Most cognitive assessments and brain imaging reports in individuals with suicidal behavior reflect prefrontal function abnormalities. Decreased orbitofrontal response to fenfluramine challenge has been associated with suicide. Asymptomatic subjects with a history of depression and suicide attempts show abnormal PFC processing of facial emotions (81), and decreased bilateral dorsolateral prefrontal cortex (DLPFC) activity during recall of suicide episodes (82). Poor performance during executive function tests is associated with decreased orbitofrontal activation in euthymic individuals with history of suicide attempts (83). Thus, abnormal PFC function seems to be a trait associated with suicidal behavior, which could represent the neurobiological correlate of impulsivity and faulty decision making.

Other recently identified biological risk factors for suicide (although mechanisms are unclear) include

infection with *Toxoplasma gondii* (84,85), human immunodeficiency virus infection (86), chronic sleep deprivation, and nocturnal sleep disturbances (87, 88). Chronic exposure to high altitudes has also been linked to suicide (89), likely mediated by depression severity (90). Another environmental factor, transient increase in particulate matter, was recently described to increase suicide risk, especially for individuals with preexisting cardiovascular disease (91).

### ***Cognitive and psychological risk factors***

In addition to a biological predisposition, suicide has been linked to personality characteristics, reactivity to stressful events, psychological states (i.e., hopelessness, anhedonia, impulsiveness, psychological pain, low self-esteem, poor anger management, or dysmorphic body image), impaired cognition, and flawed decision making. Many studies have consistently described three cognitive characteristics that distinguish depressed suicidal from depressed non-suicidal individuals: 1) attentional bias to particular life events reflecting signals of defeat (“loser” status), 2) sense of insufficient capacity to solve problems, and 3) absence of anticipation of problems, leading to hopelessness (77). It has been proposed that decreased serotonergic input to the PFC may mediate the cognitive propensity to suicidal behavior (61,92).

Cognitively, suicide is associated with impulsivity and executive function impairments. In a seminal study, Keilp, et al. (93) demonstrated substantial cognitive and executive function impairments in individuals who attempted suicide with highly lethal means. Euthymic patients with history of suicide attempts showed significant deficits in executive function suggestive of generalized PFC dysfunction (impaired visuospatial conceptualization, inhibition, and visual attention or reading fluency) (94). Impairments in executive function are reported in high-lethality suicide attempts independent of deficits associated with depression alone (93). Moreover, executive function deficits are more specific to suicidal behavior than to any given psychiatric diagnosis because this observation holds true for suicidal patients with depression, bipolar disorder, and even temporal lobe epilepsy (93-98).

Not surprisingly, poorer problem-solving abilities are also found in suicide attempters with different psychiatric disorders (99). This performance is worse in carriers of the short allele of the serotonin transporter gene (100). There is evidence that at least a subgroup of suicide attempters have poor

decision-making skills as evidenced by inability to delay gratification (101,102), and poor risk-sensitive decision making (103,104). A considerable subgroup of suicide attempters experience severe suicidal ideation in a very acute and transient fashion. For instance, 40% of suicide attempts were preceded by five minutes or less of planning (105). Impulsive suicide is traditionally associated with younger, female subjects, alcohol ingestion and availability of lethal means. Both impulsivity and inability to delay gratification are associated with hyposerotonergic states, underscoring the integration of biological and cognitive deficits in suicide. Impairments in decision making and executive function may lead susceptible individuals to get involved in dire interpersonal situations and to manage them poorly. In individuals with other risks factors, this could lead to suicidal ideation and behavior. We have previously reported transient impulsive choice abnormalities in a subset of suicide attempters, as well as in depressed patients with severe suicidal ideation (101).

Hopelessness is thought to reflect a cognitive style consisting of negative attributions about the future and about one’s helplessness to improve prospects for the future. Hopelessness is considered to be the strongest risk factor for suicide, increasing the risk more than sevenfold, and it is considered to mediate the relationship between depression and suicidal intent (106). Hopelessness and anhedonia have been described as predictors for suicide in prospective studies in patients with a variety of psychiatric diagnoses (107-111). Furthermore, hopelessness mediates the association between childhood sexual abuse and suicide attempts (112). Hopelessness is also found to predict development of suicidal ideation (113).

