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

Rhodes AE *et al.*Sex/gender and youth suicide

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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[1]. While youth suicide rates vary widely across and within countries[2,3], in developed countries, with good-quality vital registration data[1], rates are at least 2 to 3 times higher in boys than girls[4,5].Suicide rates have declined in boys since the 1990s, but there is concern that in some countries, rates have increased for girls[6] and the downward trend in boys, is now reversing[7]. However, it is unclear how best to intervene to reduce suicide risk in youth[8] - 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[9]. In particular, this paradox is age dependent. For suicide attempt rates, the sex/gender difference (F > M) increases with age peaking in mid adolescence[10-13], whereas for suicide rates, the sex/gender difference (M > F) steadily climbs until early adulthood[1]. Although suicide attempt data are self-reported, hospital presentation data reveal the same pattern[14-17] and suicide misclassification seems an unlikely explanation[18]. 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[2,19] 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[20]. “Sex/gender” is used rather than “sex” or “gender” to signify the complex interplay of social and biological determinants[21]. Most findings are limited by dichotomous measures of sex/gender[22], and to Western cultures. We defined suicidal ideation, attempts and suicide according to standard nomenclature[23]. 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[24-26].

***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[27-30] and lifetime prevalence[25,29,31,32] 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[33]. 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%)[28]. The sex/gender difference in youth suicide attempts (F > M) only diminishes among hospital presentations in medically serious suicide attempts (largely self-poisonings)[34] and reverses (M > F) with increased lethality of methods (*e.g*., hanging and firearms)[35,36].

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[10,37], is a predictor of a later attempt[24,37,38]; but more for girls than boys[10,26]. 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[10], 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[39], 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[40] 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[40].

***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[1], 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[2]; 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[2], 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[41]. Suicide risk is strongest in the year after the presentation, but remains elevated in subsequent years[42]. 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[43], in youth aged 10 to 18, a hospital presentation for self-cutting (*vs* self-poisoning) is more predictive of suicide[42], a method of lower lethality[44,45], associated with repetition[42]. Repeat (*vs* single) hospital presentations are more strongly associated with suicide, particularly in girls[46]. However, self-poisonings, usually medication overdoses in Western cultures[14], are the most common hospital presentation among youth[3] and sex/gender differences in lethality are not evident here[44].

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[35], 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[40], a Finnish birth cohort study[47] 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[48]. 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)[48], may mediate the familial transmission, and stem from genetic vulnerabilities and/or adverse early environments[49]. 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[50,51].

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”[52-56]: changes in gene expression mediated by altered chromatin without modifying the DNA sequence[57]. 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)[54,58]. There is an ongoing debate about parent-to-child transmission of epigenetic effects[59].

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[60]. 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”[61] affecting their ability to flourish cognitively, emotionally and behaviourally in their environments[40,53]. 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[62,63]. Yet, this sex/gender difference is not evident in adults[64] 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[62,64].

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[58,65,66]. However, current nosology systems [*e.g*., the Diagnostic and Statistical Manual (DSM) for Mental Disorders and the International Classification of Diseases (ICD)] 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[1]. 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)[67]. 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”[65]. 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[2]. 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[68]. 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[69]. 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)[70] - tend to become balanced by more *endogenous*, goal directed, planning behaviors[68,71]. Indeed, engagement in “risky” behaviours seems to peak during adolescence but then decline[72,73], not unlike the age-suicide attempt distribution evident in girls[10]. Given sex-by-age interactions occur in cortical development, including faster myelination in girls than boys[74], 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[75]. 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[76,77]. Girls tend to have larger left amygdala volumes than boys (aged 10 to 22 years)[78]. 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[79]. 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[80]. 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[81]. 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[82,83]. ADHD declines with age, whereas depression and substance use disorders increase[84]. Anxiety disorders tend to precede depression (with some continuing to co-occur with depression)[75]. Externalizing disorders (rather than internalizing ones) seem to precede adult substance use disorders and there is continuity between youth and adult substance use disorders[81]. Substance use disorders may be more prevalent in boys than girls[82].

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[85]. Further, the ODD link seems to be explained by irritability and has been posited as a mood disorder variant[85,86], newly captured in DSM 5 as Disruptive Mood Dysregulation Disorder (DMDD)[87]. 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[88,89] but may vary in age of onset and by sex/gender)[90,91].

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[92]. 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”[93]. 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)[93], 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[94]. Instrumental or proactive aggression has been related to psychopathy, whereas, reactive aggression is thought to arise from difficulties regulating emotional responses to threats[95].

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[96-98], disruptive disorders would seem implicated in younger youth, consistent with studies on youth suicide attempts[39,40,47]. 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[2,97-100]. 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[101,102].

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[103]. Another study (all ages), found that measures of impulsivity and aggression were associated with a younger age at suicide, independent of mental disorders[104]. It is well established that substance use disorders are associated with suicide in older youth, particularly males, but less so in older adults[104]. However, there has been less study of the acute effects of alcohol consumption on suicide among youth[105,106]. 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[107,108].

**SEX/GENDER DIFFERENCES IN PERCEIVED THREATS AND LOSSES**

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[109]. 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[110], *via* differential monitoring, rewards/punishments[109,111]. 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[112]. 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[37]. 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[76]. 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[98]. Media exposures (*e.g.,* TV, movies, online/social media) may act as a “super peer” by modeling values and behaviours[113]. Indeed, there is concern about how the growing use of less regulated, more interactive media among youth contributes to suicidal behaviours[114]. Knowledge of and access to lethal methods is socially scripted[109], and knowledge of a peer (but not necessarily a friend) who died by suicide is prospectively associated with a suicide attempt in youth[115].

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[116]. However, as mentioned, boys and girls differ in how they express aggression, which is related to how they bully[117,118]. Intimate partner violence contributes to suicide attempts, an association most evident in girls[119]. 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[120-123].

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”[124]. 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[7].

Qualitative studies illustrate how micro environments may reinforce masculine norms of personal autonomy and attainment as youth age. Mac an Ghaill *et al*[125] 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[125]. 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[126]. 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[127] but also in inferences about major causes of mortality)[128]. 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”[129], but also neuroimaging studies demonstrating pain networks are activated when social exclusion is perceived[130]. Also, according to this Interpersonal Theory[129], 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[112]. Denying or suppressing pain has been posited as more common in male youth, of relevance to the gender paradox[131].

