



Contributing Factors to Heterogeneity in the Timing of the Onset of Nonfatal Suicidal Behavior: Results From a Nationally Representative Study

Nicolas Hoertel, Julien Sabatier, Carlos Blanco, Mark Olfson, Jean-Pierre Schuster, Guillaume Airagnes, Hugo Peyre, Frédéric Limosin

► To cite this version:

Nicolas Hoertel, Julien Sabatier, Carlos Blanco, Mark Olfson, Jean-Pierre Schuster, et al.. Contributing Factors to Heterogeneity in the Timing of the Onset of Nonfatal Suicidal Behavior: Results From a Nationally Representative Study. *Journal of Clinical Psychiatry*, 2020, 81 (3), pp.19m13017. 10.4088/JCP.19m13017 . inserm-02572010

HAL Id: inserm-02572010

<https://inserm.hal.science/inserm-02572010>

Submitted on 13 May 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Word count: 2994 (<3000)

Word count (abstract only): 248 (<250)

Tables: 2

Figure: 1

**Contributing factors to heterogeneity in the timing of the onset of
nonfatal suicidal behavior: Results from a nationally representative study**

Running title: Heterogeneity in the timing of suicide attempt onset

Nicolas Hoertel, M.D., M.P.H., Ph.D.,^{a, b, c, *}

Julien Sabatier, M.D.,^a

Carlos Blanco, M.D., Ph.D.,^d

Mark Olfson, M.D., M.P.H.,^e

Jean-Pierre Schuster, M.D.,^f

Guillaume Airagnes, M.D., M.P.H.,^{a, b, g, h}

Hugo Peyre, M.D., Ph.D.,^{i, j}

Frédéric Limosin, M.D., Ph.D.,^{a, b, c}

^a Centre Ressource Régional de Psychiatrie du Sujet Agé (CRRPSA), Service de Psychiatrie et d'Addictologie de l'adulte et du sujet âgé, DMU Psychiatrie et Addictologie, AP-HP.Centre-Université de Paris.

^b Faculté de médecine Paris Descartes, Université de Paris, Paris, France.

^c Inserm U1266, Institut de Psychiatrie et Neurosciences de Paris, Paris, France.

^d Division of Epidemiology, Services, and Prevention Research, National Institute on Drug Abuse, Bethesda, Maryland, USA.

^e Department of Psychiatry, New York State Psychiatric Institute / Columbia University, New York, NY 10032, USA.

^f Old-age psychiatry service, Lausanne University Hospital, Lausanne, Switzerland

^g UMS 011, Population-based Epidemiological Cohorts, Inserm, Villejuif, France.

^h UMR 1168, VIMA, Inserm, Villejuif, France.

ⁱ Assistance Publique-Hôpitaux de Paris, Robert Debré Hospital, Child and Adolescent Psychiatry Department, Paris, France.

^j Cognitive Sciences and Psycholinguistic Laboratory, Ecole Normale Supérieure, Paris, France.

Corresponding author:

Nicolas Hoertel, M.D., M.P.H., Ph.D.,

Department of Psychiatry, Corentin Celton Hospital, Paris Descartes University

4 parvis Corentin Celton; 92130 Issy-les-Moulineaux, France

Phone: 33 (0) 1 58 00 44 21

Fax: 33 (0) 1 58 00 44 53

Email: nico.hoertel@yahoo.fr

Conflicts of interest: Pr. Limosin has received speaker and consulting fees from AstraZeneca, Janssen, Lundbeck, Otsuka Pharmaceuticals, Roche and Servier outside the submitted work. Other authors report no conflicts of interest.

Acknowledgements: The National Epidemiologic Survey on Alcohol and Related Conditions was sponsored by the National Institute on Alcohol Abuse and Alcoholism and funded, in part, by the Intramural Program, NIAAA, National Institutes of Health.

Disclaimer: The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of any of the sponsoring organizations, agencies, or the US government.

Additional information: The original data set for the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) is available from the National Institute on Alcohol Abuse and Alcoholism (<http://www.niaaa.nih.gov>).

Abstract

Introduction: It remains unclear whether specific clinical factors contribute to heterogeneity in the timing of the onset of nonfatal suicidal behavior. This knowledge could have important implications for suicide prevention.

Methods: Using a nationally representative US adult sample, the second wave of the National Epidemiologic Survey on Alcohol and Related Conditions, we compared the characteristics of 4 different suicide attempter groups: those who first attempted (i) before 18 years, (ii) between 18 and 34 years, (iii) between 35 and 49 years, and (iv) at 50 years or older. Specifically, we examined psychiatric disorders that occurred before the first suicide attempt, childhood maltreatment experiences, parental history of psychiatric disorders, and sociodemographic characteristics.

Results: Most first non-fatal suicide attempts (85.3%) occurred before age 35 years. Compared with suicide attempts occurring between 18 and 34 years, suicide attempts occurring <18 years were more strongly associated with childhood maltreatment and less strongly linked to lifetime prior psychiatric disorders, whereas first suicide attempts occurring at 35 years and older were more strongly associated with a prior lifetime history of substance use disorders, including alcohol use disorder and nicotine dependence, and mood disorders, including mania/hypomania and dysthymic disorder between 35 and 49 years, and major depressive episode at 50 years and older (all $p < 0.05$).

Conclusions: Our results suggest age differences in risk factors for first non-fatal suicide attempt. Improving early detection and treatment of psychiatric disorders and preventing childhood maltreatment may have broad benefits to reduce the burden of suicidal behavior at all ages.

Key words: Suicide attempt; age; old; young; onset; risk factors; childhood maltreatment; psychiatric symptoms.

Introduction

Suicide continues to be a leading cause of preventable death worldwide,¹ accounting for an estimated 800,000 deaths worldwide,² and there are many more suicide attempts, which are associated with significant morbidity.² Prior research suggests substantial age differences in suicide and suicide attempt rates.²⁻⁷ Although older adults attempt suicide less often than younger ones, suicide completion rates increase as a function of age for both men and women to a peak in old age.² Understanding the factors that contribute to heterogeneity in the timing of the onset of nonfatal suicidal behavior may help clinicians identify individuals who are at greater risk for a first attempt, which is particularly important in older adults where a large percentage of first attempts are fatal,⁸ and help refine prevention interventions for this major public health problem.⁹

