

## Antecedents and sex/gender differences in youth suicidal behavior

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### Abstract

Suicide is the second leading cause of death in youth globally; however, there is uncertainty about how best to intervene. Suicide rates are typically higher in males than females, while the converse is true for suicide attempts. We review this "gender paradox" in youth, and in particular, the age-dependency of these sex/gender differences and the developmental mechanisms that may explain them. Epidemiologic, genetic,

neurodevelopmental and psychopathological research have identified suicidal behaviour risks arising from genetic vulnerabilities and sex/gender differences in early adverse environments, neurodevelopment, mental disorder and their complex interconnections. Further, evolving sex-/gender-defined social expectations and norms have been thought to influence suicide risk. In particular, how youth perceive and cope with threats and losses (including conforming to others' or one's own expectations of sex/gender identity) and adapt to pain (through substance use and help-seeking behaviours). Taken together, considering brain plasticity over the lifespan, these proposed antecedents to youth suicide highlight the importance of interventions that alter early environment(s) (*e.g.*, childhood maltreatment) and/or one's ability to adapt to them. Further, such interventions may have more enduring protective effects, for the individual and for future generations, if implemented in youth.

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**Key words:** Suicide; Attempted suicide; Sex; Gender; Child; Adolescent; Review

**Core tip:** Previous research has demonstrated clear and consistent sex-/gender-specific patterns in the continuum of suicidal behaviour. Here, we review epidemiologic, genetic, neurodevelopmental and psychopathological research to identify and discuss explanations for these findings. We propose antecedents to youth suicide and highlight the importance of early intervention. Understanding the mechanisms underlying sex/gender differences in youth suicidal behaviour could help identify strategies to reduce suicide risk across the lifespan.

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## INTRODUCTION

### Problem

Suicide is the second leading cause of death among young people globally with substantial social and economic costs<sup>[1]</sup>. While youth suicide rates vary widely across and within countries<sup>[2,3]</sup>, in developed countries, with good-quality vital registration data<sup>[1]</sup>, rates are at least 2 to 3 times higher in boys than girls<sup>[4,5]</sup>. Suicide rates have declined in boys since the 1990s, but there is concern that in some countries, rates have increased for girls<sup>[6]</sup> and the downward trend in boys, is now reversing<sup>[7]</sup>. However, it is unclear how best to intervene to reduce suicide risk

in youth<sup>[8]</sup>-a problem that may be resolved, in part, by addressing sex/gender differences in suicidal behaviours.

### Gender paradox

Herein, the “gender paradox”-higher suicide attempt rates in females but higher suicide rates in males-merits attention<sup>[9]</sup>. In particular, this paradox is age dependent. For suicide attempt rates, the sex/gender difference (F > M) increases with age peaking in mid adolescence<sup>[10-13]</sup>, whereas for suicide rates, the sex/gender difference (M > F) steadily climbs until early adulthood<sup>[1]</sup>. Although suicide attempt data are self-reported, hospital presentation data reveal the same pattern<sup>[14-17]</sup> and suicide misclassification seems an unlikely explanation<sup>[18]</sup>. Why do these changes occur and could this knowledge help us reduce suicide risk in boys and girls?

### Purpose of this review

We build on developmental perspectives of youth suicidal behaviours<sup>[2,19]</sup> to advance our understanding of the mechanisms underlying the gender paradox, which may help focus approaches to youth suicide prevention. In the following sections, we examine the continuum of suicidal behaviours in boys and girls, synthesizing findings from epidemiologic, genetic, neurodevelopmental and psychopathology research to propose key mechanisms. We then highlight how these mechanisms operate within the sex/gender developmental contexts in which youth live, which if modified, may reduce their suicide risk.

### Terminology

“Boys” and “girls” refer to youth ages 10 to 24 years<sup>[20]</sup>. “Sex/gender” is used rather than “sex” or “gender” to signify the complex interplay of social and biological determinants<sup>[21]</sup>. Most findings are limited by dichotomous measures of sex/gender<sup>[22]</sup>, and to Western cultures. We defined suicidal ideation, attempts and suicide according to standard nomenclature<sup>[23]</sup>. Hereafter, hospital presentation data on self-inflicted injuries and poisonings are referred to as “hospital presentations” or when admitted, “hospital admissions”. For both, unless otherwise noted, suicidal intent was unspecified.

## SEX/GENDER DIFFERENCES IN THE CONTINUUM OF SUICIDAL BEHAVIOUR

In this section, we review the epidemiologic evidence for a proposed continuum from suicidal ideation to behaviours, with those attempting and dying by suicide experiencing a greater burden of risk<sup>[24-26]</sup>.