**SEX/GENDER DIFFERENCES IN ADAPTATIONS TO PAIN**

Fearful youth may avoid some contexts given heightened sensitivity to non-rewarding cues. Self-disclosure may be viewed as potentially harmful[110,132,133]. 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[110]. Affiliating with delinquent or substance abusing peers has been associated with a suicide attempt among youth[134,135] and contributes to adjustment difficulties among youth exposed to childhood sexual abuse[136].

***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[137,138]. Further, given opportunities to drink alcohol, youth with a history of childhood sexual abuse are more likely to do so[138] and boys (but not girls) with a history of sexual abuse tend to binge drink more than their peers[139]. While alcohol may be used to self-medicate[140], binge drinking is associated with 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[19,141,142]. 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[143]. 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)[144,145].

***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[146]. 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[147]. 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[148]. 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[140]. 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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**REFERENCES**

1 **World Health Organization.** Preventing suicide. A global imperative. Geneva, Switzerland, World Health Organization, 2014: 1-89

2 **Bridge JA**, Goldstein TR, Brent DA. Adolescent suicide and suicidal behavior. *J Child Psychol Psychiatry* 2006; **47**: 372-394 [PMID: 16492264 DOI: 10.1111/j.1469-7610.2006.01615.x]

3 **Hawton K**, Saunders KE, O'Connor RC. Self-harm and suicide in adolescents. *Lancet* 2012; **379**: 2373-2382 [PMID: 22726518 DOI: 10.1016/S0140-6736(12)60322-5]

4 **Wasserman D**, Cheng Q, Jiang GX. Global suicide rates among young people aged 15-19. *World Psychiatry* 2005; **4**: 114-120 [PMID: 16633527]

5 **Pitman A**, Krysinska K, Osborn D, King M. Suicide in young men. *Lancet* 2012; **379**: 2383-2392 [PMID: 22726519 DOI: 10.1016/S0140-6736(12)60731-4]

6 **Rhodes AE**, Skinner R, McFaull S, Katz LY. Canada-wide effect of regulatory warnings on antidepressant prescribing and suicide rates in boys and girls. *Can J Psychiatry* 2013; **58**: 640-645 [PMID: 24246435]

7 **Chang SS**, Stuckler D, Yip P, Gunnell D. Impact of 2008 global economic crisis on suicide: time trend study in 54 countries. *BMJ* 2013; **347**: f5239 [PMID: 24046155 DOI: 10.1136/bmj.f5239]

8 **De Silva S**, Parker A, Purcell R, Callahan P, Liu P, Hetrick S. Mapping the evidence of prevention and intervention studies for suicidal and self-harming behaviors in young people. *Crisis* 2013; **34**: 223-232 [PMID: 23502058 DOI: 10.1027/0227-5910/a000190]

9 **Canetto SS**. Women and suicidal behavior: a cultural analysis. *Am J Orthopsychiatry* 2008; **78**: 259-266 [PMID: 18954189 DOI: 10.1037/a0013973]

10 **Lewinsohn PM**, Rohde P, Seeley JR, Baldwin CL. Gender differences in suicide attempts from adolescence to young adulthood. *J Am Acad Child Adolesc Psychiatry* 2001; **40**: 427-434 [PMID: 11314568 DOI: 10.1097/00004583-200104000-00011]

11 **Nkansah-Amankra S**. Adolescent suicidal trajectories through young adulthood: prospective assessment of religiosity and psychosocial factors among a population-based sample in the United States. *Suicide Life Threat Behav* 2013; **43**: 439-459 [PMID: 23601148 DOI: 10.1111/sltb.12029]

12 **Thompson MP**, Light LS. Examining gender differences in risk factors for suicide attempts made 1 and 7 years later in a nationally representative sample. *J Adolesc Health* 2011; **48**: 391-397 [PMID: 21402269 DOI: 10.1016/j.jadohealth.2010.07.018]

13 **Boeninger DK**, Masyn KE, Feldman BJ, Conger RD. Sex differences in developmental trends of suicide ideation, plans, and attempts among European American adolescents. *Suicide Life Threat Behav* 2010; **40**: 451-464 [PMID: 21034208 DOI: 10.1521/suli.2010.40.5.451]

14 **Rhodes AE**, Bethell J, Spence J, Links PS, Streiner DL, Jaakkimainen RL. Age-sex differences in medicinal self-poisonings: a population-based study of deliberate intent and medical severity. *Soc Psychiatry Psychiatr Epidemiol* 2008; **43**: 642-652 [PMID: 18511993 DOI: 10.1007/s00127-008-0349-6]

15 **Colman I**, Yiannakoulias N, Schopflocher D, Svenson LW, Rosychuk RJ, Rowe BH. Population-based study of medically treated self-inflicted injuries. *CJEM* 2004; **6**: 313-320 [PMID: 17381987]

16 **Levinson D**, Haklai Z, Stein N, Gordon ES. Suicide attempts in israel: age by gender analysis of a national emergency departments database. *Suicide Life Threat Behav* 2006; **36**: 97-102 [PMID: 16676630 DOI: 10.1521/suli.2006.36.1.97]

17 **Canadian Institute for Health Information, Statistics Canada.** Health Indicators. Ottawa, ON: CIHI, 2011: 1-121

18 **Rhodes AE**, Khan S, Boyle MH, Wekerle C, Goodman D, Tonmyr L, Bethell J, Leslie B, Manion I. Sex differences in suicides among children and youth: the potential impact of misclassification. *Can J Public Health* 2012; **103**: 213-217 [PMID: 22905641]

19 **Conner KR,** Goldston DB. Rates of suicide among males increase steadily from age 11 to 21: Developmental framework and outline for prevention. *Aggress Violent Behav* 2007; **12**: 193-207 [DOI: 10.1016/j.avb.2006.07.002]

20 **Sawyer SM**, Afifi RA, Bearinger LH, Blakemore SJ, Dick B, Ezeh AC, Patton GC. Adolescence: a foundation for future health. *Lancet* 2012; **379**: 1630-1640 [PMID: 22538178 DOI: 10.1016/S0140-6736(12)60072-5]

21 **Canadian Institute of Gender and Health.** Introduction. In: Canadian Institute of Gender and Health, editor. What a difference sex and gender make - A gender, sex and health research casebook. Ottawa: Canadian Institutes of Health Research, 2012: ix-xiii

22 **Johnson J,** Repta R. Sex and gender: beyond the binaries. In: Oliffe J, Greaves L, editors. Designing and conducting gender, sex and health research. Los Angeles (CA): Sage, 2012: 17-37 [DOI: 10.4135/9781452230610.n2]

