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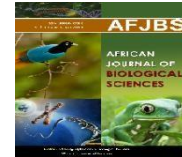
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Brief Overview about Suicidal Behavior

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Abstract: *Background:* Suicide is a complex public health problem of global importance. Suicidal behavior differs between sexes, age groups, geographic regions, and sociopolitical settings, and variably associates with different risk factors, suggesting etiological heterogeneity. Identifying and preventing suicide attempts and deaths by suicide have represented a considerable challenge for public health authorities. It is believed that the most dramatic increase in suicide mortality increase will be observed in the Third World countries, this is because the socioeconomic and behavioral factors of suicide risk are present in a higher degree than developed countries. Feelings of hopelessness and the intention to kill oneself are not common among Muslims, for whom losing hope in relief by God and self-inflicted death are blasphemous and punishable in the afterlife. However, rates of suicide attempts (parasuicide), which are more likely to be intended to elicit care, have no significant associations with religiousness among Arabs. The crude rate of suicide attempts in Cairo was found to be 38.5 per 100 000. There was a high percentage in the age group 15–44 years, with no major difference between the genders. Single patients represented 53% of the total, with students showing the highest risk (40%).

Keywords: *Suicidal Behavior*

Introduction

Suicide is a complex public health problem of global importance. Suicidal behavior differs between sexes, age groups, geographic regions, and sociopolitical settings, and variably associates with different risk factors, suggesting etiological heterogeneity **(1)**

Suicide represents one of the top fifteen causes of death for individuals of all ages in most developed countries. The World Health Organization (WHO) estimates that almost one million people die by suicide each year worldwide, representing annual global suicide mortality rate of 11.4 suicides per 100 000 people occur per year. It has long been known that young adults, ages 20–24, and the elderly, are at greater risk of dying by suicide, with death rates of 12.5 and 15.8 per 100,000, respectively. Although there is no effective algorithm to predict suicide in clinical practice, improved recognition and understanding of clinical, psychological, sociological, and biological factors might help the detection of high-risk individuals and assist in treatment selection **(1)**

Identifying and preventing suicide attempts and deaths by suicide have represented a considerable challenge for public health authorities. It is believed that the most dramatic increase in suicide mortality increase will be observed in the Third World countries, this is because the socioeconomic and behavioral factors of suicide risk are present in a higher degree than developed countries **(1)**

Presently, the WHO defines suicide as the act of deliberately killing oneself and suicide attempt as "any non-fatal suicidal behavior and refers to intentional self-inflicted poisoning, injury or self-harm which may or may not have a fatal intent or outcome." Therein, the WHO also specifies that nonfatal self-harm without suicidal intent is included. The WHO explains that this is because of the problem of evaluating suicidal intentionality due to ambivalence or even concealment on the part of the patient.

On the other hand, suicidal behavior can be "a range of behaviors that include thinking about suicide (or ideation), planning for suicide, attempting suicide and suicide itself" **(2).**

DSM-5 definition:

The DSM-5 **(3)** defines suicidal ideation as "thoughts about self-harm, with deliberate consideration or planning of possible techniques of causing one's own death," defines suicide as "the act of intentionally causing one's own death," and defines suicide attempt as "an attempt to end one's own life, which may lead to one's death."

The difficulty of establishing the intent of self-harming behaviors has hindered efforts to streamline the historically heterogeneous suicide nomenclature, but efforts, such as those resulting in the Columbia Classification Algorithm of Suicide Assessment (C-CASA), have contributed to standardising nomenclature. The severity of suicidal behavior varies, on the basis of family studies showing the progression from less to more severe forms of suicidal ideation and behavior, and from family and biological studies showing overlap between attempted and completed suicide **(4).**