Psychological pain, in the form of psychic, mental, or emotional pain, depressive turmoil, or “psychache,” has been posited to be central for the completion of suicide. It is defined as “the introspective experience of negative emotions such as dread, despair, grief, shame, guilt, frustrated love, loneliness and loss” (114). It is thought that unbearable psychological pain triggers a transitory fragmentation of the self, overwhelming a susceptible individual who chooses an impulsive escapist strategy to terminate his/her own life while disregarding all future consequences (115). Intense psychological pain has previously been reported in recent suicide attempters and in depressed patients with severe suicidal ideation (101,116).

### *Social risk factors*

The causative role of social factors in suicidal behavior is long established, and there is compelling evidence that they may contribute at least as much as genetic factors. Limited or lack of social support is recognized as a pervasive predisposing risk factor for suicide. Low socioeconomic status has been linked to suicidal behavior (117). Low levels of parental education are associated with higher adolescent suicidal risk. Additionally, low quality of life, unemployment, social deprivation, and social fragmentation independently increase the risk for suicide behavior (118). Children whose families move around frequently are more likely to make suicide attempts during adolescence, in a frequency-dependent fashion (119).

Family environment has been found consistently to be a predictor of suicidal behavior among adolescents, but can also represent stressful stimuli, chronic or episodic, that contributes to suicide risk in adulthood. The relevant family-related risk factors are parental psychopathology, family history of suicidal behavior, adoption, family discord, loss of a parent to death or divorce, poor quality of the parent-child relationship, and maltreatment (13,120,121). Additionally, same-sex sexual orientation is an independent risk factor for attempted suicide. In particular, family rejection after “coming out” increases the likelihood of attempting suicide eightfold (122).

Adverse experiences during adult life, including financial, legal, romantic or labor issues are associated with suicide. Interpersonal difficulties within family and marital contexts have also been clearly linked with suicidal behavior (123,124).

There is strong and convergent evidence that suicidal behavior in families is related to both genetic and environmental components. Social learning may be an important factor in both familial and non-familial transmission of suicidal behaviors. The concept of “suicide contagion” is based on the infectious disease model and assumes that suicidal behavior by one person may facilitate the occurrence of subsequent, similar behaviors by others (125). Clustering of suicide behavior is explained by imitation. Studies conducted primarily in adolescents revealed that up to 5% of all suicides may be the result of suicide clustering and that exposure to suicide behaviors in family and friends was predictive of suicide behavior and ideation (125). A large body of research in the last 10 years clearly

demonstrates that extensive newspaper and television coverage of suicide is associated with a significant increase in the rate of suicide (126). The magnitude of the increase is proportional to the amount, duration, and prominence of the media coverage. For instance, intense media coverage of the suicide of either an entertainment or political celebrity can increase 14 times the likelihood of a copycat than those suicides that are not covered (127). Today, the increasing popularity of the Internet and social media as a source of information and facilitation of suicide behavior is drawing increasing attention. Further research and regulation is warranted.

Regarding relationships with peers as a risk factor in suicide, bullying stands out as a robust predictor. Both bullying of others and being a victim of bullying during childhood increase the odds of suicide attempt (128). There is some evidence that conduct disorder might mediate this relationship (129). There seems to be gender specificity, with boys’ risk increased by bullying and girls’ risk elevated by victimization (128, 129).

Most theoretical models of suicidal behavior propose a diathesis-stress model in which the psychiatric, psychological, and biologic factors as described above predispose a person to suicidal ideation, while stressful life events interact with those factors to further increase risk of suicidal behavior. Consistent with such a model, suicidal behaviors often are preceded by stressful events, mostly of interpersonal nature, i.e., family or romantic conflicts, or school, work, or legal difficulties (123,124,130). The experience of persistent stress also may explain higher rates of suicidal behavior by people in certain occupations, such as physicians, military personnel, and police officers. Other highly stressful experiences such as intractable pain, pruritus, chronic or terminal illness have also been associated with suicide (41).