### Suicide attempts

Several factors complicate our understanding of suicide attempts in boys and girls as they age. First, knowledge from community-based samples (*i.e.*, school or household surveys) may be slanted to girls because girls have a higher past year<sup>[27-30]</sup> and lifetime prevalence<sup>[25,29,31,32]</sup> of suicidal ideation and attempts than boys between the ages of 12

to 24. Second, depending on the study design, younger youth may not be well-represented given the prevalence of suicide attempts is highest in mid adolescence, and the lifetime recall of suicide attempts is inconsistent, particularly at early ages<sup>[33]</sup>. Third, community-based surveys tend to represent more common, but less lethal behaviours. For example, although 8.0% of United States students (grades 9 to 12) reported a past year suicide attempt, the proportion reporting their attempt was treated by a doctor or nurse was only 2.7% (higher in girls than boys, 3.6% *vs* 1.8%)<sup>[28]</sup>. The sex/gender difference in youth suicide attempts (F > M) only diminishes among hospital presentations in medically serious suicide attempts (largely self-poisonings)<sup>[34]</sup> and reverses (M > F) with increased lethality of methods (*e.g.*, hanging and firearms)<sup>[35,36]</sup>.

With these caveats, we review prospective community-based studies where the temporal ordering between potential predictors of suicide attempts is less ambiguous, to illustrate cumulative risks and potential causal chains in boys and girls as they age. Suicidal ideation, tied to depression<sup>[10,37]</sup>, is a predictor of a later attempt<sup>[24,37,38]</sup>, but more for girls than boys<sup>[10,26]</sup>. Further, when depression and suicide attempts were compared by age in girls, suicide attempts declined in older girls (narrowing the F > M difference) but depression did not<sup>[10]</sup>, raising the question what accounted for this decline and its relevance to suicide prevention?

Other longitudinal studies have shown that suicide attempt risk is predicted by early adverse environments and early psychiatric morbidity. However, it remains unclear whether boys' and girls' pathways differed. For example, in a New Zealand birth cohort study<sup>[39]</sup>, after adjusting for predictors collected prior to ages 15 to 16: lower socio-economic status (SES) at birth, parental alcohol problems, childhood sexual abuse and poor parental attachment along with predictors collected at ages 15 to 16: neuroticism and novelty seeking, the initially higher risk of a suicide attempt in girls compared to boys between the ages of 15 to 21 was attenuated (RR = 1.73 to 1.17). While tentative, this attenuation of risk hints that the F > M difference in suicide attempts is mediated by one or more of these predictors. Also, this study noted that the predictors' effects were later largely mediated by mental disorders and stressful life events, except for low SES at birth, neuroticism and novelty seeking. That is, the predictive power of early adverse environments on suicide attempts was reduced as youth aged, mediated, in part, by psychiatric morbidity and stressful life events.

Further research indicated that for youth who attempted suicide, psychiatric morbidity was evident earlier than age 15, coinciding with environmental effects. In a study of kindergarten students<sup>[40]</sup> teacher-rated trajectories of anxiousness and/or disruptiveness (between the ages of 6 to 12) predicted lifetime suicide attempts by age 15 to 24. Sex/gender (along with childhood sexual abuse before age 18 and a family history of suicide attempts) remained predictive. Potential sex/gender differences in

these pathways and possible mediators of sex/gender differences were difficult to interpret, though, as the study attrition in boys was 50% and the temporal sequence of events, uncertain. Notably, boys were overrepresented among students with disruptiveness or both trajectories by age 12; however, girls with both trajectories were most likely to report a suicide attempt at ages 15 to 24<sup>[40]</sup>.

### Suicide

We now consider how boys and girls differ along the continuum from suicide attempts to suicide as they age. Given suicide rates are higher in boys and increase with age, samples may be slanted more towards older males. Because youth suicide is rare<sup>[1]</sup>, information from studies of community-based samples often comes from retrospective "psychological autopsies". Such studies typically have small samples and rely on informants' recall, usually family members. Informants may have difficulties reporting on more personal or distant aspects of the decedent's life (*e.g.*, childhood sexual abuse or a suicide attempt). Differential reporting may be overcome by interviewing similar informants for both controls and decedents but problems of statistical power preclude testing some associations. Suicide attempts and suicides share many predictors, including early adverse environments<sup>[2]</sup>; however, the temporal sequencing between predictors, and by sex/gender, has been harder to discern for suicide.