Several lines of evidence support potential age differences in risk factors profiles of suicide attempt. First, while the prevalence of most psychiatric disorders is lower in older than in younger adults,¹⁰⁻¹³ psychiatric disorders are among the strongest predictors of suicide attempt and completion across all ages.^{9, 14-21} Prior studies^{3, 4, 18, 22, 23} have suggested age differences in the strength of associations between psychiatric disorders and suicide risk. For example, major depression may be associated with a stronger risk of suicide in older than in younger adults, whereas substance use disorders may play a lesser role in later life suicide risk. Second, the male to female ratio of suicide attempts and completions is higher in older than in younger adults.¹⁹ Third, neurodegenerative, cerebrovascular and other chronic diseases may play a stronger contributing role in suicide risk in older than in younger adults.^{23, 24} Finally, the detrimental effect of certain socioeconomic and environmental factors, such as loneliness, financial and social difficulties and the loss of loved ones on suicide risk may differ in magnitude between younger and older adults.²⁵⁻²⁸

However, little is known about the similarities or differences between adults who first attempted suicide at an older or younger age. Because a substantial proportion of older adults who attempt suicide have a prior history of suicide attempt,¹² this distinction may help disentangle risk factors specifically related to emerging suicide risk in later life and progress in the understanding of suicidal behavior across the lifespan.²⁹ This knowledge may also have important implications for suicide prevention by informing identification of adults at greater risk for suicide attempt according to their age, and may help refine specific assessment and service provision according to the age of the first suicide attempt.

In this study, we investigated whether specific factors may explain differences in the timing of first suicide attempt across different age at first attempt groups. Specifically, we hypothesized that factors contributing to differences in the timing of first suicide attempt would include sociodemographic characteristics (sex, race/ethnicity, nativity and education), lifetime prior psychiatric disorders (i.e, disorders that occurred before the first/single suicide attempt), childhood maltreatment experiences and parental history of psychiatric disorders.

Methods

Sample

Data were drawn from the Wave 1 and Wave 2 NESARC, a nationally representative face-to-face survey of the US adult population, conducted in 2001–2002 (Wave 1) and 2004–2005 (Wave 2) by the National Institute on Alcoholism and Alcohol Abuse (NIAAA) and described in detail elsewhere.³⁰ The target population included the civilian population aged 18 years and older residing in households and group quarters. Face-to-face interviews were conducted with 43,093 respondents. The overall survey response rate was 81%. In Wave 2, attempts were made to conduct face-to-face re-interviews with all 43,093 respondents of the Wave 1 interview. The cumulative response rate at Wave 2 was 70.2%, reflecting 34,653

completed Wave 2 interviews. The Wave 2 NESARC data were weighted to be representative of the US civilian population based on the 2000 census.³⁰ The research protocol, including informed consent procedures, received full human subjects review and approval from the US Census Bureau and the Office of Management and Budget.³⁰ The present analysis included the 34,653 participants who completed both NESARC waves.

Measures

Assessment of suicide attempts and age at first suicide attempt

All NESARC respondents were asked the following questions: 1) “Did you ever attempt suicide?” and 2) “How old were you the first time it happened?” Based on prior research that identified age differences in suicide attempts rates,^{5, 12} a preliminary analysis of the distribution of age at first suicide attempt in NESARC, and assuming that we needed at least 40 suicide attempts by age group for adequate statistical power, we defined 5 mutually exclusive groups: participants who first attempted suicide (i) before 18 years, (ii) between 18 and 34 years, (iii) between 35 and 49 years, and (iv) at 50 years or older, and (v) those who never attempted suicide.

Sociodemographic characteristics

Sociodemographic characteristics included age, sex, race/ethnicity (White vs. non-White), nativity, education, and family poverty which was considered present if participants reported that their family received money from any government assistance program before they were 18 years of age.

Assessment of DSM-IV-TR Axis I and II disorders

Psychiatric disorders were assessed using the Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version (AUDADIS-IV), a structured diagnostic

instrument administered by trained lay interviewers.³⁰ Axis I diagnoses included substance use disorders (alcohol use disorder, drug use disorder and nicotine dependence), mood disorders (major depressive episode, dysthymic disorder, mania or hypomania), anxiety disorders (panic disorder with and without agoraphobia, social anxiety disorder, specific phobia, generalized anxiety disorder and post-traumatic stress disorder), pathological gambling, conduct disorder and attention deficit hyperactivity disorder. All respondents with a lifetime history of Axis I psychiatric disorders were questioned about the age at onset of disorders to determine whether these disorders occurred before the first suicide attempt. The test-retest reliability and validity of AUDADIS-IV measures of DSM-IV psychiatric disorders is good to excellent for substance use disorders and fair to good for other disorders.³⁰

Childhood traumatic experiences

Five types of childhood maltreatment were examined: emotional neglect, physical neglect, emotional abuse, physical abuse, and sexual abuse. Respondents completed 19 questions regarding exposure to the types of maltreatment occurring before age 17 years adapted from the Childhood Trauma Questionnaire (CTQ)³¹ and the Conflict Tactics Scale (CTS).³² Test-retest of these items was adequate, with Cronbach's alpha coefficients ranging from 0.78 for physical abuse to 0.90 for sexual abuse.³³ Consistent with prior work,^{9, 10, 34, 35} participants were considered to have suffered a type of childhood maltreatment (e.g., physical abuse) if they reported frequent exposure (sometimes, often or very often), except for sexual abuse, which was considered present if they indicated at least 1 episode.

Parental history of psychiatric disorders

Parental histories of alcohol use disorder, drug use disorder, major depression and antisocial personality disorder were ascertained in separate modules of the AUDADIS³⁰ and defined in our study as having at least one parent with the disorder. All respondents were

prompted with a definition that included examples for each condition. The definitions read to respondents included readily observable manifestations, since these are the most likely to be known by participants and therefore are likely to be more sensitive.³⁶ The test-retest reliability of AUDADIS family history diagnoses is very good to excellent.³⁷

Statistical analyses

Percentages and their standard errors (SE) were estimated using SUDAAN (Version 8.1 Research Triangle Institute Research Triangle Park) to adjust for the complex design of the NESARC. Binary logistic regression analyses were performed to compare the sociodemographic and clinical characteristics of each age at first suicide attempt group with the reference group of individuals who attempted suicide between 18 and 34 years. Because sex, age and race/ethnicity have been shown to influence the risk for attempting suicide,^{9, 16, 38} all analyses adjusted for these variables. Statistical significance was evaluated using a two-sided alpha set *a priori* set at 0.05.

