Suicidal thoughts and behaviours in adolescents and young adults: disentangling the role of gender and sexual orientation

Andrea Miranda Mendizabal

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THESIS DIRECTORS

Dr. Jordi Alonso

Dr. Pere Castellví

DEPARTMENT DE CIÈNCIES EXPERIMENTAL I DE LA SALUT

Universitat Pompeu Fabra Barcelona

A mis padres,

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Abstract

Suicide is the second leading cause of death among 15- to 29-year-olds. Male youths have higher risk for suicide compared to females, whereas females are at greater risk for suicidal ideation and suicide attempts. Mental disorders have been identified as one of the strongest predictors of suicidal thoughts and behaviours (STB). Among youth, sexual minority (LGB) individuals are a high-risk subpopulation because they face specific stressors (e.g. discrimination, victimisation) that further increase the probability of STB. Evidence about suicide risk and whether there are possible mechanisms by which some factors increase or diminish the risk according to gender or sexual orientation is scarce.

The general aim of this doctoral thesis is to provide new evidence about the risk for STB and potential risk and protective factors associated with STB among adolescents and young adults; and how these vary according to gender and sexual orientation. To achieve this aim, we carried out a systematic review of the literature, followed by a meta-analysis, and we analysed empirical data from a cohort study (UNIVERSAL: *University and Mental Health*) of Spanish university students.

The results show that female adolescents and young adults are at greater risk for suicide attempts compared to males. As already well known through information provided by vital statistics registries, males are at higher risk for suicide. Risk and protective factors for

STB differ by gender. Internalising disorders and interpersonal difficulties increase the risk among females, while externalising disorders, hopelessness and some stressful life events (e.g. death of any of the parents) are found to be related to STB among males. In addition, family and peer support are found to be protective factors for suicidal ideation, but only among females. LGB youth have higher risk for STB compared to heterosexuals. This risk is mediated by childhood maltreatment, bullying and a previous history of any mental disorders. Perceived sexual orientation discrimination increases the risk for any mental disorder, which, in turn, carries risk for suicidal ideation. There is a need to better understand the mechanisms underlying gender differences in the association between STB and anxiety, violence between parents, hopelessness and family support. In addition, a knowledge gap remains in terms of the protective factors of STB for adolescents and young adults. Further research in this regard is definitively needed.

This thesis has provided new evidence on a wide range of individual and community risk and protective factors for STB among adolescents and young adults, and has detected important differences across gender and sexual orientation with regard to STB risk. These results suggest that there is a need to combine preventive strategies focusing on individual risk factors (e.g. early diagnosis and treatment of mental disorders) with those with a public health population-level risk prevention approach (e.g. reinforcing community protective factors), as well as to consider the specific needs of high-risk groups.

Resumen

El suicidio es la segunda causa principal de muerte entre los jóvenes de 15 a 29 años. Los hombres jóvenes tienen un mayor riesgo de suicidio consumado en comparación con las mujeres, mientras que las mujeres tienen un mayor riesgo de ideación suicida e intentos de suicidio. Los trastornos mentales se han identificado como uno de los predictores más fuertes de los pensamientos y la conducta suicida. Entre los jóvenes, las lesbianas, gais y bisexuales (LGB) son una subpoblación de alto riesgo porque enfrentan factores estresantes específicos (por ejemplo, discriminación, victimización) que aumentan aún más la probabilidad de los pensamientos y la conducta suicida. La evidencia sobre el riesgo de suicidio y si existen posibles mecanismos por los cuales algunos factores aumentan o disminuyen este riesgo según el género o la orientación sexual es escasa.

El objetivo general de esta tesis doctoral es proporcionar nueva evidencia sobre el riesgo de los pensamientos y la conducta suicida, y los potenciales factores de riesgo y protección de los pensamientos y la conducta suicida; y cómo varían según el género y la orientación sexual en los adolescentes y adultos jóvenes. Para lograr este objetivo, se realizó una revisión sistemática de la literatura, seguida de un meta-análisis, y se analizaron datos empíricos de un estudio de cohorte (UNIVERSAL: *Universidad y Salud Mental*) de estudiantes universitarios españoles.

Los resultados muestran que las mujeres adolescentes y adultas jóvenes corren un mayor riesgo de intentos de suicidio en comparación con los hombres. Como ya se sabe a través de la información proporcionada por los registros de estadísticas de mortalidad, los hombres corren un mayor riesgo de suicidio. Los factores de riesgo y de protección para los pensamientos y la conducta suicida difieren según el género. Los trastornos mentales internalizantes y las dificultades interpersonales aumentan el riesgo de los pensamientos y la conducta suicida entre las mujeres, mientras que los trastornos mentales externalizantes, la desesperanza y algunos eventos vitales estresantes (p. ej. la muerte de cualquiera de los padres) aumentan el riesgo en los hombres. Además, el apoyo familiar y de los pares son factores protectores para la ideación suicida, pero solo entre las mujeres. Los jóvenes LGB tienen un mayor riesgo de pensamientos y conducta suicida en comparación con los jóvenes heterosexuales. Este riesgo está mediado por el maltrato infantil, el bullying y los antecedentes de cualquier trastorno mental. La discriminación percibida por orientación sexual aumenta el riesgo de cualquier trastorno mental, que, a su vez, conlleva riesgo de ideación suicida. Existe la necesidad de comprender mejor los mecanismos subyacentes a las diferencias de género en la asociación entre los pensamientos y la conducta suicida y la ansiedad, la violencia entre padres, la desesperanza y el apoyo familiar. Además, sigue habiendo una brecha de conocimiento en términos de los factores protectores de los pensamientos y la conducta suicida para los adolescentes y adultos jóvenes. Se necesita investigación adicional a este respecto.

Esta tesis proporciona nueva evidencia sobre una amplia gama de factores de riesgo y protección a nivel individual y comunitario para los pensamientos y la conducta suicida en los adolescentes y adultos jóvenes, y ha detectado diferencias importantes según el género y la orientación sexual. Estos resultados sugieren que es necesario combinar estrategias preventivas centradas en factores de riesgo individuales (p. ej. diagnóstico temprano y tratamiento de los trastornos mentales) con aquellas con un enfoque de prevención de riesgos de salud pública a nivel poblacional (p. ej. reforzar los factores de protección de la comunidad), así como considerar las necesidades específicas de los grupos de alto riesgo.

Preface

Suicide is a serious public health concern. It is the second leading cause of death among 15- to 29-year-olds. Among those, the group aged 25 to 29 has the highest suicide incidence. Despite the increasing evidence on the relation between a wide range of factors and the risk for suicidal thoughts and behaviours (STB) in this population; as well as the numerous efforts at different scales and diverse contexts to prevent STB, suicide deaths are still occurring, and young people still suffer suicidal ideation and commit suicide attempts, which are both strong predictors of suicide.

Suicide rates are twice as high among male youths compared to females, whereas suicidal ideation and suicide attempts are much more frequent among females. Gender differences in the associations with internalising and externalising mental disorders, the lethality of the method and difference in help-seeking behaviour have been mentioned as possible explanations for this gender gap. From a gender perspective, the association between suicide and masculinity may play a role in creating a genuine gender gap in suicide rates.

High-risk groups for STB among youth have been identified. Lesbian, gay and bisexual youth have higher risk for STB compared to heterosexuals. Sexual minority individuals suffer greater discrimination and stigma in different environments and face additional stress, with detrimental consequences for their mental

health, including an increased risk for STB. Similarly, prevalence estimates of STB and mental disorders among college students are consistently high. Substantial impairment in academic performance (e.g. lower grade point average) has been associated with these outcomes.

In Spain, there is a lack of robust evidence on STB risk among youth, on potential differences according to gender or sexual orientation with regard to risk for STB, and on how specific risk and protective factors interact with gender or sexual orientation. Moreover, there is a scarcity of data on the mental health of university students. This doctoral thesis aims to provide new evidence on the risk for STB in adolescents and young adults, including Spanish university students, according to gender and sexual orientation, and aims to examine by gender and sexual orientation with a wide range of risk or protective factors for STB in this relevant age group. The results from this thesis should encourage the development of evidence-based public health strategies, tailored to the needs of the target population, and increase their long-term effectiveness.

This thesis is part of "UNIVERSAL: *University and Mental Health*", which is a 4-year multi-centre cohort study following a sample of students from 5 Spanish universities who started their freshman year for the first time in the academic year of 2014-2015. The UNIVERSAL study is part of the World Mental Health International College Student (WMH-ICS) Initiative of the World

Health Organization (WHO). The study analyses the mental health needs of university students through a web-based survey, including various items on potential personal, family and community related risk and protective factors with the ultimate aim of examining patterns and predictors for the onset and persistence of common mental disorders and the consequences derived from them among freshmen students accessing the university for the first time; and their subsequent monitoring. STB are one of the main focuses of this survey.

This thesis is made up of four original articles. The first, published in the *"International Journal of Public Health"*, assesses the association between gender, suicide attempt and suicide, and identifies gender-specific risk and protective factors for these outcomes in adolescents and young adults, through a systematic review of the literature and a subsequent meta-analysis. The second article, accepted for publication in the journal *"Depression & Anxiety"*, is a cross-sectional study based on the baseline survey of the UNIVERSAL study. It examines, from a gender perspective, the differences in the associations between the identified risk factors and protective factors with suicidal ideation among Spanish university students. The third article, published in the *"The British Journal of Psychiatry"*, assesses the risk for suicide attempt and suicide death among lesbian, gay and bisexual (LGB) adolescents and young adults, and identifies risk and protective factors of these outcomes, using a systematic review and meta-analysis. Finally, the last article is based on the baseline and follow-up data of the

UNIVERSAL study. It will be submitted for publication to the *"Journal of Adolescent Health"*, and evaluates the role of childhood maltreatment and bullying on the relationship between sexual orientation, mental disorders and suicidal ideation, as well as the role of mental disorders on the relationship between perceived sexual orientation discrimination and suicidal ideation among LGB Spanish university students. The articles are complementary to each other and together provide relevant evidence on the differences in the risk for STB according to gender and sexual orientation among youth.

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1. INTRODUCTION

1.1 Incidence and global burden of suicide

Suicide is a major public health concern. Worldwide, every year nearly 800,000 people die due to suicide, which equals one person every 40 seconds. In 2016, suicide accounted for 1.4% of all deaths worldwide, making it the 18th leading cause of death. Over the past 45 years, worldwide suicide rates have increased by 60%, estimating that by 2020 suicide deaths would increase to 1.5 million. Unfortunately, both adolescents and young adults have registered the highest increase, rendering suicide the second leading cause of death among 15- to 29-year-olds. Among them, the group aged between 25 to 29 has the highest incidence [1]. In Europe, annually 125,000 deaths are due to suicide, corresponding to an annual age-standardised rate of 12 over 100,000 people [2]. Suicide has a higher incidence in Eastern countries, with Lithuania achieving the highest suicide rate (31.9 over 100,000 people) [3]. In general, among all countries suicide rate is lower for females compared to males (females *vs*. males ratio, 0.46 in 2016) [4]. In some countries, suicide overcomes the deaths due to traffic accidents and is the third cause of death among youths [2].

Nevertheless, at the global level, age-standardised suicide mortality rates have considerably reduced since 1990, with a decline in age-standardised mortality rates from suicide (32.7%), a similar decrease to the observed for all causes mortality in 2016 (30.6%) [5]. The need of determining whether the decline in suicide mortality is

due to suicide prevention activities or whether it reflects general improvements to population health has been raised [4].

In 2016, 34.6 (32.4-37.4) million years of potential life lost (YPLL) resulted from suicide, accounting for 2.18% (1.9%-2.2%) of total years of life lost worldwide [4]. The projection for 2020 is that suicide global burden of disease (GBD) will represent around 2.4% in former socialist countries and those with market economies [6]. Data from the GBD study showed that mental and substance use disorders were responsible for 22.5 million (14.8–29.8) of the 36.2 million (26.5–44.3) Disability-Adjusted Life Years (DALYs) allocated to suicide in 2010. Depression was responsible for the largest proportion of the suicide DALYs (46.1% (28.0%–60.8%)). DALYs occurred throughout the lifespan with the largest proportion found in males aged 20–30 [7]. It is estimated that suicide represents an annual economic cost of billions of dollars worldwide [6]. The economic costs and burden of suicide and suicidal behaviour have been examined in some countries including Canada, Ireland, New Zealand, the United States and Australia [8–13]. The national cost of suicides and suicide attempts in the United States was $58.4 billion in 2013. The indirect costs (lost productivity) represented 97.1% of this cost. However, the total cost raised to $93.5 when adjusted for under-reporting [10]. Other countries also reported a high percentage of the total cost of suicide is due to productivity loss (indirect costs) [10,12,13].

