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CME Objective

After studying this article, you should be able to:

- Screen patients for risk factors for suicide (eg, tobacco smoking and impulsivity) that transcend individual psychiatric disorders

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Suicide Risk in a National VA Sample:
Roles of Psychiatric Diagnosis, Behavior Regulation, Substance Use, and Smoking

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ABSTRACT

Background: Most suicides are first attempts that are difficult to predict, possibly reflecting impaired and unstable behavior regulation. We sought to identify characteristics specifically associated with severe suicidal behavior by comparing risk ratios (RRs) for severe suicidal attempts (ATTP) to RRs for suicidal ideation (SI) only in a transdiagnostic sample of Veterans, focusing on impulsive-aggressive or externalizing behavior (EB), substance use disorders (SUDs), and recurrent affective or psychotic disorders (ie, severe mental illness [SMI]).

Methods: The VA Information and Computing Infrastructure (VINCI) Data Navigators provided aggregate phenotype counts and relevant *ICD* and clinic codes from about 350,000 Veterans in the US Department of Veterans Affairs national Million Veterans Program (MVP). Data were collected by MVP between 2011 and 2017, without relationship to the current work. Work on this report and related analyses took place from April 11, 2020, to October 6, 2021.

Results: We compared 3 suicide risk groups: 1,269 Veterans with previous ATTP, 109,836 with SI only, and 242,872 without previous suicidality. Nearly three-fourths of ATTP Veterans did not have SMI diagnoses. RR for ATTP behavior was highest in Veterans with EB (25.4), followed by those with SUD (13.9); both RRs were greater than RRs for Veterans with schizophrenia (7.4) or bipolar disorder (7.8). ATTP RR was greater for smoking than for major depressive disorder (5.0 vs 3.5, respectively). RR for smoking, across clinical groups, was strongly related to RR for ATTP risk, but not for SI only.

Discussion: ATTP suicidal behavior was more strongly associated with EB and SUD than with SMI. Suicide risk is associated with SUD or EB beyond SMI, so routine clinical encounters in primary care and emergency settings must recognize EB, SUD, and smoking as risks for severe suicidal behavior.

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Clinical Points

- Three-quarters of people with high risk for suicide attempts do not have diagnoses of schizophrenia or recurrent affective disorders, and their suicide risks are more strongly associated with addictive and behavioral disorders.

- Since suicide attempts are strongly related to tobacco smoking and impulsivity, smoking cessation and impulsivity screening should become part of primary care suicide prevention programs.

CHARACTERIZATION AND TIME COURSE OF TRANSDIAGNOSTIC SUICIDE RISK

Suicide, the Leading Cause of Mortality From Injury, Is Difficult to Predict

Suicide is the leading cause of mortality from injury in the United States, exceeding motor vehicle accidents and homicide.[1,2] Among medical causes of death, it exceeds diabetes mellitus.[3] Suicide among military personnel exceeds combat mortality[4] and is the leading cause of non-combat death.[5] Yet, identification of effective prevention remains problematic.[6,7] Mechanisms underlying suicide risk cross psychiatric diagnoses beyond major affective or psychotic disorders,[8–10] making it necessary to look beyond these diagnoses to identify risk-related characteristics that may be missed in non-psychiatric settings. Severe suicide risk can develop rapidly in susceptible people, making prediction difficult.[11,12]

Levels of Suicide Risk

Because most suicides are first attempts,[13–16] susceptibility should ideally be identified before the first attempt.[13,14,16] Surviving a medically severe, potentially lethal suicide attempt is a strong predictor of 5-year all-cause mortality from accident, homicide, and other hazardous behavior, which increases 15-fold in men and 9-fold in women, with a 5,402-fold increase in suicide over the general population.[15] Risk is highest during the first year[17] and persists for over 10 years.[18] Post-hospital survival time correlated negatively with trait impulsivity.[19] Thus, impulsivity, or immediate action dysregulation, contributes to acute suicide risk.