Results

Sample characteristics

Of the 34,654 participants, 25 (<0.01%) were excluded from our analyses because of missing data for age at suicide attempt. Of the remaining 34,629 participants, 1240 (3.6%) reported a lifetime history of suicide attempt. Among these individuals, 519 (45.2% [SE=1.8]) made a first/single suicide attempt before the age of 18 years, 535 (40.1% [SE=1.8]) between 18 and 34 years, 145 (11.7% [SE=1.2]) between 35 and 49 years, and 41 (3.0% [SE=0.6]) at 50 years and older. Stratified rates per 1,000 persons of first non-fatal suicide attempts by age group revealed that first suicide attempts were significantly more common between 18 and 34 years than in other age groups ($p < 0.001$), with no significant differences between the age groups <18 years and 35-49 years, whereas first suicide attempts

were significantly less frequent among individuals aged 50 years and older than in other age groups ($p < 0.01$) (**Figure 1**).

Sociodemographic characteristics, prior lifetime psychiatric disorders, childhood maltreatment and family history of psychiatric disorders associated with age at first suicide attempt (Tables 1 and 2)

There were no significant differences across age at first suicide attempt groups in sociodemographic characteristics (i.e., sex, race/ethnicity, nativity, education and family poverty).

Compared to respondents who first attempted suicide between 18 and 34 years, those who first attempted suicide before 18 years were significantly less likely to have a prior lifetime history of psychiatric disorders, including substance use disorders, major depressive episode, mania or hypomania, panic disorder with or without agoraphobia and generalized anxiety disorder. Individuals who attempted suicide after 35 years were significantly more likely to have a prior lifetime history of alcohol use disorder and nicotine dependence than individuals who first attempted suicide between 18 and 34 years. Furthermore, individuals who first attempted suicide between 35 and 49 years were more likely to have a prior lifetime history of mania or hypomania and dysthymic disorder, and individuals who first attempted suicide at 50 years and older were significantly more likely to have a prior lifetime history of major depressive episode compared to respondents who first attempted suicide between 18 and 34 years.

All childhood maltreatment types were significantly more frequent among individuals who first attempted suicide before 18 years than in those who first attempted suicide between 18 and 34 years. There were no significant differences across the other age at first suicide attempt groups.

Finally, there were no significant differences across groups in family history of psychiatric disorders.

Discussion

In a large, nationally representative sample of adults, most first non-fatal suicide attempts (85.3%) occurred before age 35 years. Our results suggest that several clinical factors influence the timing of the onset of non-fatal suicidal behavior. Compared with first suicide attempts occurring between 18 and 34 years, first suicide attempts occurring <18 years were more strongly associated with childhood maltreatment and less strongly linked to prior lifetime psychiatric disorders, whereas first suicide attempts occurring at 35 years and older were more strongly associated with a prior lifetime history of substance use disorders, including alcohol use disorder and nicotine dependence, and mood disorders, including mania/hypomania and dysthymic disorder between 35 and 49 years, and major depressive episode at 50 years and older. Finally, we did not find any significant associations between family history of psychiatric disorders and sociodemographic characteristics (i.e., gender, race-ethnicity, nativity, education and family poverty) with age at first/single suicide attempt.

Almost half (45.2%) of individuals with a lifetime history of suicide attempt first attempted before 18 years, and most of them (85.3%) before 35 years. Several factors may contribute to explain the elevated incidence of suicide attempt in young people. First, childhood and adolescence constitute an important phase of neuropsychological development, including the development and the maturation of physical and cognitive abilities and emotional self-awareness. For example, a study³⁹ found that the dorsolateral prefrontal cortex (linked to important behavioral changes such as the ability to inhibit impulsivity and to evaluate consequences of decisions) does not reach adult dimensions until the age of 20. This lag may explain why certain vulnerable children and adolescents are prone to maladaptive emotional (e.g., emotional coping), cognitive (e.g., self-criticism) and social (e.g., isolation)

strategies⁴⁰, which may increase their risk of suicide attempt. Second, adolescence is a period marked by new social stressors (e.g., peer-rejection, bullying, academic pressure),⁴¹ less perceived support from adults⁴² and for certain adolescents by a major identity developments (e.g., sexual, social)⁴³. Finally, the decrease in incidence of suicide attempts after 35 years may be explained by the greater case-fatality rate associated with suicide attempts in later life, as the ratio between suicide and suicide attempt tend to rise as a function of age for both men and women to a peak in old age,^{2, 44} and by the fact that those who completed suicide in earlier attempts do not reach older age.

Although it is noteworthy that most psychiatric disorders increase the risk of suicide attempt at all ages^{12, 14, 16, 17, 45-48} we found that several disorders may be associated with heterogeneity in the timing of the onset of nonfatal suicidal behavior. Specifically, compared with first suicide attempts occurring between 18 and 34 years, first suicide attempts occurring in later life (i.e., at 35 years and older) were more strongly associated with mood disorders and substance use disorders, whereas first suicide attempts occurring early in life (i.e., <18 years) were less strongly related to psychiatric disorders.

Our results are in line with those of prior studies^{3, 4, 18, 22, 23, 49, 50} that have suggested that mood disorders are more strongly associated with suicide risk in older than in younger adults. There is evidence that the brain circuitry and neurochemical abnormalities related to mood disorders can disrupt the underlying neurobiological structures involved in stress response and susceptibility to environmental influences.⁵¹ Longer exposure to depression may account at least in part for the increased suicide risk in older adults,⁵² possibly through greater neuroinflammation.⁵³⁻⁵⁵

Contrasting with prior studies suggesting that substance use disorders may play a lesser role in later life suicide risk, we found that first suicide attempts occurring in later life (i.e. at 35 years and older) may be more strongly associated with alcohol use disorder and

nicotine dependence than those occurring between 18 and 34 years. Our use of a general population sample and our focus on age at first suicide attempt may partly explain these discrepancies since prior studies have often relied on clinical samples and their results might have reflected differences related to multiple suicide attempts rather than to age at first suicide attempt. A greater vulnerability to deleterious neurological effects of nicotine and alcohol in older adults, which may result from physiological changes that occur with ageing, such as reduced kidney clearance and volume of distribution,^{56, 57} might explain their stronger effect on suicide risk in older than in younger adults.

We found that all childhood maltreatment types were significantly more common among individuals who first attempted suicide before 18 years than in those who first attempted suicide between 18 and 34 years. These findings are in line with prior research showing that exposure to childhood maltreatment, which affects developmental processes related to the strengthening of interpersonal and emotion regulation,^{58, 59} possibly through epigenetic modifications,⁶⁰ can have detrimental long-term effects on suicide risk,^{10, 34} particularly when it occurs at a younger age⁶¹. The effect of maltreatment might also be less intense later in life because people may develop coping strategies as they age, decreasing its detrimental effect on suicide risk.