In addition to the disability and economic costs associated to suicide, the costs derived from suicidal thoughts and attempts must be considered. Suicidal thoughts are considered to be as disabling as alcohol dependence and severe asthma [14]. The disability related to suicide attempts has been largely attributed to the mental distress involved. Mental distress related to suicide attempts is comparable in disability to heroin dependence and initial stage of Parkinson's disease [14]. It is estimated that for each adult who died by suicide there may have been more than 20 others attempting suicide [1].

1.2 Suicidal thoughts and behaviours (STB) among adolescents and young adults

Analysis of suicide among 15- to 19-year-olds from 81 countries showed a suicide rate of 9.50 per 100,000 for males and 4.41 per 100,000 for females [15]. Globally, for the group aged 15 to 29, as it was mentioned before, suicide is the second leading cause of death. Suicide numbers differ between countries, but most of the global burden from suicide bear at the low- and middle-income countries, with an estimate of 75% of all suicides occurring in those countries [2].

Adolescence and the beginning of young adulthood are transition periods and key life stages for personal growth and development. In fact, during these periods youths improve coping strategies to manage stress and develop the skills, attitudes, values and social networks necessary to make a successful transition to adulthood [16].

The period between 18 and 25 years of age has been denominated as "*Emerging adulthood"*, which is characterised by the fact that the dependency traits associated with childhood and adolescence come to an end, while the normative responsibilities of adulthood are not yet completely faced. Emerging adulthood is a life stage which offers a variety of possible life directions in love, work and world-views to discover [17].

The first symptoms of mental disorders typically emerge in adolescence [18] and this may be related to the neurological changes that are occurring at this stage of development [19]. Different risk behaviours peak after adolescence, during young adulthood. Risks include unprotected sex, most types of substance use [20] and risky driving behaviours (e.g. driving at high speeds or while intoxicated). To some degree, emerging adulthood risk behaviours can be understood as part of self-identity explorations and desires for novel and intense experiences before settling down into the roles and responsibilities of adult life [17]. Most of the risk behaviours occurring during adolescence and young adulthood are strongly related to STB.

a) Risk and protective factors of suicidal thoughts and behaviours

Although there is now evidence about the relation between a wide range of factors and the risk for STB in this population, suicide still happens as well as there is still a high prevalence of suicidal

ideation and suicide attempts, which are strong predictors of suicide. There are few cases of attempted suicide before puberty, but a substantial increase occurs when individuals reach adolescence and young adulthood [21], especially within the ages of 19 and 23 [22]. A study including a sample of Spanish adolescents aged 14 to 19 showed that approximately 4% have attempted suicide throughout their lives [23]. Spirito et al. suggested that between 7% to 20% of adolescents will attempt suicide again 3 to 12 months after the first event [24], with an average of 10 to 20 suicide attempts before accomplishing suicide [25]. Factors related to a poor mental health, hopelessness and adolescent upbringing are associated with a higher risk for repeating suicidal behaviours [26].

Mental disorders have consistently been found associated with STB [27]. Post-traumatic stress disorder (PTSD) mood disorder and anxiety disorder have shown the highest associations with suicide attempt (SA) [28]. Evidence shows that moderate or heavy alcohol consumption, as well as an early initiation of alcohol use, are associated with STB [29–31]. Concurrent use of more than one substance is common among adolescents/young adults. Association between heavy alcohol and tobacco use with illicit substances use or a greater risk for illicit drug use after marijuana use [32] has been seen. Substance abuse disorder is strongly related to STB [33].

Prior research provides robust evidence about the increased risk for STB associated to any form of interpersonal violence: childhood maltreatment (sexual, physical, emotional or neglect), bullying,

dating violence, and community violence [34,35], and internalising and externalising symptoms [36]. Having a family member or friend who attempted or died by suicide increases significantly the risk for STB among adolescents/young adults [37,38]. After controlling for past and current mood disorders and suicide attempt history, individuals whose parent attempted suicide were approximately five times more likely to make a suicide attempt compared to their counterparts [39]. Friend's suicide seems to increase the risk for STB during the first year after the loss, but the effect disappears after more than 5 years [40].

Some other factors associated with STB among adolescents/young adults have been less investigated. STB is associated to low self-esteem [41], poor health and physical disability (68). Whereas there is contradictory evidence about family structure factors (e.g. parent's cohabitation status) or school related factors (e.g. poor school attendance, negative attitudes towards school and school work), with some studies showing increased risk for STB and some others showing no association [42].

In contrast with risk factors, much less research has been devoted to analysing potential protective factors for STB among adolescents/young adults. There is evidence on a protective effect on STB among youth of: family support [43], religiosity [44], school connectedness and social support [45,46]. Conversely, the lack of parental support during childhood or adolescence has been shown to be a strong predictor of suicidal ideation (SI), which may increase

between 4 to 9 times the risk among young adults [47]. Insufficient evidence about these factors and their influence on the risk for STB has led to a call to research on protective factors [48,49].

b) Gender differences in suicidal thoughts and behaviours

In sharp contrast with the situation for suicide death, globally, females have higher rates of suicidal ideation and attempts, but lower rates of suicide deaths than males [50–53]. This trend remains when examined longitudinally [54]. As a rough estimate, it is typically noted that female adolescents/young adults are twice as likely to report suicide ideation as males [53]. Only few studies have reported no gender differences in suicidal ideation among youth [55].

Suicide attempts are 3 to 9 times more common in females [56,57]. Evidence about a higher cumulative incidence of suicide attempts in female adolescents/young adults than in males of the same age has been observed [28,58]. On the other hand, suicide rates are 2 to 4 times higher in boys or men than girls or women. Specifically in developed countries, suicide mortality has been estimated to be 2 to 3 times higher in young males than females [59]. Suicide rates have declined in males since the 1990s; however, in some countries the suicide rates have increased for females and the downward trend in males is now reversing [60].

Gender differences in STB rates are known as the *''Gender Paradox''* [61], which is not constant within or across countries,

especially when age and ethnicity are considered [62]. In fact, it is more pronounced in industrialised and English-speaking countries. For suicide attempt rates, the gender difference (females > males) increases with age peaking in mid adolescence [54,63], whereas for suicide rates, the gender difference (males > females) steadily climbs until early adulthood [2].

Gender differences about method choices have been discussed, revealing disparate conclusions. On one hand, evidence supports that method choices would be different according to the accessibility and acceptability of those methods as more masculine or feminine within the community [62]. If completed suicide is viewed as a masculine behaviour, males would tend to choose more lethal means to reduce the likelihood of surviving [64]. While female use of less violent methods would be related with their concern for bodily appearance -how they will look in death- or because they have less desire to kill themselves. On the other hand, certain evidence has found no significant gender differences between the levels of suicidal intent [65,66].

Analysis of cultural differences provides evidence of a correspondence between cultural beliefs about suicidal behaviour and actual patterns of it. For instance, cultures differ in what they consider essential for an act to be dubbed as suicidal. One perspective is that self-harming behaviour should be intended as fatal to be considered suicidal [50]. However, it is difficult, if not impossible, to unequivocally establish fatal intent [62]. In the same

way attempting (and failing at) suicide is assumed to be feminine, whereas suicide is more usual and considered more permissible for men [50]. This belief in turn can act as a social norm and a model, discouraging female suicide [61]. In contrast, in other countries suicide is a socially sanctionable female behaviour [60].

The prevalence of mental disorders also differs across genders. Internalising disorders –depression and anxiety, including PTSD– are more prevalent in females than males. Whereas disruptive or 'externalising' disorders —attention deficit disorder with hyperactivity (ADHD), oppositional defiant disorder (ODD) and conduct disorder (CD) — are more prevalent in males [67,68]. Externalising disorders seem to precede substance use disorders occurring in young adulthood [69], which are more prevalent among males [67,68]. Internalising and externalising disorders can coexist. Their association with irritability may explain gender differences in the prevalence of both kinds of disorders. There is some evidence that among depressed youth, those most likely to be depressed and irritable are males. Notably, depressed young males more easily precipitate to anger than females [70], whereas depressed females exhibit hostile and defiant behavior. More than half of the depressed adolescents express the same depression-irritability disorder during young adulthood (ages 19 to 21). Moreover, aggression (intent to hurt or harm others) is more likely physical among boys, while it tends to be indirect (relational) among girls [71]. Probably the fact that females have been socially placed in a position of vulnerability

(receptive and passive) against males (active and aggressive) is related to the differences in the expression of aggressive behavior.

The importance of mental disorders as risk factors may change according to context. In industrialised countries the explanatory focus is on individual psychopathology, while in developing countries, it is focused on external adversities. Gender bias in the diagnosis and treatment of mental disorders has been described. On the one hand, girls and women who experience mental disorders are underdiagnosed compared to boys and men [50]. On the other hand, there is unnecessary medicalisation and over prescription for females [72]. Causes of emotional distress are mostly ignored and medicalised by erroneous symptomatic treatment strategies. Prescription of anti-anxiety drugs, sleeping pills, and medication for mental health problems is more frequent among women [73], even when symptoms are mild [72]. This reflects a probable tendency of health services professionals to either dismiss symptoms of female patients altogether or misinterpret the patients' physical symptoms as psychological issues that require drug prescription.

Help-seeking behaviours are also marked by gender differences. Over the course of adolescence, girls increasingly identify friends and professionals as likely sources of help and support with personal and emotional problems, with less dependence on family. Boys also seek for help out of family contexts, but they do not compensate with friends or professional help as much as girls.

Masculine norms of personal autonomy may prevent boys from seeking help [74].

Gender differences in the risk for STB ("*Gender Paradox*") refer mostly to the differences in the suicide method choices, in the prevalence of internalising and externalising disorders, as well as in the frequency of seeking of help observed among men and women. These differences may be caused by gender socialisation, which sets the expectations about feminine or masculine behaviour. For instance, the belief that attempting suicide is more feminine, whereas suicide is considered more permissible for males [50]. In addition, the belief of females being more vulnerable compared to males who could or should be more aggressive or 'stronger' predisposing, somehow, the female or males youth to a specific suicidal behaviour. There is the need to better understand how the gender socialisation is implicated in the gender differences of the risk for STB among youths.

c) Sexual orientation and suicidal thoughts and behaviours

It is difficult to estimate exactly the percentage of lesbian, gay and bisexual (LGB) population worldwide. Results from a survey carried out in 2016 show that 5.9% of Europeans identify as LGB. Spain is the country with the second highest LGB population (6.9%), only after Germany (7.4%). This frequency varies according to age. Thus, young people are more likely to describe their sexual orientation as something other than only heterosexual:

16% of Europeans between the ages of 14 and 29, compared to 7.5% between the ages of 30 and 65 [75].

Awareness of sexual orientation occurs between the ages of 9 and 10 [76]. Sexual minority identity development is thought to begin in adolescence with an awareness of attraction to members of the same sex; followed by sexual experimentation and self-identification as LGB, which usually happens around 16 years of age [77]. However, these processes could be delayed due to external stressors such as stigma and rejection.

Transition from adolescence to young adulthood is challenging for any youth. However, LGB youths are more exposed to stigma, discrimination and victimisation in their families and romantic relationships [25]. Bullying, including physical aggression, is also more prevalent among them [78,79]. As a result, LGB youths face a unique set of health and health-related concerns. There is evidence that some aspects of victimisation such as frequency, duration and severity increase even more the risk for negative health outcomes [80]. LGB youths present substantially more health risk behaviours and worse health outcomes across their lifespan [81–83], as well as more mental disorders [84,85] and an increased risk for STB [22,86–88] compared to their heterosexual peers.