	Definition	Comments
Suicide	A fatal self-injurious act with some evidence of intent to die	--
Suicide attempt	A potentially self-injurious behaviour associated with at least some intent to die	Some younger people who attempt suicide report that their main motivation is other than to die, such as to escape an intolerable situation, to express hostility, or to get attention; however, many nonetheless acknowledge the possibility that their behaviour could have resulted in death; suicide attempt is characterised by greater functional impairment than non-suicidal self-injury
Active suicide ideation	Thoughts about taking action to end one's life, including identifying a method, having a plan, or having intent to act	Highly specific ideation, such as having made a plan or having intent, is associated with a much greater risk of a suicide attempt within 12 months
Passive suicide ideation	Thoughts about death or wanting to be dead without any plan or intent	--
Non-suicidal self-injury	Self-injurious behaviour with no intent to die	Differs from suicide attempt in terms of motivation, familial transmission (found only in suicidal behaviour), age of onset (younger in non-suicidal self-injury), psychopathology, and functional impairment (greater in suicide attempt); non-suicidal self-injury most commonly consists of repetitive cutting, rubbing, burning, or picking; the main motivations are either to relieve distress, to "feel something", to induce self-punishment, to get attention, or to escape a difficult situation
Suicidal events	The onset or worsening of suicide ideation or a suicide attempt, an emergency referral for ideation, or suicidal behaviour	Often used as an endpoint in pharmacological studies; rescue procedures are included in this category because a patient with ideation who then received emergency intervention might have made an attempt had he or she not been recognised and treated
Preparatory acts toward imminent suicidal behaviours	--	--
Deliberate self-harm	Any type of self-injurious behaviour, including suicide attempts and non-suicidal self-injury	The combination of suicide attempts and non-suicidal self-injury into one category reflects their high comorbidity, shared diathesis, and the fact that non-suicidal self-injury is a strong predictor of eventual suicide attempt; not all events classified as a suicide attempt are motivated by a true desire to die, but rather by desires to attract attention, to escape, and to communicate hostility; however, when only deliberate self-harm is reported, suicide attempts and non-suicidal self-injury cannot be subsequently disaggregated

Table 1: Nomenclature for suicidal and related behaviors and suicidal ideation **(5).**

Due to stigma and social taboos surrounding suicidal behavior, the behavior is not always given the serious attention it merits, what often goes unrecognized is how widely pervasive suicidal behavior has become (**5**). Suicide as the cause for death might be hidden and in some areas it is completely unreported due to a number of reasons (for example religious and/or social reasons), (**6**).

Suicide is a worldwide phenomenon. As such, it has continued to be addressed by the World Health Organization (WHO) since 1950, i.e., only two years after its foundation (**2).**

Globally, suicides are the second leading cause of premature mortality in individuals aged 15 to 29 years (preceded by traffic accidents), and number three in the age-group 15–44 years (**6**). Upsettingly, in 2015, the vast majority—namely 78% of suicides—were completed in low- and middle-income countries (LMIC) **(7).**

Age

In adolescents and young adults between 15 and 29 years of age, death from suicide reaches the highest absolute numbers. The US death statistics do not include death from suicide up to the age of 10 years. However, in the age group of 10 to 14 years, suicide is the third most common cause of death, representing the second most common cause up to the age of 34 years thereafter. Overall, many more young than old individuals die from suicide, but the relative numbers per age group are up to eight times higher in the elderly. Similarly, according to the WHO, children and adolescents up to the age of 15 years exhibit the lowest global suicide rates (per 100,000 inhabitants), which steadily increase thereafter until the age of 70 years or above (**2**).