Although family history of psychiatric disorders and many psychosocial and environmental factors are established risk factors for suicide,^{62, 63} we did not find that family history of alcohol and drug use disorders, antisocial personality disorder and major depression nor gender, race-ethnicity, nativity, education and family poverty differentially influenced the timing of the first non-fatal suicide attempt. This result is consistent with prior work that showed that genetic risk profiles associated with increased risk for suicide attempt may be shared to a large degree in older and younger adults and may have enduring effects on this

risk,^{64, 65} and that socioeconomic and environmental factors are important risk factors for suicidal behavior at all ages.^{66, 67}

Our findings have important implications. First, our results support the importance of assessing age at onset of first non-fatal suicide attempt because we found substantial age differences in associated risk factors. Second, given that almost half of individuals attempted suicide before 18 years and that these individuals were frequently exposed to childhood maltreatment, all children and adolescents who attempt suicide should be systematically assessed for childhood maltreatment. Preventing child maltreatment with evidence-based interventions⁶⁸ could strongly decrease the burden of suicidal behavior. Third, older adults with mood disorders and substance use disorders should be systematically assessed for suicide risk, particularly because a large percentage of first attempts are fatal in this population.⁸ Finally, our findings underscore the importance of performing regular suicide risk assessments in individuals with any psychiatric disorder and history of childhood maltreatment at all ages and the need for close follow-up of suicide attempters to reduce the risk of suicide.

This study has several limitations. First, the participants included in our study had experienced exclusively non-fatal suicide attempts, thus the results could not be extrapolated to individuals who died by suicide. Second, we cannot establish a causal relationship between explored contributing factors and initial suicide attempts.⁶⁹ Third, the NESARC survey relies on retrospective self-reports and reporting of suicide attempts, history of psychiatric disorder and childhood maltreatment experiences may be subject to recall bias, particularly among older adults. Fourth, the number of participants who first attempted suicide at 50 years of age or older was relatively modest (N=41), which resulted in limited statistical power. Fifth, several disorders (e.g., psychotic disorders, major neurocognitive disorders) known to be linked to suicide attempts were not assessed in the NESARC. Finally, certain environmental

risk factors such as loneliness and stressful life events and factors of suicide risk reduction such connectedness with family, mental health professionals and community organizations^{4, 70, 71} were not assessed in the NESARC.

Conclusion

Our results suggest substantial age differences in risk factors for first non-fatal suicide attempt. Improving early detection and treatment of psychiatric disorders and preventing childhood maltreatment may have broad benefits to reduce the burden of suicidal behavior at all ages.

Clinical points

- In a large, nationally representative sample of adults, we found that 85.3% of first non-fatal suicide attempts occurred before age 35 years and that several clinical factors may influence the timing of the onset of non-fatal suicidal behavior
- First suicide attempts occurring <18 years may be more strongly associated with childhood maltreatment and less strongly linked to prior lifetime psychiatric disorders, whereas first suicide attempts occurring at 35 years and older may be more strongly associated with a prior lifetime history of substance use disorders, including alcohol use disorder and nicotine dependence, and mood disorders, including mania/hypomania and dysthymic disorder between 35 and 49 years, and major depressive episode at 50 years and older.
- We did not find any significant associations between family history of psychiatric disorders and sociodemographic characteristics with age at first/single suicide attempt.

- Improving early detection and treatment of psychiatric disorders and preventing childhood maltreatment may have broad benefits to reduce the burden of suicidal behavior at all ages.

References

1. Rockett IRH, Regier MD, Kapusta ND, et al. Leading causes of unintentional and intentional injury mortality: united states, 2000–2009. *American journal of public health* 2012;102(11):e84-e92.
2. World Health Organization. (2012). Public health action for the prevention of suicide: a framework.
3. Conwell Y, Van Orden K, Caine ED. Suicide in older adults. *Psychiatr Clin North Am* 2011 Jun;34(2):451-468, ix.
4. Turecki G, Brent DA. Suicide and suicidal behaviour. *Lancet* 2016 Mar 19;387(10024):1227-1239.
5. Spicer RS, Miller TR. Suicide acts in 8 states: incidence and case fatality rates by demographics and method. *Am J Public Health* 2000 Dec;90(12):1885-1891.
6. Nock MK, Borges G, Bromet EJ, Cha CB, Kessler RC, Lee S. Suicide and suicidal behavior. *Epidemiol Rev* 2008;30:133-154.
7. Olfson M, Blanco C, Wall M, et al. National Trends in Suicide Attempts Among Adults in the United States. *JAMA Psychiatry* 2017 Nov 1;74(11):1095-1103.
8. Byers A, Li Y. FATAL AND NON-FATAL FIRST SUICIDE ATTEMPTS IN LATER LIFE AND IMPLICATIONS FOR PREVENTION. *Innovation in Aging* 2018;2(Suppl 1):278.
9. Peyre H, Hoertel N, Stordeur C, et al. Contributing Factors and Mental Health Outcomes of First Suicide Attempt During Childhood and Adolescence: Results From a Nationally Representative Study. *J Clin Psychiatry* 2017 Jun;78(6):e622-e630.
10. Hoertel N, Franco S, Wall MM, et al. Childhood maltreatment and risk of suicide attempt: a nationally representative study. *J Clin Psychiatry* 2015 Jul;76(7):916-923; quiz 923.
11. McMahon K, Hoertel N, Peyre H, Blanco C, Fang C, Limosin F. Age differences in DSM-IV borderline personality disorder symptom expression: Results from a national study using item response theory (IRT). *J Psychiatr Res* 2019 Mar;110:16-23.
12. Pascal de Raykeer R, Hoertel N, Blanco C, et al. Effects of Psychiatric Disorders on Suicide Attempt: Similarities and Differences Between Older and Younger Adults in a National Cohort Study. *J Clin Psychiatry* 2018 Oct 9;79(6).
13. Hoertel N, Le Strat Y, Gorwood P, et al. Why does the lifetime prevalence of major depressive disorder in the elderly appear to be lower than in younger adults? Results from a national representative sample. *J Affect Disord* 2013 Jul;149(1-3):160-165.
14. Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. *British Journal of Psychiatry* 1997;170(3):205-228.
15. Pokorny AD. Prediction of suicide in psychiatric patients. Report of a prospective study. *Arch Gen Psychiatry* 1983 Mar;40(3):249-257.
16. Hoertel N, Franco S, Wall MM, et al. Mental disorders and risk of suicide attempt: a national prospective study. *Mol Psychiatry* 2015 Jun;20(6):718-726.