Since fatal first suicide attempts appear unrelated to any specific psychiatric diagnosis, other risk factors must be identified to prevent the transition from ideation to attempt,[13–16] including risk-related problems in potentially high-risk patients who have not received a psychiatric diagnosis.[16] As an initial step, we focused on risk factors in the electronic health record (EHR), comparing 3 risk levels: (1) suicide attempts or severe ideation/plan with hospitalizations (ATTP); (2) suicidal ideation (SI) only, and (3) no SI or behavior (SIB).

Rationale

Suicidal behavior disorder in *DSM-5-TR* crosses diagnoses.[8,9] Fatal first suicide attempts (at least 60% of suicides[13,16]) occur in persons without diagnoses commonly considered to increase suicide risk.[16] Instead, suicide may be associated with (1) clinically noted impulsive or aggressive behavior (ie, externalizing behavior [EB]) and (2) substance use disorders (SUDs), including smoking. Because suicide occurs across and beyond conventional psychiatric diagnoses, evaluation of risk requires identification of characteristics that are identifiable in non-psychiatric settings. Rather than focusing on traditional diagnoses and mental health care settings, we investigated relationships between suicide risk and clinical characteristics, with or without apparent psychiatric diagnoses. In a national community sample of 350,000 Veterans, we used EHR[20,21] data to identify susceptibility characteristics for suicide.

METHODS

Source Population

About 350,000 Veterans in the US Department of Veterans Affairs (VA) Million Veterans Project (MVP; the population recruited with available data at the time of our analyses) provided EHR data via the VA Information and Computing Infrastructure (VINCI) portal. Using the "Hands-off" approach, VINCI Data Navigators provided cross-tabulations of aggregate phenotype counts, *ICD* codes, clinic codes, and risk flags (behavioral and suicide).[20] *ICD-9* codes were converted to *ICD-10* codes. Identifying and genetic information was not available to the authors. Characteristics studied included history of suicidal ideation or behavior, smoking, alcohol and other SUD history, impulsive-aggressive behavior, and recurrent affective or psychotic disorders.

The sample was recruited and the data entered and processed by MVP between 2011 and 2017. This article was developed between April 11, 2020, and October 6, 2021.

Identification of Suicide Risk Categories

Preventing transdiagnostic SIB requires high-risk markers accessible in broad, non-psychiatric populations. We defined 3 sets of characteristics from EHR to compare across risk categories: (1) major psychiatric disorders or severe mental illness (SMI) (major depressive disorder, bipolar disorder, or schizophrenia), (2) impulsivity or impulsive aggression disorders (often referred to as EB), and (3) SUD, including smoking. The suicide risk categories were (1) ATTP (n = 1,269) suicide-risk flag plus hospitalization; (2) SI, ie, suicidal ideation without specific plans or attempts (n = 109,836); and (3) no SIB (n = 242,872). We anticipated relatively high specificity for ATTP, but less for the lower-risk SI-only group.[21]

Characteristics of suicide risk groups. We obtained demographic data from VINCI (characteristics of suicidal behavior groups) and from Radhakrishnan et al[22] (characteristics of the overall study sample). ATTP (mean ± SD age, 59.5 ± 9.1 years) or SI (61.3 ± 13 years) were younger than the general available MVP population (65.9 ± 11.7 years).[22] A higher percentage of women were in ATTP (19%) or SI (12.7%) groups than in the overall

MVP group (7.6%). A higher percentage of African Americans were in the ATTP (22.3%) or SI (23.4%) groups than in the overall MVP group (10.5%).

Definitions of clinical groups. We defined problem drinking as having an Alcohol Use Disorders Identification Test–Consumption (AUDIT-C) score > 3[23] (n = 113,224) and severe alcohol use as meeting *ICD* codes for withdrawal or detoxification (F10.23; n = 2,286). Prevalence of addictions was measured by outpatient treatment referral for SUD (n = 56,338), greater than the number with a corresponding SUD diagnosis code. We defined smoking as current cigarette use (n = 49,853).