A prior suicide attempt is one of the strongest known predictors of youth suicide<sup>[2]</sup>, but potential sex/gender differences overall, and by age of onset are unclear. Prospective hospital presentation data confirm these youth have a higher suicide risk (about 10 times) than their peers<sup>[41]</sup>. Suicide risk is strongest in the year after the presentation, but remains elevated in subsequent years<sup>[42]</sup>. However, these risks likely differ by age and method. Unlike older samples where a hospital admission with a more lethal method (*vs* self-poisoning) predicts suicide in men and women<sup>[43]</sup>, in youth aged 10 to 18, a hospital presentation for self-cutting (*vs* self-poisoning) is more predictive of suicide<sup>[42]</sup>, a method of lower lethality<sup>[44,45]</sup>, associated with repetition<sup>[42]</sup>. Repeat (*vs* single) hospital presentations are more strongly associated with suicide, particularly in girls<sup>[46]</sup>. However, self-poisonings, usually medication overdoses in Western cultures<sup>[14]</sup>, are the most common hospital presentation among youth<sup>[3]</sup> and sex/gender differences in lethality are not evident here<sup>[44]</sup>.

In a case-control study of suicidal behaviour under age 25, youth who died by suicide and those who made a medically serious suicide attempt shared most predictors, including a prior suicide attempt<sup>[35]</sup>, and only two predictors discriminated these youth: sex/gender and a current mood disorder. Compared to youth who made a medically serious suicide attempt, youth who died by suicide were more likely to be male (81.7% *vs* 45.6%) but were less likely to have a current mood disorder (30.0% *vs* 71.2%). Differential reporting of mood symptoms by the informants seemed less likely given the severity of the events being compared. Supplementary analyses revealed

that the higher proportion of boys among youth who died by suicide was explained by their lower prevalence of a current mood disorder and greater prevalence of a highly lethal method. The possibility that younger age, early adverse environments (*e.g.*, childhood sexual abuse) and dimensional measures of psychiatric morbidity (*e.g.*, impulsive aggression, defined below) might predict more lethal methods was unexplored. Compared to peers, childhood sexual abuse was associated with a medically serious suicide attempt (OR = 7.4) as well as a current substance use disorder (OR = 3.1). However, such comparisons with peers were not reported for youth who died by suicide. While not explicitly tested, a lifetime history of antisocial behaviour (26.7% *vs* 36.8%) or of care for mental health problems (50.0% *vs* 68.8%) appeared less prevalent in youth who died by suicide than among those with a medically serious suicide attempt.

In keeping with the findings on youth suicide attempts<sup>[40]</sup>, a Finnish birth cohort study<sup>[47]</sup> found parent and teacher ratings of anxiety and/or conduct disorder at age 8 predicted later hospital admissions and/or suicides among boys aged 8 to 24. Yet, measures of psychopathology at age 8 were not predictive in girls, implying different pathways and timing of effects in boys and girls.

Collectively, these studies demonstrate important differences between boys and girls in the prevalence and lethality of suicidal behaviours; however, the reasons for these differences and the timing of their effects, critical for prevention efforts, have seldom been studied. Nevertheless, community-based studies support a model of youth suicide attempts whereby their onset is predicted by early adverse environments in concert with differing, early psychiatric morbidity (*i.e.*, neuroticism, anxiousness *vs* novelty seeking, disruptiveness). Past suicidal ideation (and concurrent depression) may be more predictive of suicide attempts in girls than boys, and among girls, most predictive in mid adolescent *vs* older girls. With respect to suicide, the effect of a prior suicide attempt may differ in boys and girls, dependent on the method's lethality and care for mental health problems. Community-based and hospital presentation studies indicate that the proportion of boys (*vs* girls) with a suicide attempt increases with the attempts' lethality and at this end of the continuum, factors other than a current mood disorder seem significant. However, what these factors are (*e.g.*, early adverse environments and/or other types of psychiatric morbidity) and how they may differ in boys and girls with age, influencing mental health care is uncertain. In the following sections, we turn to other lines of evidence to improve our understanding of the inter-relationships between early environments, psychiatric morbidity, help-seeking and the gender paradox.