Moreover, the internalisation of a homophobic environment (internalised homophobia) can also lead to negative mental health outcomes. Indeed, a significant association between internalised

homophobia and mental health problems for LGB individuals has been described [89]. Previous results suggest that internalised homophobia mediate the relationship between discrimination and depressive symptoms [90]. For LGB youths between the ages of 18 and 25, perceived stigma, internalised homophobia and homophobic physical abuse increase psychological distress and the risk for STB [91]. Some studies have assessed the relation between discrimination, stigma, and internalised homophobia and psychological factors and mental disorders, principally depression, among LGB population [81,89,92].

Family connectedness, family cohesion and religiosity have been mentioned as protective factors for STB for youths. However, for some LGB youths, relationships with family and religious communities can be disrupted, especially around the time of disclosure or discovery of sexual identity, because of perceived or actual rejection [82]. On the contrary, positive school climates can moderate the impact of harassment, bullying and victimisation on the wellbeing of LGB adolescents [93,94], decreasing suicidal outcomes. However, there is still a lack of evidence about the relationship between school-based protective factors and STB among LGB youth [45].

LGB adolescents/young adults face more stressful events compared to heterosexuals of the same age. They suffer greater discrimination and stigma in different environments -family, school-, which can lead to internalise these attitudes (internalised homophobia) with the

consequent detriment of their mental health, including an increased risk for STB. In addition, there may be some differences in the protective factors for STB between heterosexual and LGB youth.

1.3 Suicidal thoughts and behaviours (STB) among university students

In the United States, about 1,100 suicides occur annually among university students [95,96]. Between 4% to 10% of college students report having had suicidal ideation during the last 12 months [97,98]. Suicide is the third cause of death among college students since the mid-20th century. Since that time, only traffic accidents have exceeded suicide as a cause of death among students [99]. Therefore, its current relevance is not a reflection of any dramatic change in the incidence of suicide in this group, but of the increased impact among university environments and society at large [96]. Some studies have suggested that suicide rates have increased on university campuses [100,101]. However this may be due to a simultaneous increase of the number of students enrolled in the university and a higher proportion of them having mental health problems [96,100–102].

Even though the first symptoms of mental disorders typically appear during adolescence, transition to university life also represents a peak period for their appearance [18,103]. This transition is itself associated with a high risk for mental disorders and STB [104]. Studies of university populations have shown high rates of mental illnesses [18,105]. More than half of freshmen students have had some lifetime disorder and co-morbidity was common, with 19.1% of the

students experiencing three or more disorders. Moreover, approximately 31% of students have suffered depression and alcohol and substance use/abuse [106,107].

For university students, probably one of the most challenging aspects is to manage the increase in psychosocial stress and academic pressure in a new and unknown environment. Students face the stress of achieving academic standards whilst learning through new, less structured methods [108]. Students themselves may have high levels of social perfectionism [109], which correlates with an increased risk for STB [110]. In addition, leaving the family home for the first time means lessened parental oversight, which can bring new opportunities to experiment with alcohol and other substances [108]. Together, these conditions create an environment that may increase the likelihood for STB among those who are vulnerable.

Mental disorders and STB during the university period are of high concern due to the associated distress they cause in an important stage of life [111] and the substantial impairment in academic performance [18,103]. For example, significantly lower final grades have been reported among university students with mental disorders and STB [105].

1.4 Suicide in Spain

The suicide rate in Spain is 8.7 per 100,000 persons [3]. According to the "Multicenter Study on Suicidal Behavior (WHO/EURO)", Spain

is one of the European countries with the lowest incidence and prevalence of both suicide and suicide attempts, respectively [112]. However, suicide deaths are not decreasing. In 2017, 3,679 people died by suicide in Spanish territory, representing 3.1% more than in 2016 and becoming the first external cause of death among males and the third among females [113]. For the group between 15 and 34 years old, suicide is the second cause of death and the first among men aged 20 to 24. In addition, suicide rates among 15- to 29-year-olds represent a 7.77% of the total suicide deaths in the country [114].

Epidemiological studies have estimated the prevalence for STB and mental disorders among clinical [115–117] or general adult population [118–123]. The studies including general adult populations were mostly cross-sectional. One study including a representative sample of the adult general population of Spain using a face-to-face household survey showed that the lifetime prevalence of suicidal ideation was between 2.3% and 4.4%; lifetime prevalence of suicidal plan, from 1.4% to 1.9%; and of suicide attempt, around 1.5%. In terms of 12-month prevalence, the results ranged between 0.7% and 0.9% for suicidal ideation and between 0.2% and 1.9%, for suicide plans. Likelihood of a suicide attempt was higher among individuals who had previous suicidal ideation with plan (73%), compared to those with no plan (14.4%)[120].

a) Suicidal thoughts and behaviours (STB) among university students in Spain

The annual university enrolment in 2018/2019 in Spain was of 1,293,892 students, of which 51.5% were 18- to 21-year-olds; while the average age was 24.3 years old, (3 out of 4 students were under 25 years old). Of all the students, 337,055 of them enrolled at university for the first time [124]. Women represented 55.2% of the total students enrolled in undergraduate studies.

There is scarcity of epidemiological data available on mental health of Spanish university students. The available data include mostly small samples from specific regions of the country. Based on a sample of 700 university students, previous research showed that 55% reported depressive symptoms and 47%, anxiety symptoms [125]. Similarly, a study which conducted interviews to a random sample of 559 college students showed that 8.7% of them had a major depressive episode at the interview time, 54.2% of the students have had a previous depressive episode, 0.6% have considered suicide and 0.2% have attempted suicide during their lifetime [126]. More recently, in a small sample of 40 students, mostly women, 33.3% of them have had suicidal ideation [127]. Another study including exclusively female college students and teachers (n=540) showed that 18.1% of the participants reported suicidal ideation in the last 12 months and 2.4% had attempted suicide in the last five years [128].

The above studies suggest that the prevalence of some mental disorders and STB are high among Spanish university students. However, to the best of our knowledge there is no previous study including a representative sample from different regions of Spain and a longitudinal data reporting about mental disorders and STB among university students. In addition, there is no available data estimating jointly risk and protective factors for STB among this group.

1.5 Conceptual frameworks of risk and protective factors of suicidal thoughts and behaviours (STB)

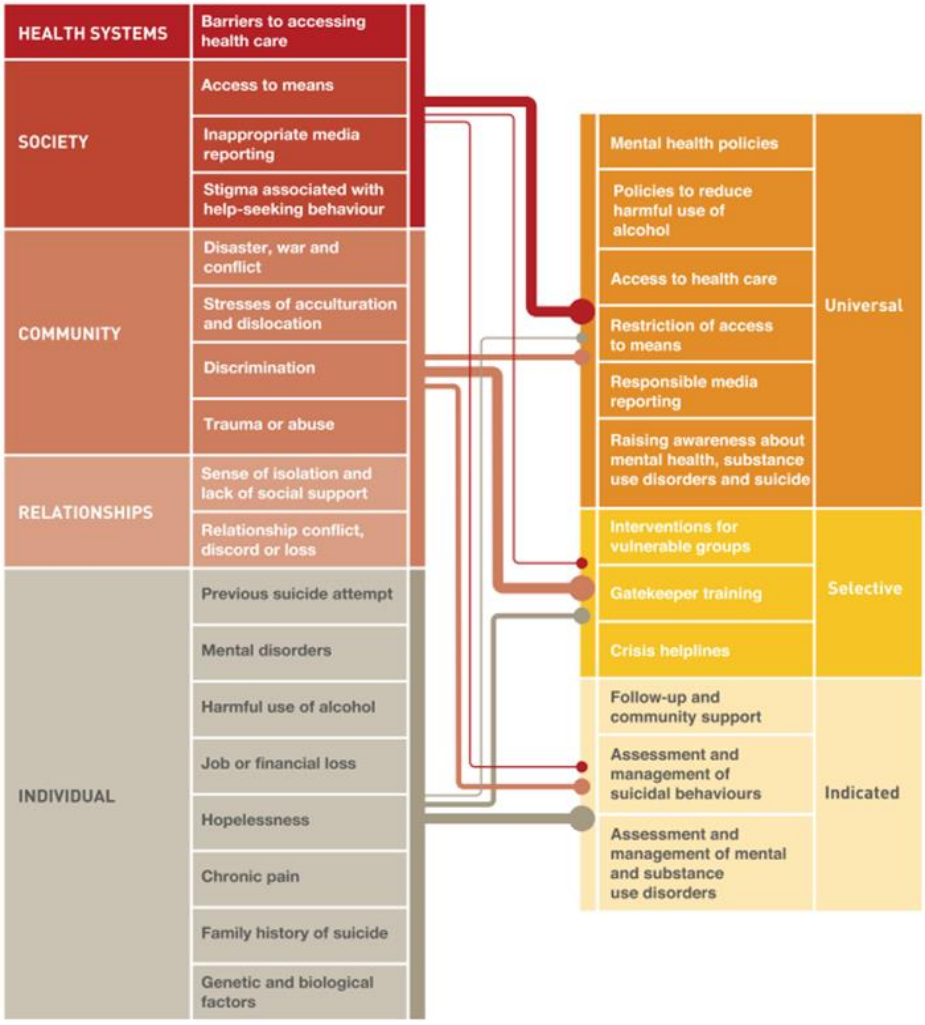
In this thesis, we used the diagram of key risk factors for suicide proposed by the World Health Organization (WHO) as a reference to classify the risk and protective factors for STB. This diagram groups the factors into different non-exclusive categories: health systems, society, community, relationships and individual. A wide range of factors can be included in each category. For the analysis of the relationship between different types of discrimination and victimisation with mental disorders and STB in adolescents/young adults LGB, we followed the minority stress model as explanatory framework, which point distal and proximal causes of distress and its impact in the mental health of LGBs [92]. More detailed information about each of them is presented above.

a) WHO model of key risk and protective factors for STB

Since there are a wide range of risk factors for STB, the WHO proposed a socio-ecological model which encompasses different areas that span across systemic, societal, community, relationship (social connectedness to immediate family and friends) and individual risk factors **(Figure 1)**. For this thesis' purposes, specifically to meet its aims, the categories proposed by the model have been slightly modified, considering that the categories proposed in the WHO model are flexible. Moreover, according to this model, the factors considered could contribute to suicidal behaviours directly, but can also contribute indirectly by influencing individual susceptibility to mental disorders. It would be a mistake to assign a clear distinction between the areas identified. Just as each individual risk factor interrelates with others, the areas are not mutually exclusive. It is far more useful to view the areas as moving from systemic through to individual. Specific risk factors could actually sit within more than one of the areas simultaneously [2].

The final categorisation used was as follows: socio-demographics and educational, individual negative life events and family adversity, recent stressful experiences, psychiatric and psychological factors, personal factors and community factors.

Figure1. World Health Organization (WHO) model of key risk factors for suicide aligned with relevant interventions.



Source: *World Health Organization. Preventing suicide, a global imperative. Geneva; 2014.*

b) Minority stress model

Minority stress model is one of the leading theoretical frameworks for understanding the processes underlying negative psychological outcomes for sexual minority individuals. The model is inferred from several sociological and social psychological theories and it focuses on the impact of external social conditions and structures on individuals. The model describes the impact of stress and coping on mental health outcomes using a distal and proximal distinction of a variety of stressors [48,129].

As mentioned, the model **(Figure 2)** describes the impact of different factors on mental health outcomes *(box i)*. Circumstances in the environment *(box a)*, including advantages and disadvantages related to factors such as socioeconomic status and a person's minority status *(box b)* are depicted as overlapping boxes in the figure to indicate that a close relationship exists between them and that one can affect to the other. Circumstances in the environment lead to exposure to stressors, including general stressors such as a job loss or death of a family member or a friend *(box c)*; minority distal stressors unique to minority group members such as discrimination and violence in different environments *(box d)*; and minority proximal stressors such as expectations of rejection or internalised homophobia *(box f)*. Similar to their source circumstances, the stressors are depicted as overlapping as well, representing their interdependency [130].