17. Hoertel N, Blanco C, Olfson M, et al. A Comprehensive Model of Predictors of Suicide Attempt in Depressed Individuals and Effect of Treatment-Seeking Behavior: Results From a National 3-Year Prospective Study. *J Clin Psychiatry* 2018 Jul 31;79(5).
18. De Leo D, Padoani W, Lonnqvist J, et al. Repetition of suicidal behaviour in elderly Europeans: a prospective longitudinal study. *J Affect Disord* 2002 Dec;72(3):291-295.
19. Wiktorsson S, Runeson B, Skoog I, Ostling S, Waern M. Attempted suicide in the elderly: characteristics of suicide attempters 70 years and older and a general population comparison group. *Am J Geriatr Psychiatry* 2010 Jan;18(1):57-67.
20. Schuster JP, Hoertel N, Le Strat Y, Manetti A, Limosin F. Personality disorders in older adults: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Am J Geriatr Psychiatry* 2013 Aug;21(8):757-768.
21. Szucs A, Szanto K, Aubry JM, Dombrovski AY. Personality and Suicidal Behavior in Old Age: A Systematic Literature Review. *Frontiers in psychiatry* 2018;9:128.
22. Szanto K, Mulsant BH, Houck P, Dew MA, Reynolds CF, 3rd. Occurrence and course of suicidality during short-term treatment of late-life depression. *Arch Gen Psychiatry* 2003 Jun;60(6):610-617.
23. Conwell Y. Suicide in later life: a review and recommendations for prevention. *Suicide Life Threat Behav* 2001 Spring;31 Suppl:32-47.
24. Minayo MC, Cavalcante FG. Suicide attempts among the elderly: a review of the literature (2002/2013). *Cien Saude Colet* 2015 Jun;20(6):1751-1762.
25. Fassberg MM, van Orden KA, Duberstein P, et al. A systematic review of social factors and suicidal behavior in older adulthood. *Int J Environ Res Public Health* 2012 Mar;9(3):722-745.
26. Turvey C, Stromquist A, Kelly K, Zwerling C, Merchant J. Financial loss and suicidal ideation in a rural community sample. *Acta Psychiatr Scand* 2002 Nov;106(5):373-380.
27. Alexopoulos GS, Bruce ML, Hull J, Sirey JA, Kakuma T. Clinical determinants of suicidal ideation and behavior in geriatric depression. *Arch Gen Psychiatry* 1999 Nov;56(11):1048-1053.
28. Pompili M, Innamorati M, Szanto K, et al. Life events as precipitants of suicide attempts among first-time suicide attempters, repeaters, and non-attempters. *Psychiatry Res* 2011 Apr 30;186(2-3):300-305.
29. Steele IH, Thrower N, Noroian P, Saleh FM. Understanding Suicide Across the Lifespan: A United States Perspective of Suicide Risk Factors, Assessment & Management. *J Forensic Sci* 2018 Jan;63(1):162-171.
30. Grant BF, Goldstein RB, Chou SP, et al. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Molecular Psychiatry* 2009;14(11):1051-1066.
31. Bernstein DP, Fink L, Handelsman L, Foote J. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *American journal of psychiatry* 1994;151:1132-1136.
32. Straus MA. Measuring intrafamily conflict and violence: The conflict tactics (CT) scales. *Journal of Marriage and the Family* 1979;41(1):75-88.
33. Ruan W, Goldstein RB, Chou SP, et al. The alcohol use disorder and associated disabilities interview schedule-IV (AUDADIS-IV): reliability of new psychiatric diagnostic modules and risk factors in a general population sample. *Drug and alcohol dependence* 2008;92(1):27-36.
34. McMahon K, Hoertel N, Olfson M, Wall M, Wang S, Blanco C. Childhood maltreatment and impulsivity as predictors of interpersonal violence, self-injury and suicide attempts: A national study. *Psychiatry Res* 2018 Nov;269:386-393.

35. McMahon K, Hoertel N, Wall MM, Okuda M, Limosin F, Blanco C. Childhood maltreatment and risk of intimate partner violence: A national study. *Journal of psychiatric research* 2015;69:42-49.
36. Slutske WS, Heath AC, Madden P, et al. Reliability and reporting biases for perceived parental history of alcohol-related problems: agreement between twins and differences between discordant pairs. *Journal of studies on alcohol* 1996;57(4):387-395.
37. Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering RP. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug and alcohol dependence* 2003;71(1):7-16.
38. Oquendo MA, Currier D, Mann JJ. Prospective studies of suicidal behavior in major depressive and bipolar disorders: what is the evidence for predictive risk factors? *Acta Psychiatr Scand* 2006 Sep;114(3):151-158.
39. Giedd JN. Structural magnetic resonance imaging of the adolescent brain. *Ann N Y Acad Sci* 2004 Jun;1021:77-85.
40. Stoep AV, McCauley E, Flynn C, Stone A. Thoughts of death and suicide in early adolescence. *Suicide Life Threat Behav* 2009 Dec;39(6):599-613.
41. Hoertel N, Le Strat Y, Lavaud P, Limosin F. Gender effects in bullying: results from a national sample. *Psychiatry Res* 2012 Dec 30;200(2-3):921-927.
42. Nansel TR, Haynie DL, Simonsmorton BG. The association of bullying and victimization with middle school adjustment. *Journal of Applied School Psychology* 2003;19(2):45-61.
43. Zhao Y, Montoro R, Igartua K, Thombs BD. Suicidal ideation and attempt among adolescents reporting "unsure" sexual identity or heterosexual identity plus same-sex attraction or behavior: forgotten groups? *J Am Acad Child Adolesc Psychiatry* 2010 Feb;49(2):104-113.
44. Bostwick JM, Pabbati C, Geske JR, McKean AJ. Suicide Attempt as a Risk Factor for Completed Suicide: Even More Lethal Than We Knew. *Am J Psychiatry* 2016 Nov 01;173(11):1094-1100.
45. Nock MK, Hwang I, Sampson NA, Kessler RC. Mental disorders, comorbidity and suicidal behavior: results from the National Comorbidity Survey Replication. *Mol Psychiatry* 2010 Aug;15(8):868-876.
46. Bostwick JM, Pankratz VS. Affective disorders and suicide risk: a reexamination. *Am J Psychiatry* 2000 Dec;157(12):1925-1932.
47. Kessler RC, Borges G, Walters EE. Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. *Archives of general psychiatry* 1999;56(7):617-626.
48. Hoertel N, Faiz H, Airagnes G, et al. A comprehensive model of predictors of suicide attempt in heavy drinkers: Results from a national 3-year longitudinal study. *Drug Alcohol Depend* 2018 May 1;186:44-52.
49. Kato K, Akama F, Yamada K, et al. Frequency and clinical features of suicide attempts in elderly patients in Japan. *Psychiatry Clin Neurosci* 2013 Feb;67(2):119-122.
50. Health NIOM. Older Adults: Depression and Suicide Facts (Fact Sheet). 2007.
51. Mann JJ. Neurobiology of suicidal behaviour. *Nature Reviews Neuroscience* 2003;4(10):819-828.
52. Zubrick SR, Hafekost J, Johnson SE, Sawyer MG, Patton G, Lawrence D. The continuity and duration of depression and its relationship to non-suicidal self-harm and suicidal ideation and behavior in adolescents 12-17. *J Affect Disord* 2017 Oct 1;220:49-56.