Access to lethal means such as firearms and high doses of medication (131) is an important risk factor for suicide, a condition that is susceptible to intervention. After some initial controversy related to confounding factors, the Behavioral Risk Factor Surveillance System (BRFSS) provided conclusive evidence about firearms and suicide. After controlling for psychological distress, rates of poverty, urbanization, unemployment, and drug and alcohol dependence and abuse, the analysis showed that household gun ownership increases the risk of firearm suicide more than threefold, but did not modify the rates of suicide

by other means (132). In particular, the presence of firearms in a home, regardless of how the weapons are stored, increases the risk of suicide not only to the gun owner but also to other household members. This increased risk is greater for young people, and greatest for those without known psychopathology (133). Possible explanations for this increased risk may lay in the abrupt and transient nature of suicidal ideation, as evidenced by the short period of time between onset of severe suicidal ideation and the actual attempt, and the relatively short duration of severe ideation with lethal intent (105,134,135).

### **Clinical risk factors**

#### *Psychiatric disorders*

In suicide cases in which psychological postmortems are conducted, more than 90% are associated with a diagnosable psychiatric disorder. Nearly all psychiatric disorders increase the risk for suicide (136). Data related to the most significant factors are described below.

#### *Depression*

Affective disorders are the most common psychiatric disorders associated with suicide, followed by substance abuse (especially alcohol) and schizophrenia. The mortality risk for suicide associated with depression is approximately 20 times the general population risk, especially in the first weeks after inpatient discharge (137). More than half of all people who die by suicide fulfill criteria for a current depressive disorder (138). On the other hand, about 4% of depressed individuals die by suicide, and the risk is greatest in males and in those who have needed psychiatric hospitalization, especially for suicidality (108). Clinical predictors of suicide in patients with major depressive disorder (MDD) include a history of attempted suicide, high levels of hopelessness, presence of comorbidity, and high ratings of suicidal tendencies (108).

One of the most effective treatments for depression is antidepressant pharmacotherapy. However, a raging controversy exists about a small but significant increased risk of suicide after initiation of antidepressant treatment, particularly in young individuals (139). This issue has led to a FDA black box warning on antidepressants about an increased risk of suicidal thinking and behaviors in children, adolescents, and young adults (18–24 years old) during the first few weeks of treatment. A dramatic

reduction in youth antidepressant prescribing occurred after the launch of this warning. On the other hand, large observational studies show that risk of suicide declines after treatment is started (140) and that geographic areas with higher rates of antidepressant use tend to have lower rates of suicide death (141, 142).

#### *Anxiety disorders*

Clinical and epidemiologic studies have demonstrated a positive association between individual anxiety disorders and suicidal ideation and attempts (143-147). However, some controversy still remains whether this high risk for suicide is mainly because of the frequent comorbidity with other psychiatric (e.g., bipolar disorder, schizophrenia, substance abuse, or major depression) or medical conditions (e.g., multiple sclerosis or coronary artery disease) (148-150). Twelve-month prevalence rates of suicide ideation have been found to be greatest in obsessive compulsive disorder (OCD) (27.3%), with attempts being most common among patients with panic disorder (3.6%), OCD (3.3%) (151) and post-traumatic stress disorder (PTSD) (2.7%) (152). Severe anxiety or intense psychological pain is found to be the strongest predictor of inpatient suicide (153). A large scale study using data from the National Comorbidity Survey, which included assessment of all anxiety disorders except OCD, found that PTSD was the only anxiety disorder significantly associated with suicidal ideation and suicide attempts, after accounting for a wide range of other sociodemographic and psychiatric comorbid disorders (152).

Because of its close association with ongoing military conflicts, PTSD has captured much media attention. However, its prevalence as a result of civilian trauma, including child abuse, is often overlooked. In the military, PTSD, along with major depression and substance use disorders, is strongly associated with elevated risk for suicide. Suicidal ideation is found in 12–21% of veterans and is associated with combat exposure, depression, PTSD, substance use disorders, particularly alcohol, poor social support, poor social satisfaction, and poor resilience (26,154-159). PTSD is an independent risk factor for suicide (154) and increases the risk for suicidal ideation even in the presence of protective factors such as positive social support (154-158). In a cohort of young adults exposed to civilian trauma, PTSD was found to be an independent predictor of suicide, even adjusting for major depression or alcohol or substance dependence

**Table 2. Protective Factors for Suicide**

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Effective clinical care for mental, physical, and substance abuse disorders
Easy access to healthcare
Family and community support (connectedness)
Support from ongoing medical and mental health care relationships
Skills in problem solving, conflict resolution, and nonviolent ways of handling disputes
Cultural and religious beliefs that discourage suicide and support instincts for self-preservation

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### *Schizophrenia*

The lifetime prevalence of suicide in schizophrenia is approximately 10%. Risk factors for suicide in schizophrenia are similar to those in the general population, including previous attempts, comorbid mood disorder, recent loss, and high risk-to-rescue ratio (referring to an increased probability of inflicting irreversible damage). Schizophrenia disease-specific factors associated with high suicide risk include the first year of illness, high level of premorbid functioning and IQ, fear of mental disintegration, agitation or restlessness, poor adherence to treatment, long duration of index hospitalization, and frequent rehospitalization (160).