EB markers were (1) restricted/monitored hospital access because of aggressive or other inappropriate behavior (n = 1,597); (2) *ICD* code for impulsivity- or aggression-related problems in EHRs, including borderline (F60.3) or antisocial (F60.2) personality disorders, intermittent explosive disorder (F63.81), and unspecified impulsive disorder (F63.9) (n = 3,097); and (3) history of arrest, probation, or incarceration (*ICD* code Z65.3) (n = 4,203). Overall, 8,146 had 1 marker, 673 had 2, and 72 had all 3. These conditions are probably underdiagnosed, especially in non-psychiatric settings, possibly reducing sensitivity but increasing specificity.

We classified major psychiatric disorders from EHRs, recognizing that potential disadvantages of EHRs[7,21,24,25] may be outweighed by their efficiency for studying large samples without additional participant burden of specialized assessments. We used multiple diagnostic codes for each disorder and characteristic[21,25,26] because these *ICD* ranges balanced clinical consistency with local or clinician-related variation and diagnostic instability. The *ICD-10* codes used were F20–F29 for schizophrenia, F30 or F31 for bipolar disorder, and F32 or F33 for major depressive disorders.

Statistical Methods

We calculated risk ratios (RRs) rather than odds ratios (ORs) along with confidence intervals (CIs) because large sample sizes distort ORs, overestimating their effects.[27] Analyses used STATA 16 (College Station, Texas).

RESULTS

Clinical and Behavioral Characteristics of Suicide Risk

Suicide risk and psychiatric diagnosis. Table 1 shows suicide-related RRs for Veterans with EHR diagnoses of SMI: major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia. For ATTP, 369 (29.1%) of 1,269 had diagnoses of

Table 1. Suicidal Ideation and Behavior: Psychiatric Diagnosis[a]

Diagnostic Group	Suicide Risk Group, n (Percent of Total Study Population)		
	ATTP, n = 1,269 (0.36%)	SI, n = 109,836 (31.03%)	No SIB, n = 242,872 (68.61%)
Depression (n = 13,842)			
n	158	10,185	3,270
RR (95% CI)	3.45 (2.96–4.12)	2.51 (2.48–2.54)	0.34 (0.33–0.35)
ES, Cohen *d*	1.04	1.67	−1.82
Bipolar disorder (n = 5,898)			
n	147	4,748	830
RR (95% CI)	7.78 (6.52–9.16)	2.67 (2.63–2.70)	0.20 (0.19–0.22)
ES, Cohen *d*	1.85	2.07	−2.55
Schizophrenia (n = 2,656)			
n	64	2,039	482
RR (95% CI)	7.35 (5.49–9.03)	2.50 (2.45–2.56)	0.26 (0.24–0.29)
ES, Cohen *d*	1.74	1.79	−2.13
Any diagnosis (n = 22,249)			
n	369	16,972	4,582
RR (95% CI)	6.07 (5.38–6.85)	2.71 (2.68–2.73)	0.315 (0.307–0.322)
ES, Cohen *d*	1.58	1.87	−1.96

[a]The table shows mean and 95% CI of RR for ATTP, SI, and No SIB in patients with depression, bipolar disorder, schizophrenia, or any of the 3 diagnoses, as defined in Methods section. No SIB reflects apparent protective effect, against SIB in general, of absence of the condition.
Abbreviations: ATTP = severe suicide attempt, ES = effect size, RR = risk ratio, SI = suicidal ideation, SIB = suicidal ideation or behavior.

SMI, compared to 15.5% of those with SI. Therefore, about 71% of ATTP did not have an SMI diagnosis. In the ATTP group, those with schizophrenia and BD had RRs significantly greater than those with MDD. Participants with BD had the highest RR for SI. RRs were higher for ATTP than for SI. ATTP RR was substantially lower in the MDD group than in the other groups. Not having one of these diagnoses reduced RR for ATTP and SI to less than 1, suggesting that not having that diagnosis had protective effects against SIB in general.