23 **Silverman MM**, Berman AL, Sanddal ND, O'carroll PW, Joiner TE. Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 2: Suicide-related ideations, communications, and behaviors. *Suicide Life Threat Behav* 2007; **37**: 264-277 [PMID: 17579539 DOI: 10.1521/suli.2007.37.3.264]

24 **Fergusson DM**, Lynskey MT. Suicide attempts and suicidal ideation in a birth cohort of 16-year-old New Zealanders. *J Am Acad Child Adolesc Psychiatry* 1995; **34**: 1308-1317 [PMID: 7592268 DOI: 10.1097/00004583-199510000-00016]

25 **Brezo J**, Paris J, Barker ED, Tremblay R, Vitaro F, Zoccolillo M, Hébert M, Turecki G. Natural history of suicidal behaviors in a population-based sample of young adults. *Psychol Med* 2007; **37**: 1563-1574 [PMID: 17927844 DOI: 10.1017/S003329170700058X]

26 **Rueter MA**, Holm KE, McGeorge CR, Conger RD. Adolescent suicidal ideation subgroups and their association with suicidal plans and attempts in young adulthood. *Suicide Life Threat Behav* 2008; **38**: 564-575 [PMID: 19014308 DOI: 10.1521/suli.2008.38.5.564]

27 **Husky MM**, Olfson M, He JP, Nock MK, Swanson SA, Merikangas KR. Twelve-month suicidal symptoms and use of services among adolescents: results from the National Comorbidity Survey. *Psychiatr Serv* 2012; **63**: 989-996 [PMID: 22910768 DOI: 10.1176/appi.ps.201200058]

28 **Kann L**, Kinchen S, Shanklin SL, Flint KH, Kawkins J, Harris WA, Lowry R, Olsen EO, McManus T, Chyen D, Whittle L, Taylor E, Demissie Z, Brener N, Thornton J, Moore J, Zaza S. Youth risk behavior surveillance--United States, 2013. *MMWR Surveill Summ* 2014; **63 Suppl 4**: 1-168 [PMID: 24918634]

29 **Evans E**, Hawton K, Rodham K, Deeks J. The prevalence of suicidal phenomena in adolescents: a systematic review of population-based studies. *Suicide Life Threat Behav* 2005; **35**: 239-250 [PMID: 16156486 DOI: 10.1521/suli.2005.35.3.239]

30 **Afifi TO**, Cox BJ, Katz LY. The associations between health risk behaviours and suicidal ideation and attempts in a nationally representative sample of young adolescents. *Can J Psychiatry* 2007; **52**: 666-674 [PMID: 18020114]

31 **Nock MK**, Green JG, Hwang I, McLaughlin KA, Sampson NA, Zaslavsky AM, Kessler RC. Prevalence, correlates, and treatment of lifetime suicidal behavior among adolescents: results from the National Comorbidity Survey Replication Adolescent Supplement. *JAMA Psychiatry* 2013; **70**: 300-310 [PMID: 23303463 DOI: 10.1001/2013.jamapsychiatry.55]

32 **Kokkevi A**, Rotsika V, Arapaki A, Richardson C. Adolescents' self-reported suicide attempts, self-harm thoughts and their correlates across 17 European countries. *J Child Psychol Psychiatry* 2012; **53**: 381-389 [PMID: 21895649 DOI: 10.1111/j.1469-7610.2011.02457.x]

33 **Hart SR**, Musci RJ, Ialongo N, Ballard ED, Wilcox HC. Demographic and clinical characteristics of consistent and inconsistent longitudinal reporters of lifetime suicide attempts in adolescence through young adulthood. *Depress Anxiety* 2013; **30**: 997-1004 [PMID: 23804209 DOI: 10.1002/da.22135]

34 **Beautrais AL**, Joyce PR, Mulder RT. Risk factors for serious suicide attempts among youths aged 13 through 24 years. *J Am Acad Child Adolesc Psychiatry* 1996; **35**: 1174-1182 [PMID: 8824061 DOI: 10.1097/00004583-199609000-00015]

35 **Beautrais AL**. Suicide and serious suicide attempts in youth: a multiple-group comparison study. *Am J Psychiatry* 2003; **160**: 1093-1099 [PMID: 12777267 DOI: 10.1176/appi.ajp.160.6.1093]

36 **Rhodes AE,** Lu H, Skinner R. Time Trends in Medically Serious Suicide-Related Behaviours in Boys and Girls. *Can J Psychiatry* 2014; **59**(3): 152–159 [PMCID: PMC4079127]

37 **Wichstrøm L**. Predictors of adolescent suicide attempts: a nationally representative longitudinal study of Norwegian adolescents. *J Am Acad Child Adolesc Psychiatry* 2000; **39**: 603-610 [PMID: 10802978 DOI: 10.1097/00004583-200005000-00014]

38 **Reinherz HZ**, Giaconia RM, Silverman AB, Friedman A, Pakiz B, Frost AK, Cohen E. Early psychosocial risks for adolescent suicidal ideation and attempts. *J Am Acad Child Adolesc Psychiatry* 1995; **34**: 599-611 [PMID: 7775355 DOI: 10.1097/00004583-199505000-00012]

39 **Fergusson DM**, Woodward LJ, Horwood LJ. Risk factors and life processes associated with the onset of suicidal behaviour during adolescence and early adulthood. *Psychol Med* 2000; **30**: 23-39 [PMID: 10722173 DOI: 10.1017/S003329179900135X]

40 **Brezo J**, Barker ED, Paris J, Hébert M, Vitaro F, Tremblay RE, Turecki G. Childhood trajectories of anxiousness and disruptiveness as predictors of suicide attempts. *Arch Pediatr Adolesc Med* 2008; **162**: 1015-1021 [PMID: 18981348 DOI: 10.1001/archpedi.162.11.1015]

41 **Hawton K**, Harriss L. Deliberate self-harm in young people: characteristics and subsequent mortality in a 20-year cohort of patients presenting to hospital. *J Clin Psychiatry* 2007; **68**: 1574-1583 [PMID: 17960975 DOI: 10.4088/JCP.v68n1017]

42 **Hawton K**, Bergen H, Kapur N, Cooper J, Steeg S, Ness J, Waters K. Repetition of self-harm and suicide following self-harm in children and adolescents: findings from the Multicentre Study of Self-harm in England. *J Child Psychol Psychiatry* 2012; **53**: 1212-1219 [PMID: 22537181 DOI: 10.1111/j.1469-7610.2012.02559.x]