53. Setiawan E, Attwells S, Wilson AA, et al. Association of translocator protein total distribution volume with duration of untreated major depressive disorder: a cross-sectional study. *Lancet Psychiatry* 2018 Apr;5(4):339-347.
54. Pandey GN, Rizavi HS, Ren X, et al. Proinflammatory cytokines in the prefrontal cortex of teenage suicide victims. *J Psychiatr Res* 2012 Jan;46(1):57-63.
55. Pandey GN, Rizavi HS, Zhang H, Bhaumik R, Ren X. Abnormal protein and mRNA expression of inflammatory cytokines in the prefrontal cortex of depressed individuals who died by suicide. *J Psychiatry Neurosci* 2018 Jun 11;43(4):170192.
56. Molander L, Hansson A, Lunell E. Pharmacokinetics of nicotine in healthy elderly people. *Clin Pharmacol Ther* 2001 Jan;69(1):57-65.
57. Kleykamp BA, Heishman SJ. The older smoker. *JAMA* 2011 Aug 24;306(8):876-877.
58. Johnson JG, Cohen P, Gould MS, Kasen S, Brown J, Brook JS. Childhood adversities, interpersonal difficulties, and risk for suicide attempts during late adolescence and early adulthood. *Arch Gen Psychiatry* 2002 Aug;59(8):741-749.
59. Etkin A, Schatzberg AF. Common abnormalities and disorder-specific compensation during implicit regulation of emotional processing in generalized anxiety and major depressive disorders. *American Journal of Psychiatry* 2011;168(9):968-978.
60. Teicher MH, Samson JA. Childhood maltreatment and psychopathology: A case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. *Am J Psychiatry* 2013 Oct;170(10):1114-1133.
61. Andersen S, Tomada A, Vincow E, Valente E, Polcari A, Teicher M. Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. *The Journal of neuropsychiatry and clinical neurosciences* 2008;20(3):292-301.
62. Qin P, Agerbo E, Mortensen PB. Suicide risk in relation to family history of completed suicide and psychiatric disorders: a nested case-control study based on longitudinal registers. *Lancet* 2002 Oct 12;360(9340):1126-1130.
63. Mann JJ. A current perspective of suicide and attempted suicide. *Ann Intern Med* 2002 Feb 19;136(4):302-311.
64. Demirkan A, Penninx BW, Hek K, et al. Genetic risk profiles for depression and anxiety in adult and elderly cohorts. *Mol Psychiatry* 2011 Jul;16(7):773-783.
65. Alexopoulos GS, Morimoto SS. The inflammation hypothesis in geriatric depression. *Int J Geriatr Psychiatry* 2011 Nov;26(11):1109-1118.
66. Roy A, Sarchiopone M, Carli V. Gene-environment interaction and suicidal behavior. *J Psychiatr Pract* 2009 Jul;15(4):282-288.
67. Osvath P, Voros V, Fekete S. Life events and psychopathology in a group of suicide attempters. *Psychopathology* 2004 Jan-Feb;37(1):36-40.
68. Mikton C, Butchart A. Child maltreatment prevention: a systematic review of reviews. *Bull World Health Organ* 2009 May;87(5):353-361.
69. Le Strat Y, Hoertel N. Correlation is no causation: gymnasium proliferation and the risk of obesity. *Addiction* 2011;106(10):1871-1872.
70. McMahon K, Herr NR, Zerubavel N, Hoertel N, Neacsiu AD. Psychotherapeutic Treatment of Bipolar Depression. *Psychiatr Clin North Am* 2016 Mar;39(1):35-56.
71. Pringle B, Colpe LJ, Heinssen RK, et al. A strategic approach for prioritizing research and action to prevent suicide. *Psychiatr Serv* 2013 Jan;64(1):71-75.

Figure 1. Rates per 1,000 persons of suicide attempts by age at first/single attempt in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (n=34,629).