Externalizing, impulsive-aggressive behavior and suicide risk. Table 2 shows that EBs expressed as impulsive and/or aggressive behavior are related to apparent suicide risk. RRs for ATTP were substantially higher among those with behavioral flags and behavior-related diagnosis than among those with recurrent psychiatric diagnoses (Figure 1). Further, RRs for ATTP were substantially higher than for SI. Veterans with impulsivity-related problems had the largest ATTP RRs (25.4) in the study population. Over three-fourths of the Veterans noted in Table 2 had histories of SI (6,448/8,146); lack of an impulsivity-related diagnosis reduced RR for SIB.

SUD and suicide risk. Table 3 shows that, for alcohol or SUD, RRs were higher for ATTP than for SI. AUDIT-C score > 3 was common in the study sample, present in half with ATTP and about one-third of the overall group with SIB. This threshold score for potential problem drinking[23] can lead to suggested referral for evaluation and treatment. History of alcohol withdrawal or need for detoxification increased the RR for ATTP by 4-fold relative to problem drinking. This finding may arise from susceptibility to bouts of out-of-control drinking, which is common immediately before suicide attempts even in those without regular drinking or a diagnosed alcohol use disorder.[28,29] Two-thirds of the Veterans in SUD treatment had histories of suicidal ideation; RR for ATTP was 5 times that for SI and almost twice the RR for ATTP in BD or schizophrenia.

Cigarette smoking and suicidal behavior. Table 3 shows RRs for smoking and suicidal behavior. About 14% (49,853) had a

Table 2. Suicidal Ideation and Behavior: Impulsivity and Aggression (Externalizing Behavior)[a]

Diagnostic Group	Suicide Risk Group (% of Total Study Population)		
	ATTP, n = 1,269 (0.36%)	SI, n = 109,836 (31.03%)	No SIB, n = 242,872 (68.61%)
Impulsivity diagnosis (n = 3,097)			
n	282	2,732	133
RR (95% CI)	25.4 (22.1–29.1)	2.89 (2.85–2.93)	0.062 (0.053–0.073)
ES, Cohen *d*	3.62	2.85	−4.88
High-risk flag (n = 1,591)			
n	103	1,121	264
RR (95% CI)	19.6 (16.1–23.8)	2.28 (2.21–2.36)	0.241 (0.216–0.269)
ES, Cohen *d*	3.16	1.43	−2.26
Incarceration/arrest (n = 4,203)			
n	94	3,237	778
RR (95% CI)	6.66 (5.41–8.20)	2.53 (2.48–2.57)	0.267 (0.251–0.285)
ES, Cohen *d*	1.68	1.81	−2.11
Any (n = 8,146)			
n	350	6,448	1,038
RR (95% CI)	16.2 (14.3–18.31)	2.65 (2.62–2.68)	0.182 (0.172–0.193)
ES, Cohen *d*	2.83	1.99	−2.74

[a]The table shows means and 95% CI of RR for ATTP, SI, and No SIB in patients with an impulsivity-related diagnosis, restriction from the facility because of ATTP disruptive behavior, incarceration/arrest, or any of these 3 conditions, as defined in Methods section. No SIB reflects apparent protective effect of absence of the condition.
Abbreviations: ATTP = severe suicide attempt, ES = effect size, RR = risk ratio, SI = suicidal ideation, SIB = suicidal ideation or behavior.

smoking-related *ICD* code. Among smokers, as with those with recurrent psychiatric disorders, RRs were significantly higher for ATTP than for SI; not smoking had a protective effect. In the ATTP group, 45% (574/1,269) were smokers, a rate 3 times greater than that for the entire MVP sample. Over 50% (27,694/49,853) of smokers had SI histories.