43 **Runeson B**, Tidemalm D, Dahlin M, Lichtenstein P, Långström N. Method of attempted suicide as predictor of subsequent successful suicide: national long term cohort study. *BMJ* 2010; **341**: c3222 [PMID: 20627975 DOI: 10.1136/bmj.c3222]

44 **Rhodes AE**, Bethell J, Carlisle C, Rosychuk RJ, Lu H, Newton A. Time trends in suicide-related behaviours in girls and boys. *Can J Psychiatry* 2014; **59**: 152-159 [PMID: 24881164]

45 **Bridge JA**, Marcus SC, Olfson M. Outpatient care of young people after emergency treatment of deliberate self-harm. *J Am Acad Child Adolesc Psychiatry* 2012; **51**: 213-222.e1 [PMID: 22265367 DOI: 10.1016/j.jaac.2011.11.002]

46 **Zahl DL**, Hawton K. Repetition of deliberate self-harm and subsequent suicide risk: long-term follow-up study of 11,583 patients. *Br J Psychiatry* 2004; **185**: 70-75 [PMID: 15231558 DOI: 10.1192/bjp.185.1.70]

47 **Sourander A**, Klomek AB, Niemelä S, Haavisto A, Gyllenberg D, Helenius H, Sillanmäki L, Ristkari T, Kumpulainen K, Tamminen T, Moilanen I, Piha J, Almqvist F, Gould MS. Childhood predictors of completed and severe suicide attempts: findings from the Finnish 1981 Birth Cohort Study. *Arch Gen Psychiatry* 2009; **66**: 398-406 [PMID: 19349309 DOI: 10.1001/archgenpsychiatry.2009.21]

48 **Brent DA**, Melhem N. Familial transmission of suicidal behavior. *Psychiatr Clin North Am* 2008; **31**: 157-177 [PMID: 18439442 DOI: 10.1016/j.psc.2008.02.001]

49 **Geulayov G**, Gunnell D, Holmen TL, Metcalfe C. The association of parental fatal and non-fatal suicidal behaviour with offspring suicidal behaviour and depression: a systematic review and meta-analysis. *Psychol Med* 2012; **42**: 1567-1580 [PMID: 22129460 DOI: 10.1017/S0033291711002753]

50 **Zalsman G**. Timing is critical: gene, environment and timing interactions in genetics of suicide in children and adolescents. *Eur Psychiatry* 2010; **25**: 284-286 [PMID: 20444577 DOI: 10.1016/j.eurpsy.2010.01.007]

51 **Bortolato M**, Pivac N, Muck Seler D, Nikolac Perkovic M, Pessia M, Di Giovanni G. The role of the serotonergic system at the interface of aggression and suicide. *Neuroscience* 2013; **236**: 160-185 [PMID: 23333677 DOI: 10.1016/j.neuroscience.2013.01.015]

52 **Labonté B**, Suderman M, Maussion G, Navaro L, Yerko V, Mahar I, Bureau A, Mechawar N, Szyf M, Meaney MJ, Turecki G. Genome-wide epigenetic regulation by early-life trauma. *Arch Gen Psychiatry* 2012; **69**: 722-731 [PMID: 22752237 DOI: 10.1001/archgenpsychiatry.2011.2287]

53 **Turecki G**, Ernst C, Jollant F, Labonté B, Mechawar N. The neurodevelopmental origins of suicidal behavior. *Trends Neurosci* 2012; **35**: 14-23 [PMID: 22177979 DOI: 10.1016/j.tins.2011.11.008]

54 **Lutz PE**, Turecki G. DNA methylation and childhood maltreatment: from animal models to human studies. *Neuroscience* 2014; **264**: 142-156 [PMID: 23933308 DOI: 10.1016/j.neuroscience.2013.07.069]

55 **Nemeroff CB**, Binder E. The preeminent role of childhood abuse and neglect in vulnerability to major psychiatric disorders: toward elucidating the underlying neurobiological mechanisms. *J Am Acad Child Adolesc Psychiatry* 2014; **53**: 395-397 [PMID: 24655648 DOI: 10.1016/j.jaac.2014.02.004]

56 **Moffitt TE**. Childhood exposure to violence and lifelong health: clinical intervention science and stress-biology research join forces. *Dev Psychopathol* 2013; **25**: 1619-1634 [PMID: 24342859 DOI: 10.1017/S0954579413000801]

57 **Lenroot RK**, Giedd JN. Annual Research Review: Developmental considerations of gene by environment interactions. *J Child Psychol Psychiatry* 2011; **52**: 429-441 [PMID: 21391998 DOI: 10.1111/j.1469-7610.2011.02381.x]

58 **Pishva E**, Kenis G, Lesch KP, Prickaerts J, Steinbusch HMW, van den Hove DLA, van Os J, Rutten BP. Epigenetic epidemiology in psychiatry: A translational neuroscience perspective. *Translational Neuroscience* 2012; **3:** 196-212 [DOI: 10.2478/s13380-012-0024-y]

59 How epigenetic memory is passed across generations. Genomics. 2014. [updated 2014 September 20; cited 2014 Sepetember 23] Available from: URL: http: //www.technologynetworks.com/Genomics/news.aspx?ID=170521

60 **Séguin M**, Renaud J, Lesage A, Robert M, Turecki G. Youth and young adult suicide: a study of life trajectory. *J Psychiatr Res* 2011; **45**: 863-870 [PMID: 21636096 DOI: 10.1016/j.jpsychires.2011.05.005]

61 **van Heeringen K,** Mann JJ. The neurobiology of suicide. *Lancet* 2014: 1-10 [DOI: 10.1016/S2215-0366(14)70220-2]

62 **Rhodes AE**, Boyle MH, Tonmyr L, Wekerle C, Goodman D, Leslie B, Mironova P, Bethell J, Manion I. Sex differences in childhood sexual abuse and suicide-related behaviors. *Suicide Life Threat Behav* 2011; **41**: 235-254 [PMID: 21477094 DOI: 10.1111/j.1943-278X.2011.00025.x]

63 **Tomasula JL**, Anderson LM, Littleton HL, Riley-Tillman TC. The association between sexual assault and suicidal activity in a national sample. *Sch Psychol Q* 2012; **27**: 109-119 [PMID: 22774785 DOI: 10.1037/a0029162]