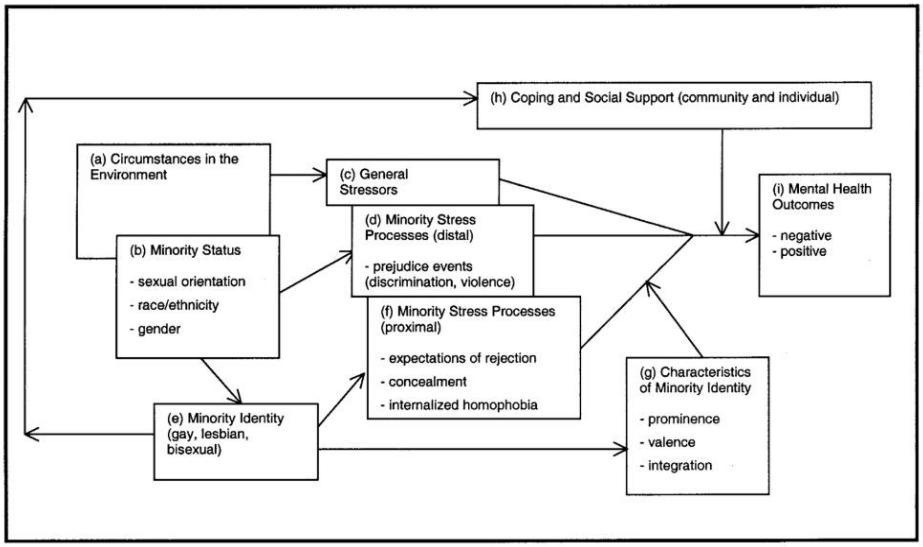
For example, an experience of antigay violence is likely to increase vigilance and expectations of rejection. Often, minority status leads to personal identification with one's minority status (minority identity) *(box e)*. In turn, such minority identity leads to additional stressors related to the individual's perception of the self as a stigmatised and devalued minority [131], a process in which societal homophobic attitudes become their own [132]. Minority identity *(box e)* is not only a source of stress, but also an important effect modifier in the stress process. It can augment or diminish the impact of stress *(box g)* or it can be a source of strength *(box h)* when it is associated with opportunities for affiliation, social support and coping that can ameliorate the impact of stress [131].

In addition, minority distal stressors *(box d)* are objective stressors, which do not depend on an individual's perceptions or appraisals, or on self-identity as LGB. However, their report depends on perception and attribution. In contrast, minority proximal stressors *(box f)* are more subjective and are, therefore, related to self-identity as LGB. Such processes vary in the social and personal meanings that are attached to them and in the subjective stress, they entail.

Minority stress is: (a) unique —meaning that it is additive to general stressors that are experienced by all people and, therefore, stigmatised people require an adaptation effort above the one required by similar others who are not stigmatised; (b) chronic — that is, minority stress is linked to relatively stable underlying social

and cultural structures; and (c) socially based —that is, it stems from social processes, institutions and structures beyond the individual [48].

Figure 2. Minority stress model of stress processes in lesbian, gay and bisexual populations.



Source: *Prejudice, Social Stress, and Mental Health in Lesbian, Gay, and Bisexual Populations: Conceptual Issues and Research Evidence. Psychol Bull. 2003;129(5):674–97.*

2. THESIS RATIONALE

Suicide is a major public health concern. Prevention of suicide has been highly recommended as a public health priority by both the European Commission and the World Health Organization (WHO). Regardless of efforts made to reduce suicide rates, they have not been considerably reduced during the last decades and both adolescents/young adults register the highest rate increments. Currently, suicide is the second leading cause of death among 15- to 29-year-olds [1]. Suicide is the ultimate stage in the spectrum of suicidal thoughts and behaviours (STB). Suicide attempts and mental disorders are the factors exerting the highest risk for suicide. Suicide attempt is rare before puberty, but a substantial increase occurs when individuals reach adolescence and young adulthood, especially for 19- to 23-year-olds. Moreover, a wide range of risk factors and protective factors for STB have been discussed.

Gender and sexual orientation differences in the risk for STB as well as the associated factors have been previously described. Female adolescents/young adults are more prone to suicidal ideation and attempts, while suicide death is more common among males. Lesbian, gay and bisexual (LGB) adolescents/young adults are also at higher risk for STB compared to heterosexuals. However, there is a lack of robust evidence on whether there are specific risk and protective factors by gender or sexual orientation, as well as on the possible mechanisms by which some factors increase and others diminish the risk for STB. Therefore, we decided to conduct a

systematic review of the literature with meta-analysis, as it has the highest quality of the evidence-based research, in order to assess the magnitude of the risk for suicide attempt and suicide death, as well as the risk and protective factors for these outcomes, according to gender and sexual orientation among adolescents/young adults.

Prevalence estimates for STB among university students are also consistently high. Probably gender differences and the greater vulnerability of LGB individuals are also higher in this subpopulation, but little is known. Similarly, the risk and protective factors for STB among university students are still quite unknown. Majority of the evidence about STB in university students comes from Anglo-Saxon countries, while the evidence in Spain is still limited, and longitudinal data about mental health of the Spanish university students is not available. Although evidence about prevention for STB in university settings is growing, only some of the implemented strategies have shown effectiveness reducing STB among university students. This makes it necessary to increase/improve the knowledge about mental health of the Spanish university students, specifically assessing the prevalence of mental disorders and STB and estimating the magnitude of the risk so as the risk and protective factors according to gender and sexual orientation. Generating reliable evidence about the mental health of Spanish university students is a requisite for the development of evidence-based public health strategies tailored to the needs of the population and for increasing its long-term effectiveness.

3. OBJECTIVES AND HYPOTHESIS

The general aim of this doctoral thesis is to provide new evidence about the risk for suicidal thoughts and behaviours (STB) and potential risk and protective factors associated with STB among adolescents and young adults; and how these vary according to gender and sexual orientation.

Specific objectives

Among adolescents and young adults:

1. To assess the risk for STB according to gender.
2. To identify risk factors and protective factors for STB and the differences in these associations according to gender.
3. To assess the risk for STB among lesbian, gay and bisexual (LGB) individuals.
4. To identify risk factors and protective factors for STB for LGB individuals.
5. To examine the role of perceived sexual orientation discrimination and internalised homophobia in the risk for STB among LGB individuals.

3.1 Hypotheses

The risk for STB among adolescents and young adults differs by gender and sexual orientation. A wide range of factors, including mental disorders, childhood and adolescent adversities, family factors and community factors are risk factors for STB. Positive

relationships with family and peers are protective for STB. The magnitude of the associations with STB for risk and protective factors differs by gender and by sexual orientation.

Specific hypotheses

1. The risk for suicidal ideation and suicide attempt is higher among female adolescents and young adults. On the contrary, the risk for suicide death is higher among male adolescents and young adults.

2. There are gender differences in the magnitude of the associations of the identified risk and protective factors with STB among adolescents and young adults (e.g. higher risk for STB for internalising mental disorders among females compared to males).

3. LGB adolescents and young adults are at higher risk for STB than their heterosexuals peers.

4. There are specific risk factors related to sexual orientation (e.g. discrimination, victimisation, internalised homophobia) and protective factors for STB for LGB adolescents and young adults.

5. Perceived sexual orientation discrimination, victimisation and internalised homophobia mediate the association between some of the identified factors and the risk for STB among LGB individuals.

4. METHODS

The analysis of this thesis are based on a broad systematic review of the literature with meta-analysis about the prevalence rates and risk factors and protective factors of suicidal attempt and suicide death in people aged 12 to 26, both inclusive; and on data from the UNIVERSAL research study (*University and Mental Health*). The results of both the systematic review and the UNIVERSAL study are complementary to each other and, together, through the 4 articles presented, try to respond the specific objectives posed in this dissertation. More specifically, the specific objectives 1 and 2 are responded in the first and second articles, while objectives 3, 4 and 5 are answered in the third and fourth articles. The methodology of both studies is described in detail in the different publications that are part of this thesis. The most relevant aspects of the methodology of both the systematic review and the UNIVERSAL study are summarised below.

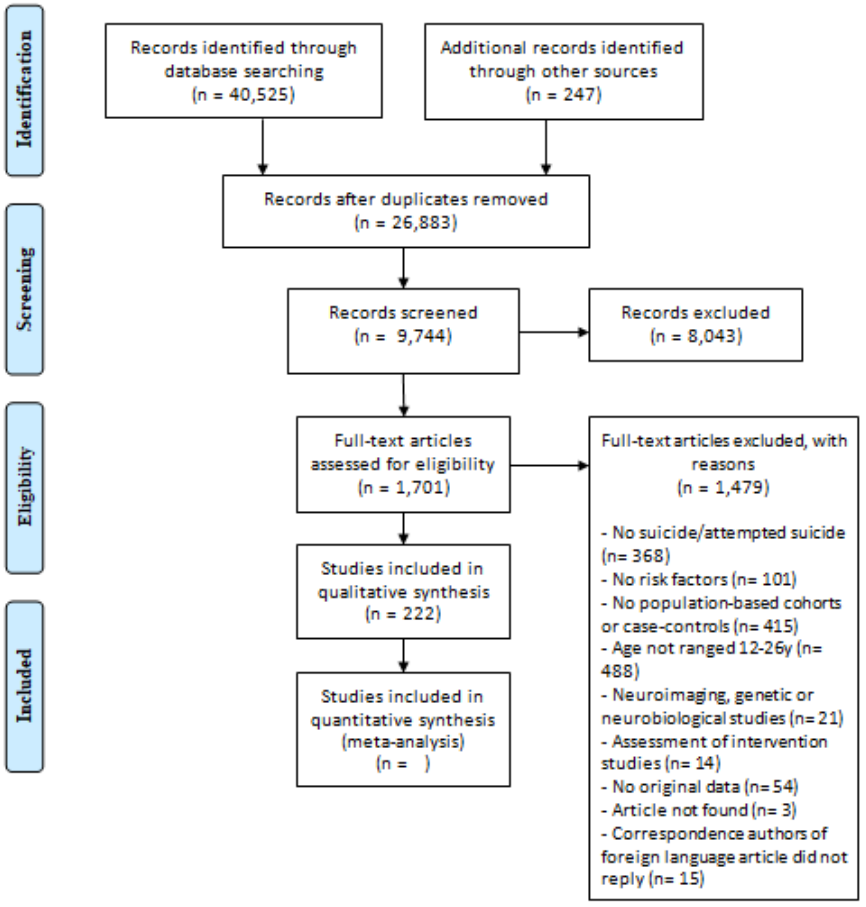
4.1 Systematic review and meta-analysis

A broad-scope and inclusive initial search strategy was carried out, with no restrictions of population, age, language or year of publication, in order to identify predictors of suicide attempt and suicide death in longitudinal studies; text-word, titles and Mesh terms were used as search terms. The search strategy was devised for Medline and then adapted for the other databases. The following databases were first searched up to October 2013 and updated twice up to June 2015 and to January 2017: Cochrane Library, Medline,

PsycINFO, EMBASE and Web of Science. OpenGrey European database was used for grey literature search. Detailed information of the search strategy is presented in annexes 2 and 3. The search was expanded using manual methods, and 212 references were identified through inspecting 254 books and reviews. No restrictions of language or year of publication were applied. We contacted the corresponding authors of articles written in languages other than Spanish and English at least three times to obtain information for inclusion/exclusion criteria, and additional data for included articles. A total of 26,882 references resulted after removal of duplicates **(Figure 3)**.

Studies were included if they met all of the following criteria: (a) reported suicide attempt or suicide as a dependent variable; (b) assessed at least one risk factor for any of these outcomes; (c) the study population age ranged between 12- to 26-year-olds, both inclusive; (d) were population-based longitudinal studies (non-clinical and non-institutional sample cohorts) or case–control studies, where the control group was of the same age range (non-clinical and non-institutional). Studies that focused on clinical, institutionalised samples were excluded to ensure that the results obtained could be generalised to a youth general population. Using these criteria, a total of 222 studies were retrieved for the qualitative synthesis. To these studies, specific selection criteria were applied to select the studies for each of the specific articles. Detailed information about these specific criteria applied in each article is presented in the results section articles 1 and 3.

Figure 3. PRISMA diagram of the included studies in the systematic review of suicidal behaviour in adolescents/young adults (covered up until January 2017).