Gender

The overall suicide rate of 10.7 per 100,000 population encompasses a male:female ratio of 1.7. Thus, men complete suicide almost twice as often as women. However, comparing the information from 183 countries which was allocated in 2015, the male:female ratio varied from 0.8 in Bangladesh and China to 12.2 in St. Vincent and the Grenadines **(8).**

A ratio below one means that the suicide rate of females exceeds that of males; this only exists in China and Bangladesh. Highest rates of suicides in women were found in China (11.5), Angola (11.6), Japan and Belgium (12.4), and—among others—Sri Lanka (13.7), India (14.3), and both Koreas (North: 15.4; South: 16.4). Also, in South East Asia, unexpectedly high suicide rates in young females aged 15–29 were reported as the primary cause of death, whereas females aged 45 or above tend to die from suicide in the Western Pacific region **(8).**

Socioeconomics

Socioeconomic variables strongly influence rates of suicide mediated by their being co-determinants of risk and, of course, of mental disorders. Several groups of determinants have been defined:

Demographic parameters: age, gender, ethnicity, and related parameters;

Social status: low income, income inequality, unemployment, low education, and low social support;

Social change: in a societal realm, e.g., urbanization, or on an individual basis, e.g., change in income;

Neighborhood: inadequate housing, overcrowding, violence and others;

Environmental incidences: climate change, natural catastrophe, war, conflict, and migration.

Suicide in Egypt

Feelings of hopelessness and the intention to kill oneself are not common among Muslims, for whom losing hope in relief by God and self-inflicted death are blasphemous and punishable in the afterlife. However, rates of suicide attempts (parasuicide), which are more likely to be intended to elicit care, have no significant associations with religiousness among Arabs **(9).**

Although the wish to die is common among people with depression in Arab cultures, it usually remains at the level of wishing that God would terminate their life and does not progress to the wish to kill themselves **(10).**

The crude rate of suicide attempts in Cairo was found to be 38.5 per 100 000. There was a high percentage in the age group 15–44 years, with no major difference between the genders. Single patients represented 53% of the total, with students showing the highest risk (40%).

Depressive illnesses, hysterical reactions and adjustment disorders were the main causes of the attempt. Overdose by tablet ingestion was the most commonly used method (80%).

Official government reports are misleading and do not represent the true rate; assuming that one in ten suicide attempts ends with actual suicide, a crude estimate of suicide in Egypt would be about 3.5 per 100 000 **(9).**

Etiology:

Genetic factors
The role of genetics in suicidal behavior has been established by twin, adoption and family studies which strongly support a role for genetics in the transmission of suicidal acts independently of the transmission of psychiatric disorders and suicidal ideation **(12).**
These effects are unlikely to result from imitation because adoption studies show concordance between biological, but not adoptive relatives (**12).**
Although psychopathological disorders also aggregate in families, the transmission of suicidal behavior seems to be mediated through the transmission of impulsive aggression **(13).**   Twin and adoption studies suggest that genetic factors account for part of the familial transmission of suicidal behavior, with estimates of heritability of 30–50% **(12).** However, when the heritability of other psychiatric conditions is taken into account, the specific heritability of suicidality is estimated as 17.4% for suicide attempts and 36% for suicide ideation **(12).** Ideation seems to be co-transmitted with mood disorders and shows a distinct pattern for transmission from suicidal behavior **(14).**
Despite consistent evidence for the heritability of suicidal behavior, the identification of specific genes associated with suicide risk remains elusive, despite several candidate-gene and genome-wide association studies, which have mostly provided inconclusive results **(14).**
Modeling the interactions between experience and genes would be useful. The many studies of the role of serotonin transporter promoter polymorphism (HTTLPR) in suicidal behavior among patients with psychiatric disorders have been reviewed by Lin and Tsai, **(2).**
Lin and Tsai concluded that the 5-HTTLPR short allele occurred significantly more often among suicide attempters than among psychiatric patients who had never attempted suicide (**15**).
Caspi et al., (16) reported an interaction between 5-HTTLPR and stressful life events for depression, suicidal ideation, and suicide attempts. The loss-of-function s allele and s-containing genotypes were again implicated. They carried out a prospective longitudinal study of 1037 Dunedin children assessed at regular intervals till the age of 26 years. They measured stressful life events occurring between the age of 21 and 26 years. Individuals with an s allele and with stressful life events after 21 years of age had an increase in depressive symptoms and suicidal behavior/ideation whereas l/l homozygotes did not.
Furthermore, when examined childhood maltreatment that occurred during the first 10 years of age they similarly found that childhood trauma predicted depression as an adult-but again only among individuals with the s allele and not among l/l homozygotes.
In addition to heritable factors, other psychosocial, demographic, and biological factors increase vulnerability to suicide (**17**).
Early-life adversity is also associated with epigenetic modification of genes involved in neuronal plasticity, neuronal growth, and neuroprotection **(18).**
Studies of brain tissue from people who completed suicide show that mRNAs encoding BDNF and its receptor TRKB are down regulated in several brain regions including the prefrontal cortex and the hippocampus, and some studies report differential methylation of BDNF and TRKB in the brains of people who died by suicide compared with in people who died from other causes **(18).**
        Another potential risk factor for suicidal behavior is infection with the brain-tropic parasite Toxoplasma gondii (**19**)
Relation with psychiatric illness
Suicide is a global public health problem and mental illness is known to be the strongest risk factor. Most individuals with psychiatric illnesses do not die by suicide, but some psychiatric illnesses are more strongly