64 **Rhodes A,** Bethell J, Tonmyr L. Child sexual abuse and youth suicide: A review of the evidence with implications for future research. *IJCYFS* 2014; **5**: 113-130. [updated 2014 January; cited 2014 September 23] Available from: URL: http: //journals.uvic.ca/index.php/ijcyfs/index

65 **Kim YS**, State MW. Recent challenges to the psychiatric diagnostic nosology: a focus on the genetics and genomics of neurodevelopmental disorders. *Int J Epidemiol* 2014; **43**: 465-475 [PMID: 24618187 DOI: 10.1093/ije/dyu037]

66 **Casey BJ**, Oliveri ME, Insel T. A neurodevelopmental perspective on the research domain criteria (RDoC) framework. *Biol Psychiatry* 2014; **76**: 350-353 [PMID: 25103538 DOI: 10.1016/j.biopsych.2014.01.006]

67 **Oquendo MA**, Baca-Garcia E. Suicidal behavior disorder as a diagnostic entity in the DSM-5 classification system: advantages outweigh limitations. *World Psychiatry* 2014; **13**: 128-130 [PMID: 24890057 DOI: 10.1002/wps.20116]

68 **Vigil P**, Orellana RF, Cortés ME, Molina CT, Switzer BE, Klaus H. Endocrine modulation of the adolescent brain: a review. *J Pediatr Adolesc Gynecol* 2011; **24**: 330-337 [PMID: 21514192 DOI: 10.1016/j.jpag.2011.01.061]

69 **Brent BK**, Thermenos HW, Keshavan MS, Seidman LJ. Gray matter alterations in schizophrenia high-risk youth and early-onset schizophrenia: a review of structural MRI findings. *Child Adolesc Psychiatr Clin N Am* 2013; **22**: 689-714 [PMID: 24012081 DOI: 10.1016/j.chc.2013.06.003]

70 **Braquehais MD**, Oquendo MA, Baca-García E, Sher L. Is impulsivity a link between childhood abuse and suicide? *Compr Psychiatry* 2010; **51**: 121-129 [PMID: 20152291 DOI: 10.1016/j.comppsych.2009.05.003]

71 **Lourenco F**, Casey BJ. Adjusting behavior to changing environmental demands with development. *Neurosci Biobehav Rev* 2013; **37**: 2233-2242 [PMID: 23518271 DOI: 10.1016/j.neubiorev.2013.03.003]

72 **Casey B**, Jones RM, Somerville LH. Braking and Accelerating of the Adolescent Brain. *J Res Adolesc* 2011; **21**: 21-33 [PMID: 21475613 DOI: 10.1111/j.1532-7795.2010.00712.x]

73 **Strang NM**, Chein JM, Steinberg L. The value of the dual systems model of adolescent risk-taking. *Front Hum Neurosci* 2013; **7**: 223 [PMID: 23750132 DOI: 10.3389/fnhum.2013.00223]

74 **Koolschijn PC**, Crone EA. Sex differences and structural brain maturation from childhood to early adulthood. *Dev Cogn Neurosci* 2013; **5**: 106-118 [PMID: 23500670 DOI: 10.1016/j.dcn.2013.02.003]

75 **Cummings CM**, Caporino NE, Kendall PC. Comorbidity of anxiety and depression in children and adolescents: 20 years after. *Psychol Bull* 2014; **140**: 816-845 [PMID: 24219155 DOI: 10.1037/a0034733]

76 **Scherf KS**, Smyth JM, Delgado MR. The amygdala: an agent of change in adolescent neural networks. *Horm Behav* 2013; **64**: 298-313 [PMID: 23756154]

77 **Malter Cohen M**, Tottenham N, Casey BJ. Translational developmental studies of stress on brain and behavior: implications for adolescent mental health and illness? *Neuroscience* 2013; **249**: 53-62 [PMID: 23340244 DOI: 10.1016/j.neuroscience.2013.01.023]

78 **Satterthwaite TD**, Vandekar S, Wolf DH, Ruparel K, Roalf DR, Jackson C, Elliott MA, Bilker WB, Calkins ME, Prabhakaran K, Davatzikos C, Hakonarson H, Gur RE, Gur RC. Sex differences in the effect of puberty on hippocampal morphology. *J Am Acad Child Adolesc Psychiatry* 2014; **53**: 341-50.e1 [PMID: 24565361 DOI: 10.1016/j.jaac.2013.12.002]

79 **Whittle S**, Lichter R, Dennison M, Vijayakumar N, Schwartz O, Byrne ML, Simmons JG, Yücel M, Pantelis C, McGorry P, Allen NB. Structural brain development and depression onset during adolescence: a prospective longitudinal study. *Am J Psychiatry* 2014; **171**: 564-571 [PMID: 24577365 DOI: 10.1176/appi.ajp.2013.13070920]

80 **Lozier LM**, Cardinale EM, VanMeter JW, Marsh AA. Mediation of the relationship between callous-unemotional traits and proactive aggression by amygdala response to fear among children with conduct problems. *JAMA Psychiatry* 2014; **71**: 627-636 [PMID: 24671141 DOI: 10.1001/jamapsychiatry.2013.4540]

81 **Copeland WE**, Adair CE, Smetanin P, Stiff D, Briante C, Colman I, Fergusson D, Horwood J, Poulton R, Costello EJ, Angold A. Diagnostic transitions from childhood to adolescence to early adulthood. *J Child Psychol Psychiatry* 2013; **54**: 791-799 [PMID: 23451804 DOI: 10.1111/jcpp.12062]

82 **Kessler RC**, Avenevoli S, Costello EJ, Georgiades K, Green JG, Gruber MJ, He JP, Koretz D, McLaughlin KA, Petukhova M, Sampson NA, Zaslavsky AM, Merikangas KR. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. *Arch Gen Psychiatry* 2012; **69**: 372-380 [PMID: 22147808 DOI: 10.1001/archgenpsychiatry.2011.160]

83 **Alisic E**, Zalta AK, van Wesel F, Larsen SE, Hafstad GS, Hassanpour K, Smid GE. Rates of post-traumatic stress disorder in trauma-exposed children and adolescents: meta-analysis. *Br J Psychiatry* 2014; **204**: 335-340 [PMID: 24785767 DOI: 10.1192/bjp.bp.113.131227]

84 **Costello EJ**, Copeland W, Angold A. Trends in psychopathology across the adolescent years: what changes when children become adolescents, and when adolescents become adults? *J Child Psychol Psychiatry* 2011; **52**: 1015-1025 [PMID: 21815892 DOI: 10.1111/j.1469-7610.2011.02446.x]