## SEX/GENDER DIFFERENCES IN GENETIC VULNERABILITIES AND SUICIDAL BEHAVIOUR

Suicidal behaviours aggregate within families after

controlling for familial transmission of mental disorders (unlike suicidal ideation) and this transmission does not seem to be explained by imitation effects<sup>[48]</sup>. Further, there is some evidence that the elevated risk of suicide among offspring exposed to a parent's suicide is highest among youth who were under the age of 17 when exposed. Impulsive aggression, (*i.e.*, reacting with hostility or aggression to frustration or provocation)<sup>[48]</sup>, may mediate the familial transmission, and stem from genetic vulnerabilities and/or adverse early environments<sup>[49]</sup>. It has been hypothesized that vulnerabilities to suicide arise from gene/environment interactions occurring during critical windows of brain development. Identifying sex/gender developmental differences may help focus targets for intervention<sup>[50,51]</sup>.

More specifically, there is evidence that early adverse life events, particularly childhood maltreatment (physical or sexual abuse, neglect), have an enduring impact on the brain both through genetic vulnerabilities (*e.g.*, variation in single nucleotide polymorphisms) and telomere erosion making some individuals more vulnerable to brain changes and through "epigenetics"<sup>[52-56]</sup>: changes in gene expression mediated by altered chromatin without modifying the DNA sequence<sup>[57]</sup>. While the genetic structure (genotype) transmitted to offspring from their parents at conception is unchanged, offspring gene expression may be modified by environmental exposures. Several epigenetic mechanisms have been proposed, which could in theory, influence sex/gender differences in psychopathology, (*e.g.*, sex hormone induced differences and/or differential exposures to environmental risk factors, including drugs of abuse and child maltreatment)<sup>[54,58]</sup>. There is an ongoing debate about parent-to-child transmission of epigenetic effects<sup>[59]</sup>.

Youth who die by suicide experience child maltreatment more often than their peers and at an earlier age than their peers—in one study the respective proportions were: 60.0% *vs* 18.0% by age 9 and 77.0% *vs* 34.0% by age 14<sup>[60]</sup>. Thus, it seems that for many youth who die by suicide, their neurodevelopment was affected, and dependent on their age, may have had an enduring impact, creating a "diathesis"<sup>[61]</sup> affecting their ability to flourish cognitively, emotionally and behaviourally in their environments<sup>[40,53]</sup>. We highlight childhood sexual abuse, as it has been found to be associated with suicide attempt(s), independently of other forms of child maltreatment in cross-sectional studies among youth. Further, the magnitude of this association is stronger in boys than girls<sup>[62,63]</sup>. Yet, this sex/gender difference is not evident in adults<sup>[64]</sup> implying the nature and timing of the abuse differs for boys and girls. In fact, there is some evidence that for boys, childhood sexual abuse typically occurs prior to puberty; is more forceful and usually perpetrated by another male. However, boys are less likely than girls to disclose the abuse. The lack of this sex/gender difference in adults may be explained, in part, by differential reporting and/or selection biases, including mortality<sup>[62,64]</sup>.

Given that brain plasticity lessens in adulthood, interventions that alter environment(s) and/or an individual's

adaptations to it, may have more enduring protective effects (*i.e.*, for those individuals and future generations) if first implemented in youth. In the next section, we describe how neurodevelopmental disruptions may give rise to different types of psychopathology in boys and girls which may then, contribute to the gender paradox.

## SEX/GENDER DIFFERENCES IN NEURODEVELOPMENTS AND PSYCHOPATHOLOGY

Increasingly, psychopathology is viewed within a neurodevelopmental lens<sup>[58,65,66]</sup>. However, current nosology systems [*e.g.*, the Diagnostic and Statistical Manual (DSM) for Mental Disorders and the International Classification of Diseases] are based on categorical clusters of signs and symptoms which lack neurobiological substrates. Thus, mental disorders are defined and measured relying heavily on how signs and symptoms are communicated and considered abnormal within cultures. Lack of knowledge, stigma and discrimination may prevent disclosing symptoms. Suicidal behaviours are still illegal in some countries<sup>[1]</sup>. It is only recently, (*i.e.*, within DSM 5), that suicidal behaviours have been identified separately from mental disorders, (*i.e.*, not presumed to be fully explained by a mental disorder)<sup>[67]</sup>. Increasingly, research is employing dimensional systems, including biological measures, to better capture sub threshold conditions and changes over time. Categorical systems have been criticized for producing somewhat arbitrary boundaries, possibly confusing temporal sequences and shared/unique etiologies. Nonetheless, standard diagnostic criteria across time and place provide useful “phenotypic” information which can be refined, iteratively, as knowledge grows about etiological substrates “ranging from environmental disruptions to genetically determined syndromes”<sup>[65]</sup>. These paradigm shifts may be particularly helpful for youth suicide prevention efforts, improving early detection. More specifically, although nearly 90% of youth who died by suicide were identified as having a mental disorder in psychological autopsy, up to 40% under age 15 did not meet diagnostic thresholds<sup>[2]</sup>. Further, many of the youth diagnosed with mental illness after death, may have been previously undiagnosed and untreated for mental illness.