Source: *Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009;6(6):e1000097.*

a) Study selection

Literature was checked by independent peer-reviewers including psychiatrists, psychologists, statisticians, epidemiologists and public health professionals. A total of 10 reviewers were divided into five groups; each pair of reviewers checked 20% of cites first by title, then by abstract and, finally, by full-text. To diminish bias, reviewers were blinded in terms of author's article, journal and publication year during the title and abstract phases. In case of discrepancy, the uncertain literature was included in the title revision phase. Regarding the abstract and full-text phases, in case of discrepancies a third reviewer checked and solved them. Where necessary, the authors of the included studies were contacted for further information.

b) Data extraction

A Cochrane Collaboration data collection form was adapted for data extraction. The following variables were extracted:

Basic information:

1) Reference
2) PMID
3) Title
4) First author
5) Publication year
6) Journal

Characteristics of the article:

At baseline:

7) Sample size included
8) Number of females/males included
9) Mean age
10) Age range
11) Sample's recruiting country
12) Study design
13) Sample anonymised
14) Outcome assessed (suicide/suicidal attempt)
15) Instruments administered for assessing suicidal behaviour
16) Type of recruited sample in cohorts, or in the case group for case-control studies (general population; primary care; students; others)
17) Mean of suicide (hanging, hooting; drowning; deliberate traffic accident; jumping from a high place; intoxication; others)
18) Ethical Committee Approval

At follow-up (cohort studies):

19) Follow-up weeks
20) Number of attritions during the follow-up
21) Number and week of the assessment
22) Number of subjects with suicidal attempt at baseline
23) Number of subjects with incidence of suicide during the follow-up
24) Number of subjects with incidence of suicidal attempt during the follow-up

Quality assessment of the included studies:

25) The Newcastle–Ottawa Scale (NOS) was used for assessing the quality of non-randomised studies [133]. Detailed information of the scale is presented in the following subsection.

Incidence assessment (only in cohort studies):

26) Number of new cases (incidence) in each assessment during the follow-up (weeks)

Suicidal risk factors assessment:

27) Identified risk or protective factors:

Dichotomous variable: number of exposed and non-exposed cases, and number of exposed and non-exposed controls.

Continuous variable: mean (standard deviation [SD] or standard error [SE]) of exposed and non-exposed cases and mean (SD or SE) of exposed and non-exposed controls.

Stratified analysis (if it is the case) was also registered.

c) Quality of included studies

New Castle Ottawa Scale (NOS) was developed to assess the quality of non-randomised studies with its design, content and ease of use directed to the task of incorporating the quality assessments in the interpretation of meta-analytic results. A 'star system' has been developed in which a study is judged on three broad

perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or the outcome of interest for case-control or cohort studies respectively. The highest-quality studies are awarded up to nine stars. Studies with up to 6 stars were considered as high quality according to the NOS.

d) Data synthesis

Study characteristics and quality of the included studies were described. In case of multiple articles of the same study including duplicated data, the longest follow-up and most completed report was considered.

To estimate the magnitude of the association of dichotomous variables, relative risk (RR) in case of cohort studies, and odds ratio (OR), in case-control studies and 95% CI, were used. Adjusted values prevailed over unadjusted ones, if not, the latter were considered if adjusted values were not available. Similarly, if meta-analysis of any found risk or protective factor could be done with both RR and OR, the assessment of RR prevailed. For continuous variables, mean differences with 95% CI were used.

When possible population attributable risk (PAR) was calculated, it indicates the number (or proportion) of cases that would not occur in a population if the risk factor were eliminated. PAR calculation uses the formula:

$$\mathrm{PAR} = \frac{P\,(RR-1)}{[1+P\,(RR-1)]}$$

P is the prevalence of the risk factor and RR is the relative risk for suicide attempt or suicide death, both obtained from data of the cohort studies included in meta-analysis. In case only OR were available, to convert OR to RR the following formula was used:

$$\mathrm{RR} = \frac{\mathrm{OR}}{(1-\mathrm{P_0})+\mathrm{P_0OR}}$$

Where OR is the odds ratio of suicide attempt or suicide death in the risk category of each assessed variable (e.g. female for suicide attempt, male for suicide), and P_0 is the prevalence of suicide attempt or incidence suicide death in the category of reference [134], calculated from data of the included studies.

Heterogeneity between the included studies was assessed by visual inspection of forest plots, by Galbraith plots, and using both Chi-square test and Higgins' test (I^2) to calculate the p-value which was considered as significant when <0.10. If there was moderate (30% to 50%) or no heterogeneity, fixed models were used for the meta-analysis. In case of severe heterogeneity (>50%), random effects models were use. To assess publication bias, funnel plots, Begg test and the degree of asymmetry, these factors were tested using Egger unweighted regression asymmetry test.

e) Reporting systematic review

Recommendations from the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for systematic reviews were followed [135]. MOOSE checklist is available at **Annex 1**.

4.2 The UNIVERSAL Study

a) Design

The UNIVERSAL study is a multicentre, observational and prospective study of freshmen university students from five Spanish universities. The study began in January 2014 and ended in December 2018.

b) Study setting and sample

Sample was recruited from five Spanish public universities from different regions: Cádiz University (UCA), Balearic Islands University (UIB), Basque Country University (UPV-EHU), Pompeu Fabra University (UPF) and Miguel Hernández University (UMH). The universities were selected for convenience and represented 8.2% of the undergraduate enrolment capacity annually offered in the country. Inclusion criteria were a) students aged 18 to 24; and b) being enrolled in the first year of university for the first time. Based on these criteria, 16,332 students were eligible to participate. To participate in the study, students had to fill out an application form

on the UNIVERSAL study website and accept the informed consent.

Sample recruitment was performed in two phases. First, university authorities sent up to four personal e-mail letters to the eligible students to invite them to participate in the study. Other invitation methods were campus advertising campaigns (e.g., information stands, university website) and classroom presentations, among others. Second, a random subsample of non-respondents of the survey was contacted by e-mail including an economic incentive of 25 € to complete the survey ("endgame strategy"). At UPV-EHU University, only the first phase was carried out.

c) Data collection

Participants underwent an online survey via a secure web-based platform designed for the study. The survey assessed extended information about mental health of the university students and their use of health services. Baseline survey (T1) included 14 sections and a specific section about suicidal thoughts and behaviours, which translated into a total of 336 items. New items were added to the follow-up survey (12-months) (T2), which had 354 items. In both surveys some items were conditioned on previous responses.

d) Analysis

To achieve the aims of the third and fourth article of this thesis, items from both baseline survey and 12-months survey of the UNIVERSAL study were selected. Detailed information about the variables assessed and the analysis conducted is presented in the results section (articles 1 and 3).

e) Ethical considerations

Protocol of the study was approved by Parc de Salut MAR-Clinical Research Ethics Committee (Reference number 2013/525/I). At the end of the surveys, all participants received information on how to access local health services. Students with positive responses on the items about suicidal thoughts or behaviours also received a specific alert approved by the ethical committee with instructions to consult with a health professional.

5. RESULTS

The four original articles that make up this thesis and respond to the objectives are:

- **Article 1.** Gender differences in suicidal behavior in adolescents and young adults: systematic review and meta-analysis of longitudinal studies. International Journal of Public Health (2019). Quartile 1. Public, environmental and occupational health. IF: 2.373.

- **Article 2.** Gender commonalities and differences in risk and protective factors of suicidal thoughts and behaviors: a cross-sectional study of Spanish university students. Depression and Anxiety (2019). Quartile 1. Psychiatry. IF: 4.935.

- **Article 3.** Sexual orientation and suicidal behaviour in adolescents and young adults: systematic review and meta-analysis. The British Journal of Psychiatry (2017). Decile 1. Psychiatry. IF: 7.233.

- **Article 4.** Suicidal ideation risk among LGB Spanish university students: the role of childhood and adolescence adversities and mental disorders. To be submitted to the Journal of Adolescent Health (2019). Decile 1. Pediatrics. IF: 3.957.

Article 1. *"Gender differences in suicidal behavior in adolescents and young adults: systematic review and meta-analysis of longitudinal studies"*

Miranda-Mendizabal A, Castellví P, Parés-Badell O, Alayo I, Almenara J, Alonso I, et al. Gender differences in suicidal behavior in adolescents and young adults: systematic review and meta-analysis of longitudinal studies. Int J Public Health. 2019;64(2):265–83.

PMID: 30635683

Supplementary material for this article can be found in ANNEX 2 (page 201).

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REVIEW

Gender differences in suicidal behavior in adolescents and young adults: systematic review and meta-analysis of longitudinal studies

Andrea Miranda-Mendizabal[1,2] · Pere Castellví[1,3] · Oleguer Parés-Badell[1] · Itxaso Alayo[1,4] · José Almenara[5] · Iciar Alonso[6] · Maria Jesús Blasco[1,2,4] · Annabel Cebrià[7] · Andrea Gabilondo[8,9] · Margalida Gili[10,11] · Carolina Lagares[12] · José Antonio Piqueras[13] · Tiscar Rodríguez-Jiménez[13] · Jesús Rodríguez-Marín[13] · Miquel Roca[10,11] · Victoria Soto-Sanz[13] · Gemma Vilagut[1,4] · Jordi Alonso[1,2,4]

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Abstract

Objectives To assess the association between gender and suicide attempt/death and identify gender-specific risk/protective factors in adolescents/young adults.

Methods Systematic review (5 databases until January 2017). Population-based longitudinal studies considering non-clinical populations, aged 12–26 years, assessing associations between gender and suicide attempts/death, or evaluating their gender risk/protective factors, were included. Random effect meta-analyses were performed.

Results Sixty-seven studies were included. Females presented higher risk of suicide attempt (OR 1.96, 95% CI 1.54–2.50), and males for suicide death (HR 2.50, 95% CI 1.8–3.6). Common risk factors of suicidal behaviors for both genders are previous mental or substance abuse disorder and exposure to interpersonal violence. Female-specific risk factors for suicide attempts are eating disorder, posttraumatic stress disorder, bipolar disorder, being victim of dating violence, depressive symptoms, interpersonal problems and previous abortion. Male-specific risk factors for suicide attempt are disruptive behavior/conduct problems, hopelessness, parental separation/divorce, friend's suicidal behavior, and access to means. Male-specific risk factors for suicide death are drug abuse, externalizing disorders, and access to means. For females, no risk factors for suicide death were studied.

Conclusions More evidence about female-specific risk/protective factors of suicide death, for adolescent/young adults, is needed.

Keywords Gender · Suicide · Suicide attempt · Adolescents · Young adults · Risk factors

Introduction

Suicide is a very serious public health concern. In 2016, there were an estimated 793,000 suicide deaths worldwide, representing an annual global age-standardized suicide rate of 10.5 per 100,000 population. Globally, it is the second leading cause of death among persons aged 15–29 years (World Health Organization 2016). In adolescents and young adults, suicide rates are 2–4 times higher in males than in females, while suicide attempts are 3–9 times more common in females (Wunderlich et al. 2001; Eaton et al. 2012). In developed countries, suicide mortality has been estimated to be 2–3 times higher in young males than females (Wasserman et al. 2005).

Within the context of suicide research, gender differences in suicidal behavior rates are known as the "Gender Paradox" (Canetto and Sakinofsky 1998). In adolescents and young adults, this paradox changes according to age (Canetto 2008; Rhodes et al. 2014a). Female suicide attempt rates increase with age, peaking in mid-adolescence (Lewinsohn et al. 2001; Boeninger et al. 2010; Thompson and Light 2011), whereas male suicide rates increase until early adulthood (World Health Organization 2014). Previous suicide attempts are one of the strongest

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✉ Jordi Alonso
jalonso@imim.es

Extended author information available on the last page of the article

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predictors of suicide death (Kokkevi et al. 2012), especially among females. Gender differences in suicidal behavior may be explained by differences in emotional and behavioral problems (Kaess et al. 2011). The higher rates of suicide deaths among male youths may be associated with a higher prevalence of externalizing disorders (e.g., conduct disorder, substance abuse disorder, deviant behavior) (Mergl et al. 2015) and a preference for highly lethal methods (Värnik et al. 2008). In contrast, females are more prone to show internalizing disorders (e.g., anxiety, mood disorders) (Fergusson et al. 1993). These disorders may mediate the association with suicidal thoughts and behaviors (Peter and Roberts 2010; Mars et al. 2014).