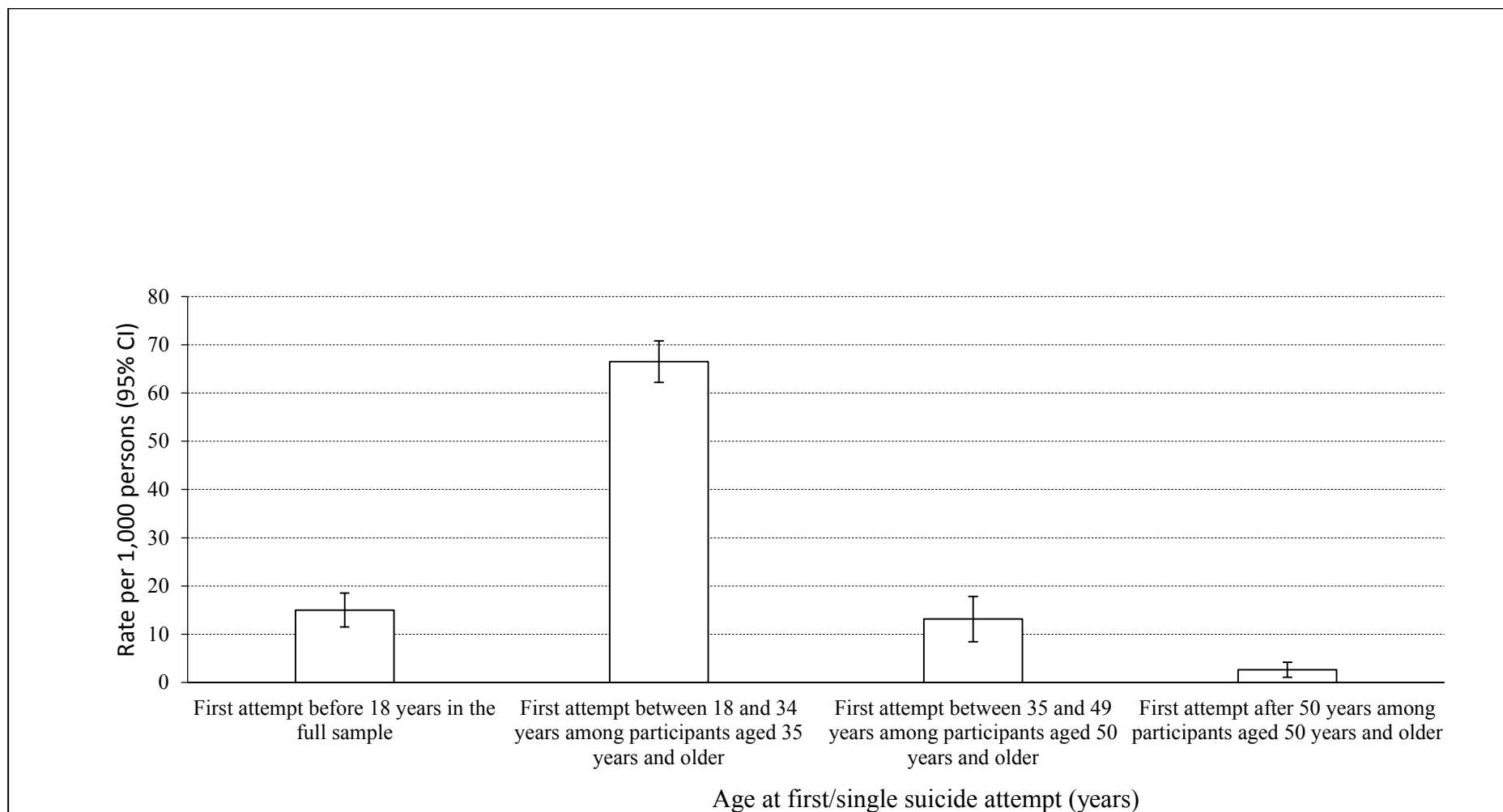


Table 1. Comparing sociodemographic characteristics and prior lifetime psychiatric disorders by age at onset of first/single suicide attempt group in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (n=34,629).

	No history of suicide attempt (A)	Age at first/single suicide attempt groups							
		Before 18 years (B)	Between 18 and 34 years (C)	Between 35 and 49 years (D)	Between 50 and 77 years (E)	A vs C	B vs C	D vs C	E vs C
	(n=33388) % (SE)	(n=519) % (SE)	(n=535) % (SE)	(n=145) % (SE)	(n=41) % (SE)				
						OR (95% CI) / p-value	OR (95% CI) / p-value	OR (95% CI) / p-value	OR (95% CI) / p-value
SOCIODEMOGRAPHICS									
Age, years	48.4 (0.2)	36.3 (0.6)	43.8 (0.6)	50.0 (0.9)	60.4 (1.3)	1.02 (1.01-1.02) / <0.001	0.95 (0.94-0.96) / <0.001	1.04 (1.03-1.06) / <0.001	1.11 (1.08-1.14) / <0.001
Sex (Male)	48.5 (0.4)	28.2 (2.6)	34.0 (2.7)	37.9 (5.6)	51.8 (9.9)	1.82 (1.44-2.31) / <0.001	0.76 (0.53-1.10) / 0.14	1.19 (0.71-1.97) / 0.51	2.08 (0.93-4.67) / 0.08
Race/ethnicity									
White	70.9 (1.6)	71.0 (2.7)	73.1 (2.2)	75.0 (3.9)	72.7 (7.9)	0.90 (0.72-1.11) / 0.31	0.90 (0.67-1.22) / 0.51	1.10 (0.69-1.76) / 0.68	0.98 (0.45-2.13) / 0.96
Non-White	29.1 (1.6)	30.0 (2.7)	26.9 (2.2)	25.0 (3.9)	27.3 (7.9)	1.00	1.00	1.00	1.00
Nativity						AOR (95% CI) / p-value ^a	AOR (95% CI) / p-value ^a	AOR (95% CI) / p-value ^a	AOR (95% CI) / p-value ^a
US-born	85.8 (1.4)	92.1 (1.9)	91.3 (1.5)	90.9 (2.3)	85.9 (6.0)	1.00	1.00	1.00	1.00
Foreign-born	14.2 (1.4)	7.9 (1.9)	8.7 (1.5)	9.1 (2.3)	14.1 (6.0)	1.75 (1.25-2.45) / 0.001	0.72 (0.38-1.38) / 0.32	1.09 (0.60-1.99) / 0.76	1.54 (0.35-6.73) / 0.56
Education									
Less than high school	5.7 (0.3)	2.4 (0.7)	3.7 (0.9)	9.4 (3.7)	13.8 (5.9)	1.15 (0.67-1.97) / 0.61	0.71 (0.30-1.67) / 0.43	2.43 (0.76-7.74) / 0.13	na
High school graduate	37.9 (0.6)	42.9 (3.1)	40.0 (2.7)	27.3 (4.2)	45.2 (9.4)	0.90 (0.72-1.13) / 0.36	0.96 (0.67-1.36) / 0.80	0.64 (0.39-1.04) / 0.07	1.69 (0.62-4.58) / 0.30
Some college or higher	56.3 (0.7)	54.7 (3.1)	56.3 (2.7)	63.3 (5.1)	41.1 (9.7)	1.00	1.00	1.00	1.00
Family poverty	12.7 (0.4)	30.5 (2.5)	29.1 (2.6)	23.2 (5.1)	20.2 (7.3)	0.39 (0.30-0.50) / <0.001	0.90 (0.65-1.26) / 0.60	0.89 (0.48-1.64) / 0.70	0.94 (0.35-2.53) / 0.90
PRIOR LIFETIME PSYCHIATRIC DISORDERS									
Substance use disorders									
Alcohol use disorder		3.5 (1.1)	27.7 (2.6)	41.8 (5.4)	39.5 (9.8)		0.10 (0.05-0.21) / <0.001	2.11 (1.21-3.68) / 0.009	2.57 (1.05-6.27) / 0.039
Drug use disorder		4.8 (1.2)	17.4 (2.1)	16.6 (4.3)	15.1 (8.7)		0.24 (0.13-0.42) / <0.001	1.32 (0.67-2.60) / 0.40	1.39 (0.29-6.68) / 0.70
Nicotine dependence		1.6 (0.6)	14.0 (1.8)	25.3 (5.2)	26.0 (8.2)		0.10 (0.04-0.23) / <0.001	2.37 (1.22-4.61) / 0.011	3.65 (1.66-9.47) / 0.008
Mood disorders									
Major depressive episode		18.9 (2.3)	33.6 (2.6)	40.0 (5.2)	43.7 (9.7)		0.44 (0.31-0.63) / <0.001	1.53 (0.91-2.57) / 0.11	3.01 (1.20-7.56) / 0.019
Mania or hypomania		5.9 (1.5)	12.7 (1.7)	22.8 (4.8)	11.6 (6.2)		0.41 (0.22-0.77) / 0.006	2.26 (1.21-4.25) / 0.011	1.27 (0.38-4.27) / 0.70
Dysthymic disorder		7.5 (1.6)	10.7 (1.5)	23.1 (4.6)	13.7 (8.7)		0.67 (0.39-1.14) / 0.14	2.84 (1.52-5.32) / 0.001	2.25 (0.49-10.2) / 0.30
Anxiety disorders									
Panic disorder with or without agoraphobia		4.0 (1.4)	9.0 (1.7)	12.7 (3.3)	14.0 (6.4)		0.39 (0.20-0.79) / 0.009	1.52 (0.77-3.00) / 0.20	2.28 (0.61-8.46) / 0.20
Social anxiety disorder		14.3 (2.1)	13.2 (1.8)	21.0 (5.1)	11.5 (5.4)		1.09 (0.69-1.71) / 0.70	1.85 (0.92-3.75) / 0.09	1.15 (0.34-3.91) / 0.80
Specific phobia		18.8 (2.4)	20.2 (2.3)	26.2 (5.2)	16.5 (8.6)		0.88 (0.59-1.32) / 0.50	1.68 (0.92-3.09) / 0.09	1.44 (0.39-5.40) / 0.60
Generalized anxiety disorder		3.7 (1.3)	9.4 (1.8)	11.6 (2.9)	9.3 (4.6)		0.37 (0.19-0.75) / 0.006	1.35 (0.70-2.63) / 0.40	1.45 (0.45-4.62) / 0.50