### *Bipolar disorder*

Up to 56% of suicide victims with bipolar disorder have had at least one previous suicide attempt. Established risk factors for suicide among those with bipolar disorder are severity of depression, agitation, hopelessness, self-blame and guilt, marital isolation and loss, long duration of illness, hopelessness, family history of suicide, adversity, early age at onset, psychiatric or medical comorbidity (161). The suicide risk in bipolar II disorder may be very high in part because of the high prevalence of comorbid anxiety disorders and substance use disorders. The most robust short-term predictors of suicide in bipolar disorder are few reasons for living, the wish to die, suicidal intent or plan, and communication of suicide intent. In contrast to classical euphoric mania, suicidal thoughts and attempts are common in dysphoric mania or the so-called mixed state (162). Recent life events, as well as psychosocial stressors (e.g., unemployment or financial problems) are risk factors for attempted suicide, particularly for individuals in a depressive or dysphoric manic episode (163).

### *Personality disorders*

Personality disorders independently increase risk of suicide attempts as a function of the severity

of the illness, particularly in women. Borderline personality disorder occupies a preeminent role as risk factor for suicide. One of the core features of borderline personality disorder is frequent suicidal ideation and suicidal behavior, as well as non-suicidal self-harmful behaviors. For instance, between 60–70% of patients with borderline personality disorder attempt suicide and up to 5–10% are successful (164). Personality traits associated with suicidal behavior are impulsivity and impulsive aggression, neuroticism, perfectionism, and sensitivity to life events (64,65).

### ***Protective factors (Table 2)***

Protective factors are those that decrease the probability of an outcome in the presence of elevated risk. Although formal tests of protective factors are rare in suicide research, several studies of factors associated with lower risk of suicidal behavior consistently point to increased sense of belonging, purpose, transcendence, and connection to others, family, friends, community or religion. Religious beliefs, religious practice, and spirituality have been associated with a decreased risk of suicide attempts (165-167). Potential mediators seem to be moral objections to suicide (168) and social support (169). Perceptions of social and family support and connectedness also have been studied outside the context of religious affiliation and have been shown to be significantly associated with lower rates of suicidal behavior (170,171). Marriage, being pregnant, and having young children in the home are also protective against suicide (172,173), even though, the presence of young children is associated with a significantly increased risk of first onset of suicidal ideation. Also, having adult roles, like parent and provider, reduces the likelihood of suicide, possibly by reducing risk-taking behaviors (174). Lastly, factors that favor social connectedness correlate negatively with suicidal behavior, including coping skills, problem solving, conflict resolution, nonviolent ways of handling disputes, resilience, and reasons for living (175,176).

## CONCLUSIONS

Suicide is one of the major causes of death worldwide. In the US, it ranks tenth among causes of death, above hypertension or homicide. Certain subpopulations are at greater risk for suicide, including teenagers, the elderly, and the psychiatrically ill. More than 90% of suicides are linked to psychiatric disorders. Depression accounts for more than half of suicide cases, though suicide is also a frequent outcome in substance abuse, bipolar disorder, and schizophrenia. A strong biological component in the diathesis for suicide is shown by its heritability and deficits in serotonergic neurotransmission, particularly to the VMPFC. Deficits in VMPFC function are associated with impulsivity and impaired decision making. Growing amounts of data suggest that other biogenic amines and the HPA axis also have a central role in suicide diathesis. Cognitive and psychological factors for high suicide risk include hopelessness, psychological pain, impulsivity and poor problem solving skills. Environmental factors related to suicide include history of childhood trauma, poor social support, recent discharge from the hospital and availability of lethal means. Despite this array of knowledge about suicide risk, predicting who is going to commit suicide continues to be a rather subjective decision in clinical practice. Further research exploring accurate objective predictive factors that could accurately inform clinicians in selecting effective preventive measures is warranted.

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