To the best of our knowledge, no previous meta-analysis has assessed the association between gender and suicidal behaviors, or gender-specific determinants, in adolescents and young adults. Accurately identifying gender-specific risk and protective factors for suicidal behaviors is important to improve knowledge and to develop more effective suicide prevention programs. Therefore, we undertook a systematic review of the literature aiming to: (1) assess the magnitude of association between gender and suicide attempts and death; and (2) to identify gender-specific risk and protective factors of suicide attempts and death in adolescents and young adults.

Methods

This article is based on a broad, comprehensive systematic review of the risk and protective factors of suicidal behaviors in adolescents and young adults aged 12–26 years. The recommendations of the MOOSE guidelines for systematic reviews were followed (Table S1) (Stroup et al. 2000). The original search protocol was registered at PROSPERO. More information about the search strategy and selection criteria is provided in Text S1 (available online).

For this article, specific selection criteria were applied, including: (1) cohort studies assessing the association between gender and suicide attempts or death; and (2) cohort or case–control studies evaluating risk or protective factors for suicide attempts or death stratified by sex. For the assessment of gender with suicidal behaviors, case–control studies were excluded because the subjects were matched by sex, which may lead to underestimation of risk. To assess suicide attempts, we considered females as the subpopulation at risk, with males as the comparison group; for suicide death, males were the subpopulation at risk (World Health Organization 2014). An exhaustive peer review process was used to classify risk and protective factors according to their definition in the primary studies, a previous exhaustive review of the literature (Evans et al. 2004) and the World Health Organization's socio-ecological model (World Health Organization 2014). The principal categories were as follows: sociodemographic and educational, individual negative life events and family adversity, psychiatric/psychological factors, personal factors and community factors.

A Cochrane Collaboration data collection form was adapted for data extraction (Higgins and Green 2008). Data were extracted by two reviewers, and a third assessed whether the information was entered properly and attempted to complete any missing data. If there were discrepancies, consensus was established among reviewers. The following data were extracted from each article: (1) sample size, (2) prevalence of females and males, (3) age range, (4) mean age, (5) country of recruitment, (6) study design, (7) suicide outcome, (8) type of sample recruited, (9) adjustment variables, and (10) ethics committee approval. For cohort studies, additional data extraction included: (1) weeks of follow-up, (2) number of suicide attempts or suicide deaths during follow-up, and (3) attrition rates. Information about sex-stratified risk and protective factors was obtained as follows: odds ratio (OR) and 95% confidence intervals (95% CI) or beta coefficients and standard errors (SE). Multivariate analyses were selected over bivariate analyses. If there were multiple publications on the same sample and factors, the results of the largest sample and longest follow-up were selected for the analyses.

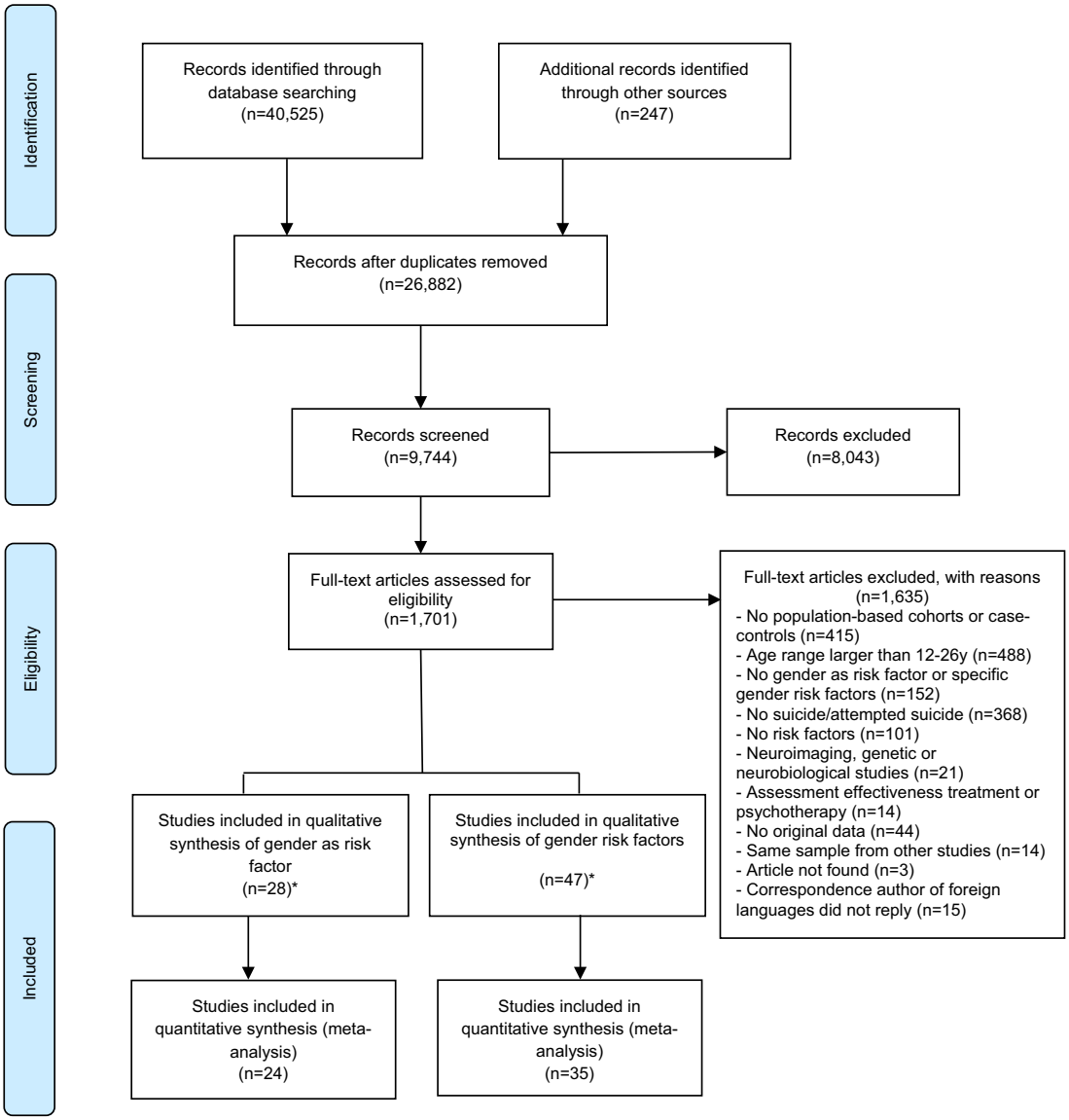
Quality assessment

The Newcastle–Ottawa scale (NOS) was used to assess the quality of non-randomized studies (Wells et al. 2013), including: (1) selection of study groups, (2) comparability between groups, and (3) exposure in case–control studies or outcome in cohort studies. The NOS includes eight questions (four in selection, one in comparability, and three in exposure or outcome) with various response options; the response indicating the highest quality is assigned 1 point. One point can be granted for each question within the selection and exposure or outcome categories. For comparability, a maximum of 2 points can be given. The highest quality studies may receive a maximum of 9 points.

Data synthesis

Meta-analyses were performed when there were a minimum of two studies with usable data; random effect methods were used. Heterogeneity was assessed by visual inspection of forest plots, Galbraith plots, a Chi-square test to calculate p value, and the Higgins test (I^2), which describes the percentage of observed heterogeneity that would not be expected by chance. Heterogeneity was considered to be significant when p was < 0.10, and was

classified as low (< 30%), moderate (30%–50%), and severe (> 50%) (Higgins and Thompson 2002). Small study effects (including publication bias) were assessed through visual inspection of funnel plots and the Egger test. Sensitivity analyses were only conducted for the analysis of gender as a risk factor, according to two criteria: (1) publication year (studies published before the year 2000) and (2) NOS scale < 6 points. Meta-analyses assessing the effects of risk and protective factors on suicide attempts and death were carried out. Due to the large number of



*Including 8 studies which assess gender as risk factor and specific gender risk factors.

Fig. 1 Modified version of PRISMA diagram of the included studies in the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)

Table 1 Characteristics of the included studies in the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)

Author (study)	Country	Follow-up	Sample at baseline (% of women)	Sample at the end of follow-up (% of attrition)	Percentage of suicide attempts or deaths during the follow-up	Population	Age range (years)	Mean age (standard deviation)	Meta-analysis (gender, risk and protective factors or both)
Studies assessing suicide attempt									
Cohort studies									
Kaplan and Pokonny (1976)	USA	3 years	7618	3148 (58.7)	NI	High school	NI	NI	None
Reinherz et al. (1995)	USA	14 years	404	385 (4.7)	4.2	High school	18	17.9	Gender
Silverman et al. (1996)	USA	17 years	777 (49.9)	375 (51.7)	2.7	General	15–21	NI	Risk and protective factors
McKeown et al. (1998)	USA	2 years	359 (56)	359	1.7	High school	NI	NI	Gender
Wichstrom (2000)	Norway	2 years	11,918 (41.1)	9679 (18.8)	8.2	High school	14–22	NI	Both
Borowsky et al. (2001)	USA	1 year	20,745 (52)	13,110 (37)	36	Students	13–19	16	None
Lewinsohn et al. (2001)	USA	8 years	1709 (57)	941 (45)	13,2	Students	24	24	Risk and protective factors
Sourander et al. (2001, 2009)	Finland	8 years	6017	580 (90.4)	0.46	General	16	16.0 (0.5)	Both
Fergusson et al. (2003) (Christchurch)	New Zealand	21 years	1265 (49.8)	1063 (15.9)	7.3	General	21–25	NI	Gender
Bearman et al. (2004)	USA	1 year	20,745	13,465 (35)	NI	High school	NI	NI	Risk and protective factors
Ialongo et al. (2004)	USA	11 years	1197 (56)	747 (38)	44.1	Students	19–20	NI	Risk and protective factors
ÓAugelli et al. (2005)	USA	2 years	528	361 (31.6)	17	LGB	15–19	NI	Both
Feigelman et al. (2006), Thompson et al. (2007), Exner-Cortens et al. (2013), Van Dulmen et al. (2013), Abrutyn et al. (2014), Turanovic and Pratt (2015) (Add Health)	USA	14 years	20,745	13,110 (36.8)	3.6	High school	NI	NI	Both
Kidd et al. (2006)	USA	1 year	12,105	9142 (24.5)	NI	High school	12–17	16.0	Gender
Rodríguez-Cano et al. (2006)	Spain	2 years	1776 (49.9)	1076 (39.4)	3.8	High school	13–15	NI	Gender
Ackard et al. (2007)	USA	5 years	3074	1710 (44.4)	3.9 females dating violence; 4.4 males dating violence	Students	NI	20.4 (0.8)	Risk and protective factors
Brezo et al. (2007, 2008) (Quebec)	Canada	22 years	3017 (47.2)	1776 (41.1)	9.3 any; 1.8 repeated	Students	19–24	21.4	Gender

Table 1 (continued)