85 **Copeland WE**, Shanahan L, Erkanli A, Costello EJ, Angold A. Indirect comorbidity in childhood and adolescence. *Front Psychiatry* 2013; **4**: 144 [PMID: 24204349 DOI: 10.3389/fpsyt.2013.00144]

86 **Stringaris A**, Zavos H, Leibenluft E, Maughan B, Eley TC. Adolescent irritability: phenotypic associations and genetic links with depressed mood. *Am J Psychiatry* 2012; **169**: 47-54 [PMID: 22193524 DOI: 10.1176/appi.ajp.2011.10101549]

87 **Copeland WE**, Shanahan L, Egger H, Angold A, Costello EJ. Adult diagnostic and functional outcomes of DSM-5 disruptive mood dysregulation disorder. *Am J Psychiatry* 2014; **171**: 668-674 [PMID: 24781389 DOI: 10.1176/appi.ajp.2014.13091213]

88 **Sparks GM**, Axelson DA, Yu H, Ha W, Ballester J, Diler RS, Goldstein B, Goldstein T, Hickey MB, Ladouceur CD, Monk K, Sakolsky D, Birmaher B. Disruptive mood dysregulation disorder and chronic irritability in youth at familial risk for bipolar disorder. *J Am Acad Child Adolesc Psychiatry* 2014; **53**: 408-416 [PMID: 24655650 DOI: 10.1016/j.jaac.2013.12.026]

89 **Tijssen MJ**, van Os J, Wittchen HU, Lieb R, Beesdo K, Mengelers R, Wichers M. Prediction of transition from common adolescent bipolar experiences to bipolar disorder: 10-year study. *Br J Psychiatry* 2010; **196**: 102-108 [PMID: 20118453 DOI: 10.1192/bjp.bp.109.065763]

90 **Merikangas KR**, Jin R, He JP, Kessler RC, Lee S, Sampson NA, Viana MC, Andrade LH, Hu C, Karam EG, Ladea M, Medina-Mora ME, Ono Y, Posada-Villa J, Sagar R, Wells JE, Zarkov Z. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. *Arch Gen Psychiatry* 2011; **68**: 241-251 [PMID: 21383262 DOI: 10.1001/archgenpsychiatry.2011.12]

91 **Merikangas KR**, Lamers F. The 'true' prevalence of bipolar II disorder. *Curr Opin Psychiatry* 2012; **25**: 19-23 [PMID: 22156934 DOI: 10.1097/YCO.0b013e32834de3de]

92 **Stringaris A**, Lewis G, Maughan B. Developmental pathways from childhood conduct problems to early adult depression: findings from the ALSPAC cohort. *Br J Psychiatry* 2014; **205**: 17-23 [PMID: 24764545 DOI: 10.1192/bjp.bp.113.134221]

93 **Stringaris A**, Maughan B, Copeland WS, Costello EJ, Angold A. Irritable mood as a symptom of depression in youth: prevalence, developmental, and clinical correlates in the Great Smoky Mountains Study. *J Am Acad Child Adolesc Psychiatry* 2013; **52**: 831-840 [PMID: 23880493 DOI: 10.1016/j.jaac.2013.05.017]

94 **Cleverley K**, Szatmari P, Vaillancourt T, Boyle M, Lipman E. Developmental trajectories of physical and indirect aggression from late childhood to adolescence: sex differences and outcomes in emerging adulthood. *J Am Acad Child Adolesc Psychiatry* 2012; **51**: 1037-1051 [PMID: 23021479 DOI: 10.1016/j.jaac.2012.07.010]

95 **Hubbard JA**, McAuliffe MD, Morrow MT, Romano LJ. Reactive and proactive aggression in childhood and adolescence: precursors, outcomes, processes, experiences, and measurement. *J Pers* 2010; **78**: 95-118 [PMID: 20433614 DOI: 10.1111/j.1467-6494.2009.00610.x]

96 **Grøholt B**, Ekeberg O, Wichstrøm L, Haldorsen T. Suicide among children and younger and older adolescents in Norway: a comparative study. *J Am Acad Child Adolesc Psychiatry* 1998; **37**: 473-481 [PMID: 9585647 DOI: 10.1097/00004583-199805000-00008]

97 **Shaffer D**, Gould MS, Fisher P, Trautman P, Moreau D, Kleinman M, Flory M. Psychiatric diagnosis in child and adolescent suicide. *Arch Gen Psychiatry* 1996; **53**: 339-348 [PMID: 8634012 DOI: 10.1001/archpsyc.1996.01830040075012]

98 **Brent DA**, Baugher M, Bridge J, Chen T, Chiappetta L. Age- and sex-related risk factors for adolescent suicide. *J Am Acad Child Adolesc Psychiatry* 1999; **38**: 1497-1505 [PMID: 10596249 DOI: 10.1097/00004583-199912000-00010]

99 **Fleischmann A**, Bertolote JM, Belfer M, Beautrais A. Completed suicide and psychiatric diagnoses in young people: a critical examination of the evidence. *Am J Orthopsychiatry* 2005; **75**: 676-683 [PMID: 16262523 DOI: 10.1037/0002-9432.75.4.676]

100 **Renaud J**, Berlim MT, McGirr A, Tousignant M, Turecki G. Current psychiatric morbidity, aggression/impulsivity, and personality dimensions in child and adolescent suicide: a case-control study. *J Affect Disord* 2008; **105**: 221-228 [PMID: 17568682 DOI: 10.1016/j.jad.2007.05.013]

101 **Messias EL**, Chen CY, Eaton WW. Epidemiology of schizophrenia: review of findings and myths. *Psychiatr Clin North Am* 2007; **30**: 323-338 [PMID: 17720026 DOI: 10.1016/j.psc.2007.04.007]

102 **Gould MS**, Greenberg T, Velting DM, Shaffer D. Youth suicide risk and preventive interventions: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry* 2003; **42**: 386-405 [PMID: 12649626 DOI: 10.1097/01.CHI.0000046821.95464.CF]

103 **Brent DA**, Johnson BA, Perper J, Connolly J, Bridge J, Bartle S, Rather C. Personality disorder, personality traits, impulsive violence, and completed suicide in adolescents. *J Am Acad Child Adolesc Psychiatry* 1994; **33**: 1080-1086 [PMID: 7982858 DOI: 10.1097/00004583-199410000-00003]