linked to suicidal behaviors than others. Major depressive episodes associated with major depressive disorder or bipolar disorder, account for at least half of suicide deaths **(18)**.

Among patients with <u>bipolar disorder</u>, mixed state episodes are most strongly associated with suicide attempts, with risk increasing according to the amount of time spent in mixed depressive episodes; suicide risk is highest within the first year of illness and associates with feelings of hopelessness **(18)**.

Adults with <u>schizophrenia</u> and other psychotic disorders are also at heightened risk. the main clinical predictors of suicide include the presence of depressive symptoms, young age, male sex, education, positive symptoms, and illness insight **(20)**.

Multiple other factors, such as <u>alcohol and drug related disorders</u>, are common in people who die by suicide and might exacerbate underlying risk or interact with depression to increase the risk of engaging in suicidal behaviors **(21)**.

Other illnesses common in people who die by suicide include eating disorders and personality disorders; particularly cluster B personality disorders such as borderline and antisocial personality disorder, which are characterized by aggressive and impulsive traits (**22**).

People who die by suicide often have a history of more than one disorder, and in individuals with psychiatric illnesses such as depression, which is associated with suicide ideation, comorbidity with disorders characterized by severe anxiety or agitation or poor impulse control predicts suicidal behavior (**22**).

In addition to methodological factors, age, geographic location, and sex largely explain the variability between studies. Younger age at suicide is associated with comorbidity, particularly with cluster B personality pathology and substance misuse disorders **(13)**.

In middle aged people, alcohol and substance misuse, high anxiety, and comorbid major depression disorder are associated with suicide risk, whereas in older people there is a stronger association between suicide and psychopathology, particularly major depressive disorder (**23**).