In recent years, structural and functional magnetic resonance imaging studies have illustrated normal and abnormal brain development in youth. Puberty begins around age 8 to 11 for girls and for boys, on average, one year later<sup>[68]</sup>. During puberty, the brain is more “plastic”, allowing youth to explore and master changing environments requiring greater autonomy. Over time, grey matter peaks and then declines while white matter increases (myelination), reflecting the brain’s organizational changes where the most frequently used connections are strengthened and preserved. Disrupting these processes can influence the onset of mental disorder. For example,

accelerated grey matter loss has been found in youth who transition to psychosis<sup>[69]</sup>. With maturation, the prefrontal cortex becomes increasingly involved in modulating responses to novel or rewarding events. Exogenous behaviours (automatic responses to external stimuli – one definition of impulsivity)<sup>[70]</sup> -tend to become balanced by more endogenous, goal directed, planning behaviors<sup>[68,71]</sup>. Indeed, engagement in “risky” behaviours seems to peak during adolescence but then decline<sup>[72,73]</sup>, not unlike the age-suicide attempt distribution evident in girls<sup>[10]</sup>. Given sex-by-age interactions occur in cortical development, including faster myelination in girls than boys<sup>[74]</sup>, disruptions in neurodevelopment, prior to or during this time may solidify with maturation contributing to the onset of different psychopathologies in boys and girls.

The way youth exert cortical control in response to threats and rewards depends upon the subcortical brain. Indeed, heightened behavioural inhibition has been posited to place youth at greater risk for mood and anxiety disorders<sup>[75]</sup>. It is noteworthy then, that the amygdala is highly connected to both cortical and subcortical brain regions and is one of the few regions known to contain sex hormone receptors. Thus, dependent on early social and biological environmental exposures, which may vary by sex/gender, amygdala development seems critical in how boys and girls appraise and respond emotionally and behaviourally to their environments. The amygdala is involved in face processing (social cues), fear learning and extinction and can modulate HPA activity (the fight or flight stress response). The rate of amygdala growth is related to pubertal development in boys and girls<sup>[76,77]</sup>. Girls tend to have larger left amygdala volumes than boys (aged 10 to 22 years)<sup>[78]</sup>. Further, a recent longitudinal study found that increased amygdala growth from ages 12 to 16 years was associated with onset of depression in girls (ages 12 to 18) but not boys<sup>[79]</sup>. Reduced amygdala activity has been linked to callous-unemotional traits, such as reduced responses to other’s fear, mediating proactive (*vs* reactive) aggression in conduct disordered youth<sup>[80]</sup>. The above neurodevelopmental findings have some consistencies with knowledge about sex/gender differences in youth mental disorders. In the following section, we review sex/gender differences in the general population of youth and then, among youth who die by suicide.

## SEX/GENDER DIFFERENCES IN TYPES OF MENTAL DISORDERS AND SUICIDE

Prospective and retrospective studies confirm that 50%-70% of adults with a mental disorder had one in their youth<sup>[81]</sup>. In particular, disruptive or “externalizing” disorders: Attention Deficit Disorder with Hyperactivity (ADHD), Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD), are more prevalent in boys than girls, and internalizing disorders: Depression, Anxiety, including Post-Traumatic Stress Disorder, more prevalent in girls than boys<sup>[82,83]</sup>. ADHD declines with age, whereas

depression and substance use disorders increase<sup>[84]</sup>. Anxiety disorders tend to precede depression (with some continuing to co-occur with depression)<sup>[75]</sup>. Externalizing disorders (rather than internalizing ones) seem to precede adult substance use disorders and there is continuity between youth and adult substance use disorders<sup>[81]</sup>. Substance use disorders may be more prevalent in boys than girls<sup>[82]</sup>.

A puzzling question pertaining to sex/gender differences in psychopathology is why do seemingly different psychopathologies, internalizing and externalizing, co-occur? Population-based research indicates that ODD is linked to such co-occurrences, not CD or ADHD<sup>[85]</sup>. Further, the ODD link seems to be explained by irritability and has been posited as a mood disorder variant<sup>[85,86]</sup>, newly captured in DSM 5 as Disruptive Mood Dysregulation Disorder<sup>[87]</sup>. Still, the need to better characterize irritability and its persistence over time is recognized given that irritability may precede and/or be better explained by other disorders (*i.e.*, personality and/or bipolar spectrum disorders often not identified in population-based studies of youth<sup>[88,89]</sup> but may vary in age of onset and by sex/gender)<sup>[90,91]</sup>.