104 **McGirr A**, Renaud J, Bureau A, Seguin M, Lesage A, Turecki G. Impulsive-aggressive behaviours and completed suicide across the life cycle: a predisposition for younger age of suicide. *Psychol Med* 2008; **38**: 407-417 [PMID: 17803833 DOI: 10.1017/S0033291707001419]

105 **Borges G**, Loera CR. Alcohol and drug use in suicidal behaviour. *Curr Opin Psychiatry* 2010; **23**: 195-204 [PMID: 20308904 DOI: 10.1097/YCO.0b013e3283386322]

106 **Bagge CL**, Lee HJ, Schumacher JA, Gratz KL, Krull JL, Holloman G. Alcohol as an acute risk factor for recent suicide attempts: a case-crossover analysis. *J Stud Alcohol Drugs* 2013; **74**: 552-558 [PMID: 23739018]

107 **Jones AW**, Holmgren A, Ahlner J. Toxicology findings in suicides: concentrations of ethanol and other drugs in femoral blood in victims of hanging and poisoning in relation to age and gender of the deceased. *J Forensic Leg Med* 2013; **20**: 842-847 [PMID: 24112333 DOI: 10.1016/j.jflm.2013.06.027]

108 **Kaplan MS**, McFarland BH, Huguet N, Conner K, Caetano R, Giesbrecht N, Nolte KB. Acute alcohol intoxication and suicide: a gender-stratified analysis of the National Violent Death Reporting System. *Inj Prev* 2013; **19**: 38-43 [PMID: 22627777 DOI: 10.1136/injuryprev-2012-040317]

109 **Payne S,** Swami V, Stanistreet DL. The social construction of gender and its influence on suicide: a review of the literature. *J Mens Heatlh* 2008; **5**: 23-35 [DOI: 10.1016/j.jomh.2007.11.002]

110 **Nolen-Hoeksema S**. Emotion regulation and psychopathology: the role of gender. *Annu Rev Clin Psychol* 2012; **8**: 161-187 [PMID: 22035243 DOI: 10.1146/annurev-clinpsy-032511-143109]

111 **Chapple CL**, Johnson KA. Gender differences in impulsivity. *Youth Violence and Juv Justice* 2007; **5**: 221-34 [DOI: 10.1177/1541204007301286]

112 **O'Connor R,** Nock MK. The psychology of suicidal behaviour. *Lancet* 2014; **1:** 73-85 [DOI: 10.1016/S2215-0366(14)70222-6]

113 **Windle M**, Spear LP, Fuligni AJ, Angold A, Brown JD, Pine D, Smith GT, Giedd J, Dahl RE. Transitions into underage and problem drinking: summary of developmental processes and mechanisms: ages 10-15. *Alcohol Res Health* 2009; **32**: 30-40 [PMID: 23104445]

114 **Pirkis J,** Robinson J. Improving our understanding of youth suicide clusters. *Lancet* 2014; **1**: 5-6 [DOI: 10.1016/S2215-0366(14)70227-5]

115 **Swanson SA**, Colman I. Association between exposure to suicide and suicidality outcomes in youth. *CMAJ* 2013; **185**: 870-877 [PMID: 23695600 DOI: 10.1503/cmaj.121377]

116 **van Geel M**, Vedder P, Tanilon J. Relationship between peer victimization, cyberbullying, and suicide in children and adolescents: a meta-analysis. *JAMA Pediatr* 2014; **168**: 435-442 [PMID: 24615300 DOI: 10.1001/jamapediatrics.2013.4143]

117 **Klomek AB**, Sourander A, Niemelä S, Kumpulainen K, Piha J, Tamminen T, Almqvist F, Gould MS. Childhood bullying behaviors as a risk for suicide attempts and completed suicides: a population-based birth cohort study. *J Am Acad Child Adolesc Psychiatry* 2009; **48**: 254-261 [PMID: 19169159 DOI: 10.1097/CHI.0b013e318196b91f]

118 **Brunstein Klomek A**, Sourander A, Gould M. The association of suicide and bullying in childhood to young adulthood: a review of cross-sectional and longitudinal research findings. *Can J Psychiatry* 2010; **55**: 282-288 [PMID: 20482954]

119 **Devries KM**, Mak JY, Bacchus LJ, Child JC, Falder G, Petzold M, Astbury J, Watts CH. Intimate partner violence and incident depressive symptoms and suicide attempts: a systematic review of longitudinal studies. *PLoS Med* 2013; **10**: e1001439 [PMID: 23671407 DOI: 10.1371/journal.pmed.1001439]

120 **Russell ST**, Toomey RB. Men's sexual orientation and suicide: evidence for U.S. adolescent-specific risk. *Soc Sci Med* 2012; **74**: 523-529 [PMID: 20833460 DOI: 10.1016/j.socscimed.2010.07.038]

121 **Haas AP**, Eliason M, Mays VM, Mathy RM, Cochran SD, D'Augelli AR, Silverman MM, Fisher PW, Hughes T, Rosario M, Russell ST, Malley E, Reed J, Litts DA, Haller E, Sell RL, Remafedi G, Bradford J, Beautrais AL, Brown GK, Diamond GM, Friedman MS, Garofalo R, Turner MS, Hollibaugh A, Clayton PJ. Suicide and suicide risk in lesbian, gay, bisexual, and transgender populations: review and recommendations. *J Homosex* 2011; **58**: 10-51 [PMID: 21213174 DOI: 10.1080/00918369.2011.534038]

122 **Marshal MP**, Dietz LJ, Friedman MS, Stall R, Smith HA, McGinley J, Thoma BC, Murray PJ, D'Augelli AR, Brent DA. Suicidality and depression disparities between sexual minority and heterosexual youth: a meta-analytic review. *J Adolesc Health* 2011; **49**: 115-123 [PMID: 21783042 DOI: 10.1016/j.jadohealth.2011.02.005]

123 **Bauer G,** Pyne J, Francino M, Hammond R. Suicidality among trans people in Ontario: Implications for social work and social justice. *Service Social* 2013; **59:** 35-62 [DOI: 10.7202/1017478ar]

124 **Möller-Leimkühler AM**. The gender gap in suicide and premature death or: why are men so vulnerable? *Eur Arch Psychiatry Clin Neurosci* 2003; **253**: 1-8 [PMID: 12664306 DOI: 10.1007/s00406-003-0397-6]

125 **Mac An Ghaill M**, Haywood C. Understanding boys': thinking through boys, masculinity and suicide. *Soc Sci Med* 2012; **74**: 482-489 [PMID: 20833461 DOI: 10.1016/j.socscimed.2010.07.036]