Neurobiology

Our knowledge about the neurobiology of suicidal behavior is still limited. Technical limitations and the complexity of the CNS are major obstacles. Neurobiological correlates of the stress-diathesis model for suicidal acts point to the involvement of the serotonergic and noradrenergic systems, and the ventro-medial prefrontal cortex behavioral inhibition. A failure of behavioral restraint mechanisms may result in a predisposition to suicidal behavior (**24**).
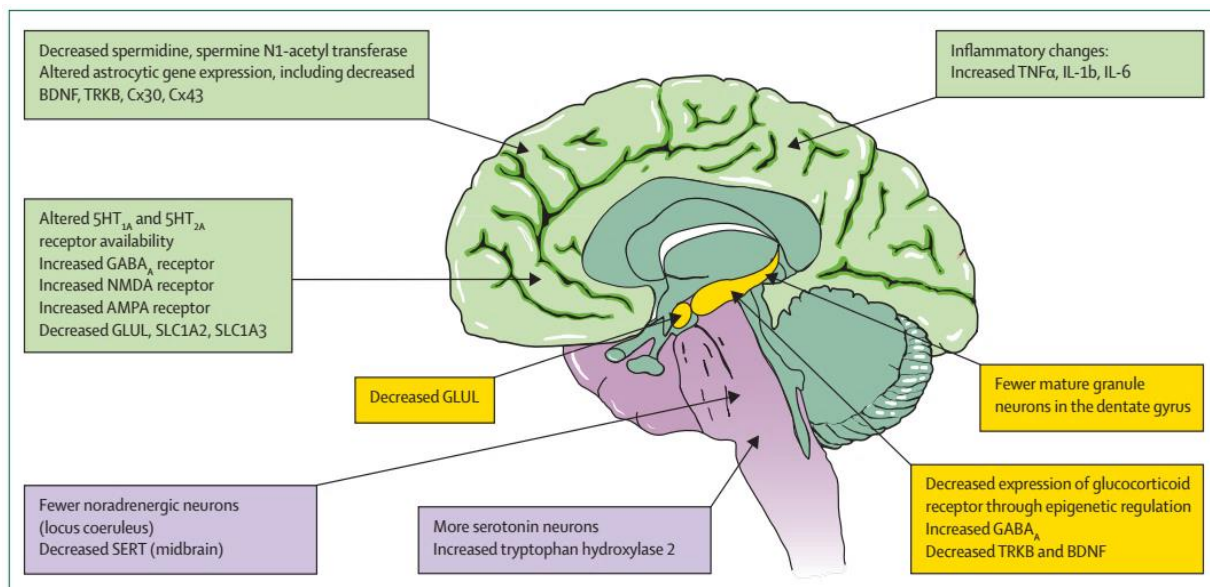

<u>Figure 1:</u> Biological changes in the brains of people with suicidal behaviors (**1**)

5HT=5-hydroxytryptamine, or serotonin. AMPA=α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid. BDNF=brain-derived neurotrophic factor. Cx=connexin. GABA=γ-aminobutyric acid. GLUL=glutamine synthetase. IL=interleukin. NMDA=N-methyl-D-aspartic acid. SERT=serotonin transporter. SLC=solute carrier family. TNF=tumor necrosis factor. TRKB=tropomyosin receptor kinase B.

Serotonin:

Among the first to be described was the altered levels of serotonin and serotonin signaling in individuals exhibiting suicidal behaviors. Several studies link disrupted serotonin expression to suicide attempt or suicide, and despite discrete differences in serotonin receptor and transporter expression between patients with depression and those who exhibit suicide ideation or suicidal behaviors (**24).**, it is unclear to what extent altered serotonin signaling in people who die by suicide can be distinguished from changes associated with depression because these two phenotypes often occur together **(25).**

There is evidence that individuals exhibiting suicidal behaviors have unique serotonin genotype and expression patterns, and low serotonin is associated with personality traits linked to suicidality, such as impulsive aggression (**26).**

Tryptophan-hydroxylase (TPH) is the key enzyme in the biosynthesis of serotonin (**24).**TPH2 was only found in the central nervous system, mostly in the brain stem. It was reported that different haplotypes of TPH2 could be risk factors for suicidal behavior (**27**).

Glutamate and GABA:

Other neurotransmitters implicated in depression and suicide are glutamate and γ-aminobutyric acid, It is demonstrated that glutamatergic enhancement increases aggression raising the possibility of excitation/inhibition imbalance. Treatments targeting the glutamate pathway, such as ketamine, have yielded some promising initial results in the treatment of severe depression and suicide ideation (**28**).

Inflammation:

Aside from neurotransmitters, inflammatory responses have been linked to suicidal behavior, with some evidence suggesting that inflammation linked to suicidality might occur both in the central nervous system and in peripheral tissues, as detected in blood samples (**28**).