For example, there is some evidence that when externalizing behaviours (especially those before age 13) precede depression, youth are more likely to experience an irritable depression at age 18<sup>[92]</sup>. Further, among depressed youth, those most likely to be depressed and irritable (*vs* depressed, not irritable) were boys (OR = 4.26). Notably, depressed boys did not differ from depressed girls on non-episodic irritability but rather, “a change in the child’s usual liability to be precipitated into anger”<sup>[93]</sup>. In contrast, when girls were depressed and irritable, they exhibited more CD (but not ODD symptoms) than boys. Most of the depressed youth (70%), stayed in the same depression-irritability group into adulthood (ages 19 to 21)<sup>[93]</sup>, implying that reactive (*vs* proactive) aggression persisted among depressed and irritable boys (*vs* girls). Aggression, (intent to hurt or harm another) is more likely physical in boys and indirect (relational) in girls<sup>[94]</sup>. Instrumental or proactive aggression has been related to psychopathy, whereas, reactive aggression is thought to arise from difficulties regulating emotional responses to threats<sup>[95]</sup>.

As noted earlier, nearly all youth who died by suicide were identified in studies as having a mental disorder. The most common, strongest risk factors were prior mood, substance-use and disruptive disorders. Combinations of these disorders lead to higher risks. Given mental disorders, particularly mood and substance use disorders, are more common in suicides among older youth<sup>[96-98]</sup>, disruptive disorders would seem implicated in younger youth, consistent with studies on youth suicide attempts<sup>[39,40,47]</sup>. Compared to girls, boys’ suicides more often include prior disruptive and substance use disorders. In contrast, girls’ suicides are more likely to include prior mood or eating disorders<sup>[2,97-100]</sup>. Schizophrenia, though rare, is also a strong risk factor. Still, it may be more common in boys than girls, due to earlier onset in boys<sup>[101,102]</sup>.

Few studies of youth suicide have employed dimensional measures of psychiatric morbidity. In one, dimensional measures of harm avoidance (correlated with anxiety and mood disorders) and irritability (correlated with substance abuse) and aggressive acts (correlated with CD) distinguished youth who died by suicide from their peers<sup>[103]</sup>. Another study (all ages), found that measures of impulsivity and aggression were associated with a younger age at suicide, independent of mental disorders<sup>[104]</sup>. It is well established that substance use disorders are associated with suicide in older youth, particularly males, but less so in older adults<sup>[104]</sup>. However, there has been less study of the acute effects of alcohol consumption on suicide among youth<sup>[105,106]</sup>. Alcohol may proximally enable suicidal acts, by decreasing arousal or fear and/or inhibitions to act (*i.e.*, decrease anxiousness but increase impulsivity). Studies examining alcohol concentrations among those who died by suicide indicate about one third were intoxicated at the time of their death. In fact, alcohol (at any level) was higher among males than females and younger persons<sup>[107,108]</sup>.

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## SEX/GENDER DIFFERENCES IN PERCEIVED THREATS AND LOSSES

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Sex/gender differences in adverse early environments not only shape early risks, but may be compounded by social expectations or norms, arising in subsequent developmental contexts, influencing not only how youth perceive threats or losses, but how they adapt to them. Gender has been described as a relational concept, something that is performed, which may be relatively stable in some contexts but not others<sup>[109]</sup>. While youth are not passive, their micro and macro level social contexts may model and reinforce conformity to expected “masculine” or “feminine” perceptions, emotions and behaviours<sup>[110]</sup>, *via* differential monitoring, rewards/punishments<sup>[109,111]</sup>. The degree of monitoring and rewards/punishments likely varies across cultures and within social networks but may be differentially directed to boys or girls and developmentally conditioned.

Conflicts arise when youth are unable to meet their own or other’s sex/gender expectations, hopes or aspirations, and specific developmental contexts may be particularly adverse or threatening. Feelings of defeat/humiliation or entrapment (*i.e.*, inability to escape), with low levels of social support may increase risk of a suicide attempt<sup>[112]</sup>. The transition to adulthood is accompanied by numerous changes, challenging youth’s sense of self or identity. Perceived pubertal timing (earlier in girls, later in boys) has been found to prospectively predict youth suicide attempts<sup>[57]</sup>. In addition to the biological and physical changes of puberty, youth face varying sex/gender expectations to master transitions to adulthood, including: academic performance; entering the labour force; forming new social networks/peers outside the family, including romantic partner(s) and possibly, having children/parenting.