Figure 1 contrasts the differences in the strengths of association between smoking RR and the RR for two types of suicidal behaviors (ATTP vs SI only) across MDD, BD, schizophrenia, posttraumatic stress disorder (PTSD), SUD, and EB. The ATTP group shows a strong linear trend by disorder between the RR for smoking and the RR for suicide attempts (r^2 of 0.95, $P < .001$), whereas within the SI group there was no association by disorder ($r^2 = 0.09$, NS). In the overall model, there was a highly significant interaction between RR for smoking and RR for SI vs ATTP ($F_{3,11} = 88.3$, $P < .001$; interaction $P < .001$). Therefore, in addition to its direct effects on suicidal behavior, smoking increased apparent susceptibility to conditions with high RR for ATTP, without effect on RR for SI.

DISCUSSION

Identifying Risk in General Clinical Settings: Mechanisms and Clinical Features

Suicidality in Veterans was related to SMI, impulsive-aggressive EB, and SUDs, including alcohol abuse and smoking. Notably, about 71% (900/1,269) of the ATTP group did not an SMI diagnosis (Table 1), implicating transdiagnostic mechanisms in suicidality.[8,9,16] The ATTP group had high RR for ATTP, suggesting that concurrent or preexisting EBs or SUDs are likely to increase suicide risk in Veterans with SMI.

Community- or medical system–based practices can assess these SUD and EB risk factors in EHRs.[22] Problems related to EB had the strongest relationship to suicide risk (Table 2). EBs are typically underreported, but clearly merit more careful consideration and screening in primary care settings. The EHR provides indirect measures of behavior regulation; more validated, clinically feasible, direct measures of these EBs are needed.

Neurobehavioral Mechanisms Potentially Underlying Suicide Risk and Behavior

Suicidal behavior links long-term sensitization to addictive or other sensitizing stimuli and immediate impulsive behavior dysregulation.[30,31] Table 1 shows that nearly three-fourths of the ATTP sample did not have schizophrenia or a major affective disorder, though suicidality is strongly associated with impulsivity.[10] Tables 2 and 3 show that risk for suicide was strongly related to EB and SUD. Effects of smoking as an SUD on suicidality may be enhanced by prominent roles of nicotinic brain receptors in impulsivity and sensitization related to other stimuli,[32–36] as discussed later in this section.

Persistent effects on immediate behavior: sensitization and SUD. In susceptible individuals, highly stressful or rewarding stimuli produce behavioral sensitization and cross-sensitization, disrupting regulation of reward, arousal, and action.[31] Sensitization combines anhedonia and impulsivity and predisposes to addictive and suicidal behavior.[35–37] Table 3 shows that high risk for suicide was strongly related to SUD. Further, suicide risk had a dose-response relationship to the severity of alcohol problems with substantially higher risk for alcoholism with severe complications than for problem drinking (AUDIT-C score > 3) (Table 3). Smoking increased

Figure 1. Risk Ratios for Smoking and Suicidal Behaviors[a]
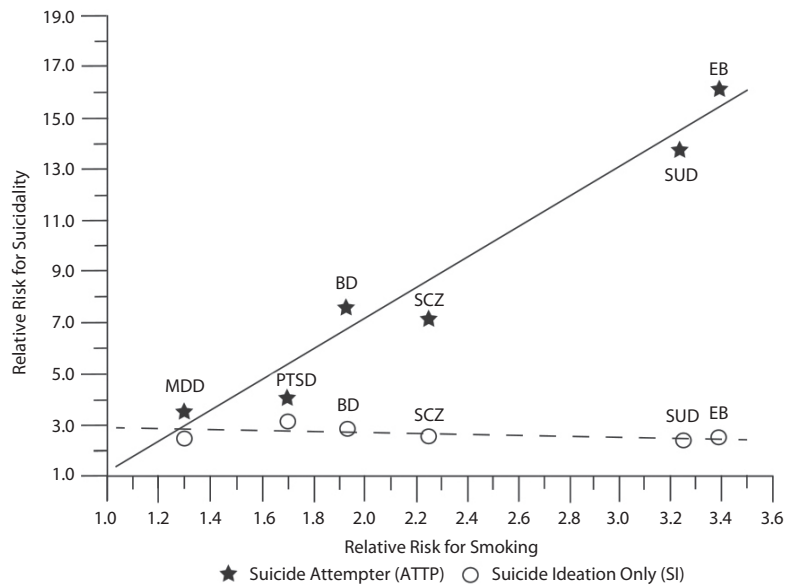
[a]The figure shows risk ratios (RRs) for smoking versus RR for suicide attempter (ATTP) and suicidal ideation only (SI). The regression line for ATTP has an r^2 of 0.95 ($P < .001$); for SI, $r^2 = 0.09$. The overall model has $F_{3,11} = 88.3$, ($P < .001$); interaction between ATTP and SI has $P < .001$. EB includes participants with at least 1 of the 3 conditions in Table 2.
Abbreviations: BD = bipolar disorder, EB = externalizing behavior, MDD = major depressive disorder, SCZ = schizophrenia, SUD = substance use disorder.