Hypothalamic–Pituitary–Adrenal (HPA) Axis:

There is clear evidence that the activity of three neurobiological systems has a role in the pathophysiology of suicidal behavior. This includes hyperactivity of the hypothalamo-pituitary-adrenal axis, dysfunction of the serotonergic (5-HTergic) system, and excessive activity of the noradrenergic system. While the first and the last system appear to be involved in response to stressful events, dysfunction of the serotonergic system is thought to be trait-dependent and associated with disturbances in the regulation of anxiety, impulsivity, and aggression. It can be then hypothesized that neurobiological dysfunctions mediate the occurrence of suicidal behavior through the disturbed modulation of the basic neuropsychological functions (**29**)

The hypothalamic–pituitary–adrenal axis regulates physiological responses to stress to facilitate coping with changing environments or challenging events, mainly through cortisol regulation. Individuals who have experienced early-life adversity often have a hyperactive hypothalamic–pituitary–adrenal axis and an increased stress response (**29**)

FKBP5 inhibits glucocorticoid receptor signal transduction and might contribute to the risk of suicidal behavior; FKBP5 sequence variants are associated with an increased risk of suicidal behavior, especially in people who have had early-life adversity (**1**).

Brain changes:

Altered responses to stressful social situations might lead to psychopathological disorders and suicidal behavior, with evidence that suicidality is associated with several changes in the brains of people with suicidal ideation or behaviors **(25).** Glial cell function might also be disrupted in people who show suicidal behaviors, where astrocyte-specific genes linked to structural integrity are down regulated, and neurotrophic factors such as the BDNF receptor TRKB are expressed differently in people who die by suicide and controls (**25**).

Psycho -Social factors

Living alone.

High introversion.

Extreme hopelessness, helplessness and worthlessness, or defeat and   entrapment, which may result from depressive psychopathology.

Traumatic events in adulthood.

Interpersonal stressors.

Loss or bereavement: causes emotional distress, can lead to an enduring inability to cope with the loss; complicated grief and development of suicide ideation or behavior is more likely in cases of bereavement caused by a violent death such as suicide

Financial or legal difficulties.

Physical illnesses with concurrent depression: respiratory diseases such as chronic obstructive pulmonary disorder and asthma (for death by suicide vs other causes, odds ratio 1.5–2.1), cardiovascular diseases such as coronary heart disease and stroke (1.53–1.54), degenerative diseases such as osteoporosis and multiple sclerosis (2.33–2.54); differs by sex, with increased risk for women (**28).**

Chronic diseases acting independently of mental disorders: inflammatory bowel disease, migraine, and epilepsy **(20**).

Sleep disturbances and insomnia: increased risk of suicide ideation or suicidal behaviors can be independent of depression; might be mediated by increased impulsivity, negative cognitive bias, and reward-seeking.

Traumatic brain injury: athletes and war veterans who have sustained chronic traumatic encephalopathy are especially vulnerable; possibly mediated by a decrease in impulse control following repeated injuries; lifetime occurrence of a psychiatric disorder associated with a greater risk of suicide in patients with traumatic brain injury. **(1)**

Family History

Suicidal behaviors run in families, Family studies show that the risk of attempts is higher in relatives of people who died by suicide, and that the risk of dying by suicide is higher in relatives of people with a history of suicide attempts **(4).**

Family, twin, and adoption studies provide evidence of the heritability of suicide and attempted suicide, in part independent of the familial transmission of major psychiatric disorders. The estimates of heritability for suicide range between 21–50%, and 30–55% for a broader phenotype of suicidal behavior and ideation (**21**).

Adoption and family studies indicate that suicidal acts have a genetic contribution in terms of cause or diathesis that is independent of the heritability of major psychiatric disorders **(4).**

The data from twin studies (**22**) show a much higher concordance rate for monozygotic than for dizygotic twins (13.2% versus 0.7%) which is strongly supportive of a genetic component in suicidal behavior.

Clinical indicators of suicide risk:

The Columbia Suicide Severity Rating Scale is a widely-used measure to establish the degree of suicide risk.

Previous SA and method of SA predict increased suicide risk.

Suicide completers are likely to have had repeated hospital admissions; recurrence of self-harming is most likely within 3–6 months of the first presentation.

Ambivalence, worthlessness, helplessness, and notably, hopelessness are key indicators of heightened suicide risk.