Younger youth may be influenced more by adults (parents, teachers); whereas, older youth, by their peers<sup>[76]</sup>.

Among youth who died by suicide, interpersonal stressors have been associated with suicide and vary with age. Before age 16, family conflicts were apparent; whereas, in older youth, conflicts occurred within a romantic relationship<sup>[98]</sup>. Media exposures (*e.g.*, TV, movies, online/social media) may act as a “super peer” by modeling values and behaviours<sup>[113]</sup>. Indeed, there is concern about how the growing use of less regulated, more interactive media among youth contributes to suicidal behaviours<sup>[114]</sup>. Knowledge of and access to lethal methods is socially scripted<sup>[109]</sup>, and knowledge of a peer (but not necessarily a friend) who died by suicide is prospectively associated with a suicide attempt in youth<sup>[115]</sup>.

Before we highlighted how early adverse environments, in particular child maltreatment, may differ for boys and girls, increasing their suicide risk. As youth age and their social environments expand, they may face new, adverse or threatening environments which vary by sex/gender and developmental context. For example, peers may discriminate against sexual minorities and/or promote unrealistic expectations such as an idealized physical appearance. Bullying involves an imbalance in power, is intentional and repeated, occurring online and offline. Both bullies and those who are bullied are more likely to experience suicidal ideation and attempt suicide. Although the association with being bullied (peer victimization) and suicidal ideation does not seem to differ by sex/gender, it is unclear whether is true for suicidal behaviour<sup>[116]</sup>. However, as mentioned, boys and girls differ in how they express aggression, which is related to how they bully<sup>[117,118]</sup>. Intimate partner violence contributes to suicide attempts, an association most evident in girls<sup>[119]</sup>. Sexual minority youth are known to be at a greater risk of suicide attempts. Not only do they encounter bullying from their peers, but they may also face rejection, maltreatment and discrimination from family and others during a critical time in their development<sup>[120-123]</sup>.

It has been postulated for boys beginning to define themselves as adult men. It may be especially difficult to attain “masculine” norms of personal autonomy and attainment. Such ideals may be discrepant with actual achievements and/or broader socio-economic realities, undermining the “human need to belong and form lasting significant personal relationships”<sup>[124]</sup>. Men have been found to have greater mental health risks than women during acute economic downturns, (*i.e.*, increased unemployment). In particular, European men aged 15 to 24 were most affected by the 2008 global economic recession, with an 11.7% increase in suicide rates<sup>[7]</sup>.

Qualitative studies illustrate how micro environments may reinforce masculine norms of personal autonomy and attainment as youth age. Mac An Ghail *et al.*<sup>[125]</sup> 2012 described how British pre-adolescent boys were confused and unhappy with treatment from teachers. For example, teachers praised girls for being good pupils, and physically separated boys from “their mates” encouraging isolation and competition between them. Further, among

their peers, boys learned not to speak of being scared by “real things” to avoid exclusion<sup>[125]</sup>. In another study, Irish men (aged 18 to 30 years) seen in hospital after attempting suicide identified that their lower educations limited their opportunities, including moving out of their environments<sup>[126]</sup>. Given their backgrounds, they did not recognize their experience as connected to mental illness, nor did they see treatment as relevant. Some spoke of being unable to “come out” as gay. (A problem inherent in suicide risk determination in psychological autopsy studies<sup>[127]</sup> but also in inferences about major causes of mortality)<sup>[128]</sup>. Instead, men tried to mask their “pain” through alcohol and/or drugs to project strength. When their “pain” worsened, including sleeplessness, they did not tell others as they feared being rejected by their peers for being weak and burdening their partners, who might leave them.

These experiences not only mirror “thwarted belongingness and perceived burdensomeness”<sup>[129]</sup>, but also neuroimaging studies demonstrating pain networks are activated when social exclusion is perceived<sup>[130]</sup>. Also, according to this Interpersonal Theory<sup>[129]</sup>, the acquired ability for suicide comprises habituation to pain. Still, most research on pain sensitivity has examined non-suicidal self-injury rather than suicidal behaviours in youth<sup>[112]</sup>. Denying or suppressing pain has been posited as more common in male youth, of relevance to the gender paradox<sup>[131]</sup>.