Table 3. Suicidal Ideation and Addictive Behavior[a]

Diagnostic Group	Suicide Risk Group (% of Total Study Population)		
	ATTP, n = 1,269 (0.36%)	SI, n = 109,836 (31.03%)	No SIB, n = 242,872 (68.61%)
SUD treatment (n = 56,338)			
n	919	35,276	19,224
RR (95% CI)	13.87 (12.27–15.68)	2.50 (2.48–2.52)	0.454 (0.449–0.459)
ES, Cohen d	2.57	1.37	−1.53
	2.57	1.37	−1.53
Alcohol withdrawal/detoxification (n = 2,286)			
n	77	1,689	520
RR (95% CI)	9.94 (7.92–12.47)	2.40 (2.34–2.46)	0.34 (0.306–0.356)
ES, Cohen d	2.16	1.62	−1.79
AUDIT-C score > 3 (n = 113,224)			
n	672	43,724	68,156
RR (95% CI)	2.39 (2.14–2.67)	1.41 (1.39–1.42)	0.829 (0.825–0.834)
ES, Cohen d	0.70	0.40	−0.44
Cigarettes (n = 49,853)			
n	574	27,694	21,585
RR (95% CI)	5.04 (4.51–5.63)	2.06 (2.04–2.08)	0.34 (0.33–0.35)
ES, Cohen d	1.38	1.03	−1.03

[a]The table shows means and 95% CI of RR for ATTP, SI, and No SIB in patients with assignment to SUD treatment, alcohol withdrawal or detoxification, AUDIT-C score > 3, or cigarette smoking, as defined in Methods section. No SIB reflects apparent protective effect of absence of the condition.
Abbreviations: ATTP = severe suicide attempt, AUDIT-C = Alcohol Use Disorders Identification Test–Consumption, ES = effect size, RR = risk ratio, SI = suicidal ideation, SIB = suicidal ideation or behavior.

severe suicide risk independently, but also was increased in the Veterans with SMI and other SUDs, which additively increase risk. Nicotine directly and indirectly increases sensitization[38,39]: in addition to being a sensitizing stimulus, nicotinic activation is required for sensitization to other stimuli,[39,40] consistent with the relationships between RRs for smoking and severe suicidal behavior noted in Figure 1. However, sensitization is not due to nicotinic mechanisms alone, and it requires other factors including dopaminergic D_2,[41] noradrenergic $α_1$,[41] and glutamatergic[42] activation. Thus, medicines that reduce sensitization would potentially prevent smoking and suicide.

Development of SUD may require behavioral sensitization.[43,44] Cross-sensitization occurs across SUD substances[45]; for example, early onset of smoking and alcohol use together is strongly associated,[46] and alcohol dependence

and smoking each increases the likelihood of the other by about 4-fold.[33] Cross-sensitization also occurs between SUD and stress-related stimuli[37] as shown in humans with PTSD-inducing stressors.[47] Susceptibility to sensitization varies widely across individuals, potentially modifying behavior, comorbidities, and illness, but developing SMI does not appear to require sensitization.[48,49] Apparent sensitization from coexisting SUD, previous trauma, or many previous suicide attempts is associated with increased risk for suicidal behavior in bipolar disorder and across diagnoses.[13,32,33] Therefore, suicide risk in Veterans with SMI may be related to coexisting sensitization-related disorders such as SUD or EB[22,33] (Table 3).