Post-traumatic stress disorder	16.5 (2.0)	20.5 (2.0)	29.2 (5.2)	19.0 (7.7)	0.78 (0.54-1.12) / 0.18	1.78 (0.99-3.19) / 0.053	1.44 (0.49-4.30) / 0.50
Attention deficit-hyperactivity disorder	15.4 (2.1)	13.2 (1.8)	9.0 (2.4)	7.1 (5.2)	1.17 (0.73-1.88) / 0.50	0.71 (0.35-1.42) / 0.30	0.78 (0.15-4.19) / 0.80
Pathological gambling	0.0 (0.0)	0.1 (0.1)	1.4 (1.0)	1.4 (1.4)	na	na	na
Conduct disorder	12.7 (2.1)	11.8 (1.9)	11.6 (4.2)	12.9 (6.6)	1.13 (0.66-1.93) / 0.70	1.05 (0.41-2.72) / 0.90	1.41 (0.45-4.41) / 0.50
At least one Axis I disorder	54.7 (3.0)	56.6 (2.8)	70.5 (4.5)	70.5 (4.5)	0.85 (0.61-1.17) / 0.30	2.08 (1.29-3.36) / 0.003	1.17 (0.48-2.86) / 0.70

Percentages are weighted.
^a Adjusted for sex, race/ethnicity (White vs non-White) and age at Wave 2.

Table 2. Comparing childhood maltreatment experiences and parental history of psychiatric disorders by age at onset of first/single suicide attempt group in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (n=34,629).

	No history of suicide attempt (A)	Age at first/single suicide attempt groups				A vs C	B vs C	D vs C	E vs C
		Before 18 years (B)	Between 18 and 34 years (C)	Between 35 and 49 years (D)	Between 50 and 77 years (E)				
		(n=33388) % (SE)	(n=519) % (SE)	(n=535) % (SE)	(n=145) % (SE)				
						OR (95% CI) / p-value	OR (95% CI) / p-value	OR (95% CI) / p-value	OR (95% CI) / p-value
CHILDHOOD MALTREATMENT									
Physical neglect	6.0 (0.0)	8.4 (0.2)	7.7 (0.2)	7.8 (0.4)	8.2 (0.9)	0.85 (0.84-0.87) / <0.001	1.03 (1.01-1.06) / 0.009	1.00 (0.96-1.04) / >0.90	1.02 (0.95-1.10) / 0.60
Emotional abuse	4.3 (0.0)	7.7 (0.2)	6.8 (0.2)	6.9 (0.4)	6.7 (0.7)	0.78 (0.76-0.80) / <0.001	1.06 (1.02-1.10) / 0.003	1.01 (0.96-1.07) / 0.70	1.02 (0.93-1.12) / 0.60
Physical abuse	2.8 (0.0)	4.9 (0.2)	4.3 (0.1)	4.5 (0.3)	4.3 (0.5)	0.70 (0.67-0.73) / <0.001	1.02 (1.04-1.16) / <0.001	1.02 (0.94-1.12) / 0.60	1.02 (0.89-1.17) / 0.80
Sexual abuse	4.3 (0.0)	7.2 (0.2)	6.4 (0.2)	6.1 (0.4)	5.4 (0.5)	0.78 (0.76-0.80) / <0.001	1.04 (1.01-1.07) / 0.009	0.99 (0.94-1.05) / 0.80	0.98 (0.88-1.08) / 0.60
Emotional neglect	8.1 (0.0)	12.2 (0.3)	10.9 (0.3)	11.4 (0.6)	11.3 (0.9)	0.89 (0.88-0.91) / <0.001	1.04 (1.02-1.07) / 0.001	1.01 (0.97-1.04) / 0.70	1.00 (0.95-1.05) / >0.90
FAMILY HISTORY OF PSYCHIATRIC DISORDER									
Alcohol abuse	21.3 (0.4)	48.7 (2.7)	41.4 (2.7)	51.7 (5.7)	39.3 (9.5)	0.42 (0.34-0.52) / <0.001	1.28 (0.94-1.74) / 0.12	1.59 (0.96-2.65) / 0.07	1.15 (0.48-2.75) / 0.70
Drug abuse	3.4 (0.1)	18.0 (2.3)	10.5 (1.7)	9.0 (3.3)	5.2 (5.0)	0.39 (0.26-0.58) / <0.001	1.36 (0.83-2.24) / 0.20	1.13 (0.45-2.84) / 0.80	1.09 (0.14-8.43) / 0.90
Major depression	23.5 (0.5)	56.9 (3.0)	53.6 (3.0)	54.0 (6.3)	33.6 (10.4)	0.30 (0.24-0.37) / <0.001	1.02 (0.76-1.38) / 0.90	1.10 (0.64-1.90) / 0.70	0.60 (0.22-1.60) / 0.30
Antisocial personality disorder	8.1 (0.3)	31.2 (2.9)	24.6 (2.3)	30.6 (5.3)	16.3 (8.0)	0.31 (0.24-0.40) / <0.001	1.17 (0.82-1.68) / 0.40	1.57 (0.89-2.75) / 0.12	0.88 (0.27-2.79) / 0.80

Percentages are weighted.

^a Adjusted for sex, race/ethnicity (White vs non-White) and age at Wave 2.