Author (study)	Country	Follow-up	Sample at baseline (% of women)	Sample at the end of follow-up (% of attrition)	Percentage of suicide attempts or deaths during the follow-up	Population	Age range (years)	Mean age (standard deviation)	Meta-analysis (gender, risk and protective factors or both)
Crow et al. (2008)	USA	5 years	3672	2516 (22.6)	8.7 females; 3.5 males	General	NI	17.2 high school; 20.4 young adults	Risk and protective factors
Dupéré et al. (2008)	Canada	10 years	4951	2776 (43.9)	NI	General	12–19	NI	Gender
Lambert et al. (2008)	USA	3 years	678 (46.5)	473 (30.2)	NI	Students	13–14	13.8 (0.3)	None
Nrugham et al. (2008, 2015)	Norway	6 years	2464 (50.8)	265 (89.2)	1.50	Students	18–21	20 (0.6)	Risk and protective factors
Wong et al. (2008)	China	12 months	1747 (34)	1099 (37.1)	NI	Students	12–18	14.5	Both
Wilcox et al. (2009)	USA	17 years	2311 (50.2)	1570 (47.2)	2.38	Students	20–23	21	Both
Batty et al. (2010)	Sweden	24 years	1,379,531	1,133,019 (17.9)	NI	General	16–25	18	None
Tracey et al. (2010) (NLSCY)	Canada	5 years	25,781	2499 (90.3)	45.9	General	15–18	NI	Both
Roberts et al. (2010)	USA	1 year	4500	3134 (30.3)	0.84	General	11–17	NI	Gender
Klomek et al. (2011)	USA	4 years	2342	342	NI	High school	13–18	14.8 (1.2)	Risk and protective factors
Young et al. (2011)	UK	8 years	2586 (50.4)	1860 (28.1)	6.1	High school	15	NI	Gender
Fried et al. (2012)	USA	2 years	27,000	1728 (93.6)	0.5	Students	16–18	16.7 (0.6)	Gender
Guan et al. (2012)	USA	2.5 years	712 (54.8)	399 (44)	5.2	High school	NI	NI	Gender
Hurtig et al. (2012)	Finland	16 years	9215	273 (97.1)	0.086	General	15–18	NI	Gender
Nkansah-Amankra et al. (2012)	USA	14 years	20,715	9412 (54.6)	1.9	General	18–26	NI	Risk and protective factors
Wanner et al. (2012)	Canada	22 years	3017 (47.2)	1776 (41.1)	2.3	Students	19–24	21.4	Risk and protective factors
Winterrowd and Canetto (2013)	USA	3 years	295 (59)	253 (14.2)	9	General	19–23	19.5 (1.1)	None
Chang et al. (2014) (ALSPAC)	UK	17 years	14,062	3560 (74.6)	1.61	General	16–17	16.8 (2.9)	None
Chuan-Yu et al. (2014)	China	1 year	9393	7313 (44)	NI	General	15–24	NI	Risk and protective factors
Conner et al. (2014)	USA	5 years	NI	418	4.54	General	12–19	NI	Gender

Table 1 (continued)

Author (study)	Country	Follow-up	Sample at baseline (% of women)	Sample at the end of follow-up (% of attrition)	Percentage of suicide attempts or deaths during the follow-up	Population	Age range (years)	Mean age (standard deviation)	Meta-analysis (gender, risk and protective factors or both)
Luntano et al. (2014)	Finland	16 years	6017	5416 (6.8)	0.88	General	NI	NI	Risk and protective factors
Mars et al. (2014)	UK	16 years	14,062	4799 (65.9)	3.5	General	16–17	NI	Gender
Miranda et al. (2014)	USA	6 years	1729	506 (70.7)	2.4	Students	12–20	15.6 (1.4)	Gender
Soller et al. (2014)	USA	12 years	5316	4459 (16.1)	4.72	Students	NI	NI	Risk and protective factors
Swanson et al. (2014)	USA	10 years	228	199 (12.7)	NI	Students/ females	16–22	19.6	Risk and protective factors
Scott et al. (2015)	USA	16 years	2450	1950 (20.4)	1.47	General/ females	17–21	NI	Risk and protective factors
You et al. (2015)	China	1 year	5423 (53)	3600 (34)	2,9	Students	12–18	14.63 (1.3)	Both
Conway et al. (2016)	Denmark	9 months	99 (88.9)	85 (14.1)	14.1	General	NI	16.3 (1.6)	None
Meza et al. (2016)	USA	10 years	228 (100)	216 (5)	NI	General	17–24	19.6	None
Mok et al. (2016)	Denmark	30 years	1,743,525 (48.7)	1,743,525	2.6	General	NI	21.6	None
Hishinuma et al. (2017) (HHSHS study)	USA	5 years	2133	2083 (2.34)	2.7 females; 1.6 males	Native Hawaiians/ non–Hawaiians	14–17	NI	None
Case–control studies									
King et al. (1990)	USA	*a*	19 cases vs. 21 controls (100)	*a*	*a*	General/ Women	NI	14.9 (1.2)	None
Rotheram-Borus and Shrout (1990)	USA	*a*	77 cases vs. 63 controls (100)	*a*	*a*	Primary health care	12–17	14.7	Risk and protective factors
Garnefski et al. (1992)	The Netherlands	*a*	285 cases vs. 285 controls (64.9)	*a*	*a*	Students	13–20	16	Risk and protective factors
Adams et al. (1994)	USA	*a*	91 cases vs. 155 controls	*a*	*a*	High school	12–17	NI	None

Table 1 (continued)

Author (study)	Country	Follow-up	Sample at baseline (% of women)	Sample at the end of follow-up (% of attrition)	Percentage of suicide attempts or deaths during the follow-up	Population	Age range (years)	Mean age (standard deviation)	Meta-analysis (gender, risk and protective factors or both)
Beautrais et al. (1998)	New Zealand	*a*	129 cases vs. 153 controls	*a*	*a*	General	18–24	19.4 (3.0) cases; 21.4 (1.6) controls	Risk and protective factors
Lyon et al. (2000)	USA	*a*	38 cases vs. 76 controls (18.4)	*a*	*a*	Primary care	12–17	14.8	Risk and protective factors
Ikeda et al. (2001)	USA	*a*	153 cases (37) 513 controls (40)	*a*	*a*	General	13–24	NI	Risk and protective factors
Donald et al. (2005)	Australia	*a*	95 cases vs. 380 controls (48)	*a*	*a*	General	18–24	NI	Risk and protective factors
Bilgin et al. (2007)	Turkey	*a*	52 cases vs. 52 controls (100)	*a*	*a*	High school	14–18	16	None
Freitas et al. (2008)	Brazil	*a*	110 cases vs. 110 controls (100)	*a*	20 cases, 6.3 controls (prevalence)	Primary health care	14–18	NI	Risk and protective factors
Christiansen et al. (2011, 2012)	Denmark	*a*	3465 cases vs. 69,300 controls (78.7)	*a*	4.8	General	16–22	16.8 (2.3) females; 17.8 (2.4) males	Risk and protective factors
Studies assessing suicide death									
Cohort studies									
Finkelstein et al. (2015)	Canada	12 years	1,044,405	1,043,958 (0.042)	0.039	General	17–26	NI	Gender
Feigelman et al. (2016) (Add Health study)	USA	7 years	20,771	10,122	21	General/men	20–26	NI	None
Weiser et al. (2016)	Israel	16 years	988,847	634,655 (35.8)	0.07	General/men	16–17	16.9 (0.5)	None
Case–control studies									
Salk et al. (1985)	USA	*a*	52 cases vs. 104 controls (17.3)	*a*	*a*	General	12–20	NI	None
Brent et al. (1993, 1999)	USA	*a*	67 cases vs. 67 controls; 140 cases vs. 131 controls (22)	*a*	*a*	General	13–19	14	Risk and protective factors

Table 1 (continued)

Author (study)	Country	Follow-up	Sample at baseline (% of women)	Sample at the end of follow-up (% of attrition)	Percentage of suicide attempts or deaths during the follow-up	Population	Age range (years)	Mean age (standard deviation)	Meta-analysis (gender, risk and protective factors or both)
Shaffer et al. (1996)	USA	*a*	120 cases vs. 147 controls	*a*	*a*	General	20	15.9 females; 16.9 males	Risk and protective factors
Cheng et al. (2014)	China	*a*	500 cases vs. 15,000 controls (47.6)	*a*	*a*	General	15-19	NI	Risk and protective factors
Studies assessing suicide death and suicide attempt									
Case–control studies									
Ostry et al. (2007)	Canada	*a*	827	*a*	*a*	General	NI	NI	Risk and protective factors

NI no information, *a* not applicable

figures, those not presented in this article are available upon request. STATA software version 13 was used.

Results

Of 26,882 potentially suitable articles, we identified 1701 full-text articles for eligibility. Of these, 1635 were excluded. Reasons for exclusion are detailed in Fig. 1. A total of 77 articles or publications were included, representing 67 distinct studies. Ten articles were excluded from the analyses as they reported results from the same samples but with shorter follow-up periods and without providing any additional information. The references of all included articles are provided in supplementary Text S2. Nineteen studies assessed the association between gender and suicide attempts; one assessed the association between gender and suicide death; 39 assessed sex-specific risk and/or protective factors for the outcomes; and eight assessed both gender and sex-specific risk and/or protective factors. Results are presented separately for suicide attempts and suicide death.

Quality of reviewed studies

No relevant differences between the included studies were observed in the selection domain. For comparability, 39 studies achieved two points. The lowest scores were found in exposure or outcome domains: Only 15 studies achieved 1 point in the question about the ascertainment of the outcome or exposure, because most studies included self-reported data without confirmatory records; 34 studies received 1 point because the length of follow-up was $\geq$ 6 years; and 25 studies received 0 points for adequacy of follow-up (attrition rates were $>$ 25%). More information is detailed in Table S2 (available online).

Gender as a risk factor for suicidal behavior

Suicide attempts

Articles were published between 1995 and 2017, including samples predominantly from the USA (n = 13) and Canada (n = 4). Participation rates ranged from 3% to almost 98%. A summary of the most relevant characteristics of the included studies is presented in Table 1.

Of the 27 studies assessing the association between gender and suicide attempts, 24 were included in the meta-analysis. Three studies were excluded because the data were either non-extractable or did not allow comparisons. Compared with males, females showed a significantly higher pooled risk of suicide attempts (OR 1.96, 95% CI 1.54–2.50), although high heterogeneity was observed

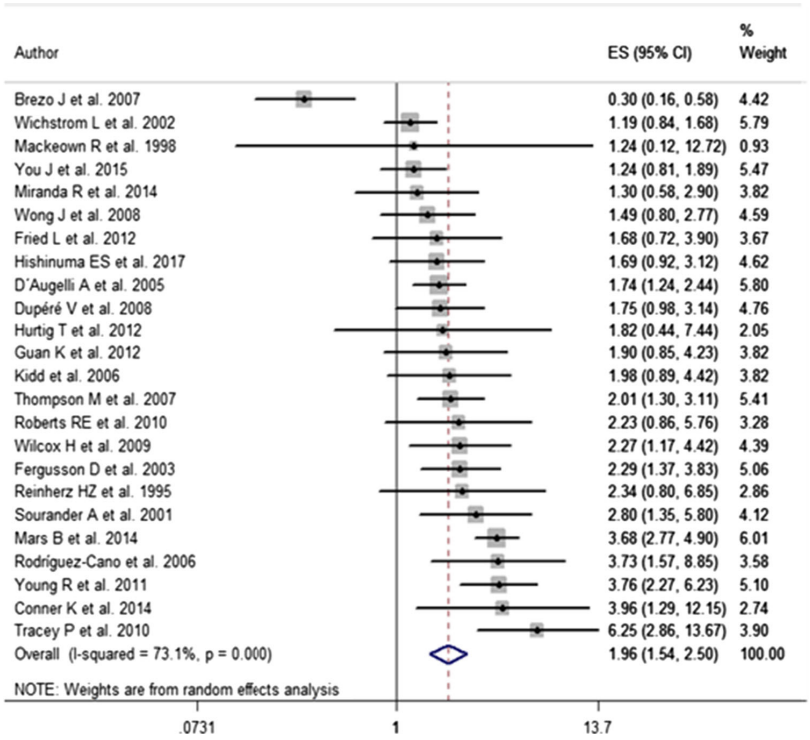


Fig. 2 Forest plot of being female as risk factor of suicide attempt—results of the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)

(I^2= 73.1%; $p < 0.001$) (Fig. 2). The funnel plot appeared asymmetric, but the Egger test did not suggest the existence of any publication bias ($p = 0.847$). After sensitivity analyses, according to publication year and quality score, no significant changes were seen.

Suicide death

One cohort study explored the association between gender and suicide death, including a sample of 1,043,958 subjects. A total of 20,471 surviving adolescents (median age 16 years; IQR 15–18), attended in the emergency department for a first self-poisoning episode, were followed from the date of discharge until death or the end of the study, whichever occurred first. Fifty matched population-based reference individuals were selected for each surviving adolescent (n = 1,023,487). After a median follow-up time of 7.2 years (IQR 4.2–9.7), the results showed that 126 individuals (0.6%) in the self-poisoning group and 286 (0.03%) in the reference group died by suicide. After a self-poisoning episode, death from suicide was more than twice as likely among males compared with females (HR 2.5, 95% CI 1.8–3.6) (Finkelstein et al. 2015).