Smoking may promote sensitization directly and indirectly. Smoking, a common SUD, has a transdiagnostic effect on suicide risk (Table 3) and a strong association with EB for ATTP (Figure 1). Figure 1 further shows that RRs between clinical groups and smoking correlated strongly for ATTP ($r^2 = 0.95$) but not for SI ($r^2 = 0.09$), with a highly significant interaction between smoking and suicide risk for the ATTP group ($P < .001$). Nicotine-related mechanisms may, therefore, interact with other characteristics to specifically increase RR for ATTP suicidal behavior across a range of clinical conditions. These two strong associations for smoking may reflect an underlying disruption of action regulation that is increased because smoking delivers nicotine rapidly to the brain.[13,17–19,34–37] Nicotine inhalation through vaping also delivers nicotine rapidly to the brain and increases suicidal behavior and attempts, perhaps especially in adolescents.[50] Adolescent nicotine use predicts adult suicide.[51] Retrospective[52,53] and prospective[54–57] studies in large non-psychiatric populations, including Veterans and non-Veterans, show that smoking is associated with increased suicide. Greater smoking severity increases suicide risk, regardless of diagnosis and adjusted for demographic and health characteristics.[9,52–57] This association suggests involvement of nicotine in transdiagnostic mechanisms of risk. A meta-analysis[58] based on a sample of 1.4 million adults reported increased suicide rates by 24% for each 10 cigarettes smoked daily (RR = 1.24; 95% CI, 1.20–1.28). A more recent meta-analysis[59] showed that ORs for smoking and suicide increased progressively from ideation to attempt to death. People at high risk of suicide also have increased mortality from accidental injuries; death from injury is greater in heavier than in lighter smokers, independent of age, race, gender, alcohol use, seat belt use, education, and marital status.[58] Smoking also predicts suicide risk in patients with major depressive[60] and bipolar[61] disorders. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; n = 34,653), a national American adult survey, found that lifetime and past-year nicotine dependence was associated with lifetime and past-year suicide attempts, regardless of diagnoses.[62] Suicide risk was lower in nicotine-dependent people who had quit than in current smokers.[62]

Immediate regulation: impulsivity. Table 2 shows that the strongest predictors of risk were EBs. Impulsivity as manifested in EB results from an imbalance between facilitation and inhibition of action[36] and predisposes to suicide.[33,36] Trait impulsivity predisposes to behavioral sensitization,[31] increasing addiction risk. Impulsivity-related noradrenergic hyper-functioning[36,63] impairs prefrontal cortex inhibitory protections against suicide.[63,64] Action-impulsivity, with impaired regulation of behavioral inhibition, occurring before conscious awareness,[65] predisposes to suicidal and other ATTP-related behavior.[31,66]

Two aspects of impulsivity are especially relevant to suicide: (1) "Impulsive" versus "planned" attempts is a false dichotomy. Impulsivity is integral to suicidal behavior, but its role and interactions with other characteristics vary.[31] Trait impulsivity is higher with both a suicide plan and an attempt than with an attempt or plan alone.[67] Momentary impulsivity can make someone more likely to act on a previously formulated plan.[11,12,65,66] (2) People are generally not impulsive all the time. Impulsivity appears in susceptible individuals[11,12] as a latent trait, elicited by overstimulation or stressors and facilitated by behavioral sensitization.[31]

Combined impulsivity and hopelessness in ATTP behavior. Impulsivity combined with hopelessness may predict overt suicidal behavior more than either alone.[68,69] Impulsive individuals can experience hopelessness, dissociated from depressed mood, predisposing to suicidality.[31,69–71] State-dependent impulsivity combined with stress or depressive symptoms can produce negative urgency,[35,71–73] combining impulsivity and anhedonia across diagnoses and linking smoking to suicide.[65,74] Smoking increases stress-induced risk-taking; cumulative stressors can combine with nicotine-facilitated sensitization and exacerbate suicide risk,[32] perhaps especially in those already predisposed to impulsivity or negative urgency (Figure 1).