High-risk cases should be followed closely post-discharge **(5).**

Prevention

The Collaborative Assessment and Management of Suicidality (CAMS) is one such therapeutic relationship approach that has been shown to enhance treatment retention and reduce suicidal ideation initially and at one-year follow-up **(30**). This approach involves a range of four to 12 sessions during which the clinician and patient collaboratively engage in a structured assessment of the patient's suicidal thoughts and treatment planning.

Several reviews of the efficacy of different prevention practices have been published **(30).**School, workplace, and community-based interventions, and multicomponent primary care interventions, can reduce the incidence of suicide or suicidal behavior.

School-Based Interventions:

School-based interventions reduce the incidence of suicide ideation or suicidal behavior. The Good Behavior Game, a teacher-led classroom intervention for children aged 6–7 years, reduced suicide ideation and suicidal behavior in one of two randomized trials (the other trial was underpowered), and the Signs of Suicide (SOS) program, which educates students about the relation between mental disorders and suicide, self-identification of depression and suicidal risk, and encourages appropriate help-seeking, also reduced the incidence of suicide attempts **(31**).

Studies of post-high school suicide prevention similarly showed no effect for educational or gatekeeper interventions, but one quasi-experimental study showed that method restriction and mandatory professional assessment of students who exhibit suicidal behaviors reduced the suicide rate **(30).**

Multi-Component Intervention:

A multi-component preventive intervention programme in the US Air Force, including leadership and gatekeeper training, increased access to mental health services, coordination of care for high-risk individuals, and a higher level of confidentiality for those who disclosed suicidality reduced suicide rates by 35% **(31).**

Interventions for Elderly People:

Among elderly people, some evidence suggests that interventions to decrease isolation and augment social support through activity groups and telephone outreach might also reduce mortality caused by suicide (**28**).

Primary Care Interventions:

A substantial proportion of patient's access primary care within 1 month of suicide but are rarely diagnosed with a mental disorder. Education programs for primary care doctors targeting identification and treatment of depression can decrease regional suicide rates, particularly in women, but need continued education and additional physician support to improve patient outcomes **(32).**

In particular, websites for physicians, increasing contact between physicians and psychiatric facilities, public education campaigns to train key community facilitators in recognition of depression and suicide risk, and a suicide hotline might all be important aspects of prevention strategies **(32).**

Post-Discharge Interventions:

Patients recently discharged from psychiatric inpatient units are at very high risk for completed suicide. Through decades of research, concerning with assessing the relation between regional changes in suicide rate and the level of regional implementation of the recommended systems modifications (**30**).

Declining regional suicide rates are related to the extent of care, clear policies for the management of dual diagnosis patients, and multidisciplinary reviews of suicide deaths. The effect of means restriction is estimated on the basis of before-and-after or other types of quasi-experimental designs. Means restriction strategies are guided by the assumption that many suicides are impulsive, and restricting access to lethal methods might forestall a suicidal crisis; even if method substitution takes place, the person will have access to less lethal, potentially non-fatal means of suicide **(33).**

Means Restrictions:

The effect of means restriction on attempting or completing suicide has been assessed in case-control studies and regional comparisons of suicide rates and methods. The rate of suicide by a given method, whether firearms, natural gas, car exhaust, paracetamol, substitution of less toxic drugs (e.g., selective serotonin reuptake inhibitors vs tricyclic antidepressants), pesticides, or jumping from bridges, is related to the ease of access **(33).**

Laws that impede access to a method, whether stricter firearms control laws, detoxification of domestic gas or car exhaust, limitation of access and use of blister packs for paracetamol, lockboxes for pesticides, or bridge barriers (often combined with a telephone hotline for crisis intervention), reduce suicides by that method, although some method substitution might occur. Briefly, individual level interventions to encourage safe

storage of hazardous items such as pesticides or firearms can work, although the effect of these interventions on morbidity or mortality has not been recorded **(33)**

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