126 **Cleary A**. Suicidal action, emotional expression, and the performance of masculinities. *Soc Sci Med* 2012; **74**: 498-505 [PMID: 21930333 DOI: 10.1016/j.socscimed.2011.08.002]

127 **Plöderl M**, Wagenmakers EJ, Tremblay P, Ramsay R, Kralovec K, Fartacek C, Fartacek R. Suicide risk and sexual orientation: a critical review. *Arch Sex Behav* 2013; **42**: 715-727 [PMID: 23440560 DOI: 10.1007/s10508-012-0056-y]

128 **Hottes T**, Ferlatte O, Gesnick D. Suicide and HIV as leading causes of death among gay and bisexual men: a comparison of estimated mortality and published research. *Critical Public Health* 2014: 1-14 [DOI: 10.1080/09581596.2014.946887]

129 **Joiner T**. Why do people die by suicide? Cambridge: Harvard University Press, 2005

130 **Eisenberger NI**. The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. *Nat Rev Neurosci* 2012; **13**: 421-434 [PMID: 22551663]

131 **Witte T**, Gordon KH, Smith PN, Van Orden KA. Stoicism and Sensation Seeking: Male Vulnerabilities for the Acquired Capability for Suicide. *J Res Pers* 2012; **46**: 384-392 [PMID: 22736874 DOI: 10.1016/j.jrp.2012.03.004]

132 **Daniel SS**, Goldston DB, Erkanli A, Franklin JC, Mayfield AM. Trait anger, anger expression, and suicide attempts among adolescents and young adults: a prospective study. *J Clin Child Adolesc Psychol* 2009; **38**: 661-671 [PMID: 20183651 DOI: 10.1080/15374410903103494]

133 **Levi-Belz Y**, Gvion Y, Horesh N, Apter A. Attachment patterns in medically serious suicide attempts: the mediating role of self-disclosure and loneliness. *Suicide Life Threat Behav* 2013; **43**: 511-522 [PMID: 23662907 DOI: 10.1111/sltb.12035]

134 **Fergusson DM**, Beautrais AL, Horwood LJ. Vulnerability and resiliency to suicidal behaviours in young people. *Psychol Med* 2003; **33**: 61-73 [PMID: 12537037 DOI: 10.1017/S0033291702006748]

135 **Winterrowd E**, Canetto SS. The long-lasting impact of adolescents' deviant friends on suicidality: a 3-year follow-up perspective. *Soc Psychiatry Psychiatr Epidemiol* 2013; **48**: 245-255 [PMID: 22717595 DOI: 10.1007/s00127-012-0529-2]

136 **Lynskey MT**, Fergusson DM. Factors protecting against the development of adjustment difficulties in young adults exposed to childhood sexual abuse. *Child Abuse Negl* 1997; **21**: 1177-1190 [PMID: 9429770 DOI: 10.1016/S0145-2134(97)00093-8]

137 **Keyes KM**, Schulenberg JE, O'Malley PM, Johnston LD, Bachman JG, Li G, Hasin D. Birth cohort effects on adolescent alcohol use: the influence of social norms from 1976 to 2007. *Arch Gen Psychiatry* 2012; **69**: 1304-1313 [PMID: 22868751 DOI: 10.1001/archgenpsychiatry.2012.787]

138 **Benjet C**, Borges G, Medina-Mora ME, Méndez E. Chronic childhood adversity and stages of substance use involvement in adolescents. *Drug Alcohol Depend* 2013; **131**: 85-91 [PMID: 23276477 DOI: 10.1016/j.drugalcdep.2012.12.002]

139 **Hamburger ME**, Leeb RT, Swahn MH. Childhood maltreatment and early alcohol use among high-risk adolescents. *J Stud Alcohol Drugs* 2008; **69**: 291-295 [PMID: 18299771]

140 **Czyz EK**, Horwitz AG, Eisenberg D, Kramer A, King CA. Self-reported barriers to professional help seeking among college students at elevated risk for suicide. *J Am Coll Health* 2013; **61**: 398-406 [PMID: 24010494 DOI: 10.1080/07448481.2013.820731]

141 **Fergusson DM**, Boden JM, Horwood LJ. Tests of causal links between alcohol abuse or dependence and major depression. *Arch Gen Psychiatry* 2009; **66**: 260-266 [PMID: 19255375 DOI: 10.1001/archgenpsychiatry.2008.543]

142 **Schuckit MA**. Alcohol-use disorders. *Lancet* 2009; **373**: 492-501 [PMID: 19168210 DOI: 10.1016/S0140-6736(09)60009-X]

143 **Gould MS**, Fisher P, Parides M, Flory M, Shaffer D. Psychosocial risk factors of child and adolescent completed suicide. *Arch Gen Psychiatry* 1996; **53**: 1155-1162 [PMID: 8956682 DOI: 10.1001/archpsyc.1996.01830120095016]

144 **Brent DA**, Perper JA, Moritz G, Baugher M, Roth C, Balach L, Schweers J. Stressful life events, psychopathology, and adolescent suicide: a case control study. *Suicide Life Threat Behav* 1993; **23**: 179-187 [PMID: 8249030]

145 **Brent DA**. Risk factors for adolescent suicide and suicidal behavior: mental and substance abuse disorders, family environmental factors, and life stress. *Suicide Life Threat Behav* 1995; **25** Suppl: 52-63 [PMID: 8553429]

146 **Rickwood D**, Deane FP, Wilson CJ, Ciarrochi JV. Young people's help-seeking for mental health problems. *Aust E J Adv Ment Health* 2005; **4** (3 Suppl): 1-34 Available from: URL: http: //ro.uow.edu.au/hbspapers/2106/

147 **Gould MS**, Velting D, Kleinman M, Lucas C, Thomas JG, Chung M. Teenagers' attitudes about coping strategies and help-seeking behavior for suicidality. *J Am Acad Child Adolesc Psychiatry* 2004; **43**: 1124-1133 [PMID: 15322416 DOI: 10.1097/01.chi.0000132811.06547.31]

148 **Lake AM**, Kandasamy S, Kleinman M, Gould MS. Adolescents' attitudes about the role of mental illness in suicide, and their association with suicide risk. *Suicide Life Threat Behav* 2013; **43**: 692-703 [PMID: 23952811 DOI: 10.1111/sltb.12052]

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**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 (*e.g.*, disclosure, and to whom) and suicide attempt methods |