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## SEX/GENDER DIFFERENCES IN ADAPTATIONS TO PAIN

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Fearful youth may avoid some contexts given heightened sensitivity to non-rewarding cues. Self-disclosure may be viewed as potentially harmful<sup>[110,132,133]</sup>. Further, if youth are oppositional and/or aggressive, they may be unwantedly or unexpectedly rejected by their peers. Affiliation with more “deviant” peers may be rewarding, provided such peers can be found and are more tolerant. However, isolation may be reinforced, and the impact of threats or loss, stronger<sup>[110]</sup>. Affiliating with delinquent or substance abusing peers has been associated with a suicide attempt among youth<sup>[134,135]</sup> and contributes to adjustment difficulties among youth exposed to childhood sexual abuse<sup>[136]</sup>.

### Substance use

Given “masculine” norms of personal autonomy, boys may try managing pain through substance use. In some contexts, including birth cohorts, alcohol use is more socially acceptable and males provided more drinking opportunities<sup>[137,138]</sup>. Further, given opportunities to drink alcohol, youth with a history of childhood sexual abuse are more likely to do so<sup>[138]</sup> and boys (but not girls) with a history of sexual abuse tend to binge drink more than their peers<sup>[139]</sup>. While alcohol may be used to self-medicate<sup>[140]</sup>, binge drinking is associated with

**Table 1 Proposed sex/gender antecedents of youth suicide**

Genetic vulnerabilities and sex/gender differences in early adverse environments affect neurodevelopment and sex/gender differences in:
Early internalizing and externalizing (co)morbidity where ODD ± anxiety symptoms or disorders precede:
Irritable depression with more reactive or “impulsive” aggression in boys
Irritable depression with more proactive or “planned” aggression in girls
Substance misuse
Mood and/or substance use disorders (not necessarily diagnosed or treated)
Sex/gender differences in perceived threats and losses
Sex/gender differences in adaptations to pain ( <i>e.g.</i> , disclosure, and to whom) and suicide attempt methods

ODD: Oppositional Defiant Disorder.

a temporary increase in depression which improves after 2 to 4 wk abstinence. Thus, if drinking is stopped or controlled, it may not be perceived as problematic. However, if it continues, intake will likely increase contributing to social isolation/exclusion, *e.g.*, through academic/work difficulties and/or aggressive acts<sup>[19,141,142]</sup>. Notably, an interpersonal loss, (*e.g.*, a romantic breakup), has been found to independently increase the risk of suicide for boys (under age 20 years), but not girls, possibly because girls had more confidants<sup>[143]</sup>. Further, such interpersonal loss has been more strongly associated with youth suicide in the presence of substance abuse and the absence of conduct disorder (but not influenced by depression)<sup>[144,145]</sup>.

### Help-seeking

Masculine norms of personal autonomy may also prevent boys from seeking help. Youth help-seeking preferences have been examined in relation to: the source of help (*i.e.*, informal: family and friends or formal: health professionals), the type of problem and timing. Surveys of high school students suggest that the developmental trends differ in boys and girls. That is, over the course of high school, girls increasingly identify friends and professionals as likely sources for help with personal-emotional problems, with less dependence on family. Although boys also report seeking out family members less, they do not compensate with friends or professional help as much as girls<sup>[146]</sup>. Others have examined help-seeking attitudes in boys and girls. In a self-report attitude survey (in six high schools) on managing suicidal behaviour and depression, boys were more likely to endorse items consistent with avoidant strategies (including not telling others). In contrast, girls, scored higher on approach strategies<sup>[147]</sup>. Further, while both boys and girls tended to connect suicide with adverse life experiences rather than mental disorder, this was truer for boys than girls<sup>[148]</sup>. Such a stance may reinforce the desire for self-management. In a study among university students who screened positive for depression, alcohol use or prior suicide attempt, the main reason for not seeking professional help was their problems were minor or transient, most apparent among heavy alcohol users<sup>[149]</sup>. In sum, youths' interactions with others in specific contexts may not only contribute to perceived threats and losses and pain and but also, how youth adapt to these experiences.

## CONCLUSION

The age-dependent gender paradox observed in youth may be explained by several factors that vary according to genetic vulnerabilities and the contexts boys and girls are born into and interact with as they age. In this final section, we return to the premise, introduced earlier, that given brain plasticity lessens in adulthood, interventions that alter environment(s) and/or a youth's abilities to adapt to them, may have more enduring protective effects (*i.e.*, for those individuals and future generations) if first implemented in youth. Integrating findings on sex/gender differences in the continuum of suicidal behaviour with genetic, neurodevelopment, psychiatric (co)morbidity and social contexts that shape sex/gender perceived threats and losses and adaptations to pain, we propose the following antecedents to youth suicide (Table 1) which, if acted on, may reduce suicide risk in boys and girls.

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