Limitations and Future Study Implications

Our study has several limitations. (1) RRs were not adjusted for specific demographic characteristics due to the deidentified nature of the database. (2) Clinical psychiatric rating scales, formal diagnostic interviews and details of suicide-related attempts, plans, and hospitalizations were not available for the sample. However, presence of suicide risk flags or hospitalizations increased our sensitivity for severe disturbances. (3) We could not directly assess interactions across risk factors. (4) This EHR-based study had variations in record-keeping across facilities and underdiagnosis or underrecognition of relevant disorders and problems. (5) The time covered by EHRs varied widely over the sample, with little information about relative timing of events, but we used EHRs to identify trait-like measures, reducing the importance of apparent time courses in the EHR. (6) The "SI" group was large and may have overestimated the number of Veterans with sustained or serious rather than transient SI. (7) While Figure 1 demonstrates a strong potential relationship between smoking and disorders specifically associated with high suicide risk, it is likely that the disorder groups overlapped, though this would not alter the direction of these relationships. In summary, this routinely available

clinical information provided pragmatic access to a large and generalizable sample, minimizing participant burden and enabling feasible data collection.[24]

suggest an important role of transdiagnostic mechanisms of sensitization and impulsivity,[31] possibly modeled by smoking effects,[30] as targets for suicide prevention.

We suggest two main clinical implications. (1) Patients should be screened efficiently for impulsive behaviors (ie, EB) and SUD, including sporadic bouts of binge substance use. (2) Nicotine-related interactions with cholinergic, noradrenergic and glutamatergic systems may be a neurobiological model for suicide risk[38,39,41] offering novel pharmacologic or psychotherapeutic targets.

Conclusions

Recognizing SUD and EB could improve identification of Veterans and other community members at risk for attempting and committing suicide and improve design of effective early interventions. Overall, suicide may be more strongly related to SUD or EB than to SMI, and we

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POSTTEST

To obtain credit, go to CMEInstitute.com to take this Posttest and complete the Evaluation. A $10 processing fee is required.

1. **A 32-year-old man was brought to the emergency department (ED) because of intrusive, threatening behavior. He appears irritable, impulsive, and labile but denies depressed mood or suicidal ideation. On interview, he criticizes your appearance and interviewing technique. A brief record review shows that he was recently started on venlafaxine treatment for major depressive disorder (MDD). You decide that**

    a. Because he had not received a specific diagnosis of schizophrenia or bipolar disorder, no intervention related to suicide prevention is needed.

    b. Regardless of the clinical diagnosis he received, his appearance and behavior are not consistent with suicide risk and thus no intervention related to suicide prevention is needed.

    c. Combined or alternating depression and activation can be associated with rapidly fluctuating suicide risk; careful observation and probable admission are needed.

    d. His symptoms indicate high risk for suicidal gestures but not for severe suicidal behavior.

2. **Cigarette smoking**

    a. Can increase suicidality but not in people who already have a major psychiatric disorder.

    b. Increases suicidality, but only in late life.

    c. Should be replaced with vaping to reduce suicide risk.

    d. Increases suicide risk directly and heightens susceptibility to conditions with high suicide risk.

3. **A woman and her husband are arguing in the ED. She states he has taken her gun away; he says he "got rid of it." She states that she does not feel safe without it because she is being watched by people who plan to kill her. On interview, she is frightened and withdrawn. Both smell like alcohol but deny habitual drinking. Relevant factors include**

    a. Alcohol can protect against suicidal behavior because of its activating effects.

    b. About twice as many people die from homicide as suicide.

    c. She appears to have a psychotic disorder, so her risk for suicide is lower than it would be with MDD.

    d. Through sensitization, early trauma can increase drug use associated with more recent trauma.