Specific risk factors for suicidal behavior stratified by gender

A full summary of results for all risk and protective factors assessed is detailed in Table 2.

Suicide attempts

Individual negative life events and family adversity Risk factors for suicide attempts common to both genders included bullying (females: OR 6.30, 95% CI 1.53–25.90; males: OR 3.8, 95% CI 1.01–14.30), childhood maltreatment (females: OR 3.77, 95% CI 2.13–6.68; males: OR 2.76, 95% CI 1.20–6.36), community violence (females: OR 1.68, 95% CI 1.42–1.99; males: OR 1.83, 95% CI 1.48–2.26), and a family history of mental disorders, alcohol or drug abuse (females: OR 2.27, 95% CI 1.78–2.89; males: OR 2.63, 95% CI 1.99–3.47). Dating

Table 2 Meta-analysis results of gender risk and protective factors of suicidal behavior among adolescents and young adults—results of the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)

Factor(s)	Female					Male				
	Studies (*n*)	Samples (*n*)	OR	95% CI	I^2	Studies (*n*)	Samples (*n*)	OR	95% CI	I^2
Suicide attempt										
Sociodemographic and educational										
Academic factors	3	3	0.94	0.80–1.11	0	3	3	1.41	0.72–2.74	79.8
Low socioeconomic status	2	3	1.52	0.89–2.58	99.1	2	3	1.65	0.83–3.27	98.1
Parental education	2	2	1.78	0.91–3.47	0	2	2	0.99	0.51–1.92	0
Race/ethnicity	3	3	0.98	0.68–1.41	0	2	2	0.93	0.53–1.61	0
Individual negative life events and family adversity										
Any negative life event [a]	6	6	1.31	0.93–1.86	94.7	6	6	1.22	0.98–1.51	75.8
Bullying	**1**	**1**	**6.30**	**1.53–25.90**	**NA**	**1**	**1**	**3.8**	**1.01–14.30**	**NA**
Childhood maltreatment	**3**	**5**	**3.77**	**2.13–6.68**	**69.6**	**3**	**4**	**2.76**	**1.20–6.36**	**72.8**
Community violence	**3**	**3**	**1.68**	**1.42–1.99**	**0**	**2**	**2**	**1.83**	**1.48–2.26**	**0**
Conflicts with partner	2	2	1.2	0.87–1.65	67.6	1	1	1.05	0.52–2.13	NA
Dating violence	**2**	**3**	**2.19**	**1.29–3.71**	**0**	3	3	1.45	0.54–3.86	32.3
Parental separation or divorce	7	8	1.07	0.88–1.29	27.2	**7**	**8**	**1.56**	**1.01–2.41**	**73.4**
Family history of mental disorders and abuse	**2**	**3**	**2.27**	**1.78–2.89**	**18.8**	**3**	**6**	**2.63**	**1.99–3.47**	**98.6**
Family previous suicidal behavior	2	3	2.10	0.97–4.58	93.2	**3**	**4**	**2.84**	**1.87–4.33**	**42.4**
Interpersonal difficulties	**2**	**3**	**1.13**	**1.03–1.24**	**0**	1	2	1.04	0.90–1.21	0
Psychiatric and psychological										
Psychiatric										
ADHD	3	4	0.79	0.19–3.21	78.8	1	1	4.50	0.96–21.20	NA
Alcohol abuse disorder	**2**	**2**	**2.69**	**1.32–5.50**	**0**	**2**	**2**	**2.14**	**1.09–4.20**	**0**
Alcohol use	3	3	1.16	0.83–1.62	78.0	3	3	1.10	0.94–1.27	6.3
Anxiety disorder	**3**	**4**	**2.03**	**1.77–2.33**	**0**	**3**	**5**	**3.79**	**2.05–7.01**	**91.8**
Any mental disorder or abuse	**10**	**36**	**3.37**	**2.52–4.51**	**88.4**	**6**	**27**	**4.23**	**3.28–5.47**	**0.8**
Bipolar disorder	**2**	**2**	**1.43**	**1.20–1.70**	**0**	No data				
Conduct disorder	1	1	2.31	0.50–10.65	NA	1	1	0.80	0.10–6.53	NA
Drug abuse disorder	**3**	**6**	**4.44**	**2.51–7.83**	**72.2**	**2**	**5**	**3.11**	**2.01–4.84**	**0**
Drugs use	3	3	3.2	0.68–14.95	78.9	3	3	3.03	0.64–14.32	87.7
Eating disorder	**1**	**2**	**5.27**	**2.04–13.60**	**0**	No data				
Gambling disorder	1	1	4.13	0.54–31.85	NA	1	1	1.01	0.14–7.35	NA
Major depressive disorder	**4**	**5**	**4.49**	**2.18–9.23**	**78.4**	**3**	**4**	**6.07**	**1.74–21.20**	**83.6**
NSSI	2	2	2.03	0.52–7.89	88.2	1	1	1.00	0.92–1.09	NA
Personality disorder	**1**	**2**	**7.89**	**3.81–16.35**	**0**	**2**	**2**	**5.13**	**2.63–10.01**	**0**
PTSD	**2**	**2**	**2.96**	**1.32–6.62**	**38.6**	1	1	3.57	0.58–22.16	NA
Previous suicidal ideation	**4**	**4**	**4.39**	**2.31–8.34**	**77.5**	**4**	**4**	**3.97**	**1.40–11.24**	**84.5**
Previous suicide attempts	**5**	**7**	**6.96**	**3.75–12.91**	**58.2**	**1**	**2**	**31.33**	**9.36–104.88**	**0**
Psychological										
Aggressiveness	No data					1	1	1.15	0.67–1.98	NA
Anxiety symptoms	No data					1	1	0.64	0.40–1.03	NA
Depressive symptoms	**10**	**10**	**1.15**	**1.04–1.28**	**66.9**	6	6	1.26	0.98–1.62	61.5
Disruptiveness	3	5	2.54	0.67–9.60	80.7	**2**	**3**	**8.78**	**2.77–27.84**	**75.6**
Hopelessness	3	3	1.55	0.71–3.42	69.4	**3**	**3**	**1.74**	**1.04–2.94**	**0**
Low self-esteem	4	4	1.46	0.78–2.74	87.0	4	4	1.22	0.95–1.57	0

Table 2 (continued)

Factor(s)	Female					Male				
	Studies (*n*)	Samples (*n*)	OR	95% CI	I^2	Studies (*n*)	Samples (*n*)	OR	95% CI	I^2
Self-concept	3	4	1.35	0.92–1.96	50.0	3	4	1.51	0.93–2.44	57.2
Personal										
Abortion	**1**	**2**	**1.3**	**1.09–1.55**	0	NA				
Any medical condition	3	5	1.01	0.98–1.04	0	2	3	1.21	0.84–1.72	43.7
Body mass index	2	2	1.01	0.98–1.05	0	2	2	0.98	0.93–1.03	0
Dating	1	5	1.03	0.95–1.11	35.0	1	5	0.97	0.82–1.14	42.6
Eating behaviors	3	5	1.26	0.91–1.75	72.8	3	4	1.06	0.95–1.19	0
Pregnancy in females	2	2	1.65	0.36–7.56	82.3	NA				
Religiosity	2	3	0.87	0.67–1.12	0	2	3	1.12	0.76–1.63	0
Somatic symptoms	2	3	1.48	0.82–2.68	29.7	1	2	1.38	0.63–3.03	0
Sexual intercourse	3	3	1.50	0.97–2.32	45.3	3	3	1.43	0.91–2.23	0
Community										
Access to means	Data uncomplete					**1**	**1**	**1.6**	**1.04–2.45**	**NA**
Any social support	5	12	1	0.88–1.13	57.7	5	12	0.97	0.91–1.02	0
Family support	4	5	1.12	0.89–1.41	70.5	4	5	0.95	0.90–1.01	0
Peer support	3	3	1.1	0.88–1.38	21.3	3	3	1.17	0.80–1.70	45.3
Social support	3	4	0.76	0.56–1.04	38.0	3	4	1	0.72–1.39	15.3
Suicidal behavior of a friend	2	2	0.85	0.14–5.01	70.1	**2**	**2**	**1.65**	**1.07–2.56**	**0**
Suicide death										
Individual negative life events and family adversity										
Any negative life event[a]	**2**	**3**	**1.99**	**1.08–3.68**	**32.1**	**2**	**3**	**2.56**	**1.65–3.97**	**0**
Childhood maltreatment	**1**	**2**	**11.2**	**1.71–73.21**	**0**	**1**	**2**	**33.77**	**6.43–117.42**	**0**
Dysfunctional family	Data uncomplete					2	2	2.05	0.74–5.72	87.2
Family history of mental disorders and abuse	Data uncomplete					2	2	0.70	0.04–11.80	79.6
Family previous suicidal behavior	**1**	**2**	**5.68**	**1.51–21.38**	**4.9**	**1**	**2**	**7.03**	**2.79–17.71**	**0**
Psychiatric and psychological										
Psychiatric										
Antisocial disorder	No data					**1**	**6**	**4.19**	**2.31–7.61**	**19.9**
Any mental disorder or abuse	**2**	**8**	**3.64**	**1.11–11.88**	**50.9**	**2**	**11**	**4.92**	**3.52–6.87**	**0**
Conduct disorder	1	3	1.58	0.42–5.97	0	**2**	**3**	**5.02**	**1.91–13.15**	**0**
Drug abuse	Data uncomplete					**2**	**2**	**5.26**	**2.27–12.19**	**0**
Community										
Access to means	1	5	2.81	0.60–13.12	99.4	**2**	**4**	**4.00**	**3.69–4.34**	**0**

95% CI 95% confidence intervals, *OR* odds ratio, *PTSD* posttraumatic stress disorder, *ADHD* attention deficit hyperactivity disorder, *NSSI* non-suicidal self-injuries, *NA* not applicable

[a]Death of a parent, parental divorce, losing boy/girlfriend, trauma exposure, major events

violence (OR 2.19, 95% CI 1.29–3.71) and having experienced interpersonal difficulties were associated with higher rates of suicide attempts in females (OR 1.13, 95% CI 1.03–1.24). Parental separation or divorce (OR 1.56, 95% CI 1.01–2.41) and previous suicidal behavior in the family (OR 2.84, 95% CI 1.87–4.33) were associated with suicide attempts only among males.

Psychiatric and psychological The risk factors for suicide attempts, common to both genders, included previous suicidal ideation (females: OR 4.39, 95% CI 2.31–8.34; males: OR 3.97, 95% CI 1.40–11.24), previous suicide attempts (females: OR 6.96, 95% CI 3.75–12.91; males: OR 31.33, 95% CI 9.36–104.88), and a history of any mental disorder (females: OR 3.37, 95% CI 2.52–4.51; males: OR 4.27, 95% CI 3.28–5.47), specifically anxiety disorder (females: OR 2.03, 95% CI 1.77–2.33; males: OR 3.79, 95% CI 2.05–7.01), major depressive disorder (MDD) (females: OR 4.49, 95% CI 2.18–9.23; males: OR 6.07, 95% CI 1.74–21.20), and personality disorders (females: OR 7.89, 95% CI 3.81–16.35; males: OR 5.13, 95% CI 2.63–10.01). Other risk factors were alcohol abuse (females: OR 2.69, 95% CI 1.32–5.50; males: OR 2.14, 95% CI 1.09–4.20) and drug abuse (females: OR 4.44, 95% CI 2.51–7.83; males: OR 3.11, 95% CI 2.01–4.84).

Factors that increased the risk of suicide attempts only among females were bipolar disorder (OR 1.43, 95% CI 1.20–1.70), eating disorders (OR 5.27, 95% CI 2.04–13.60), posttraumatic stress disorder (PTSD) (OR 2.96, 95% CI 1.32–6.62), and depressive symptoms (OR 1.15, 95% CI 1.04–1.28). Factors significantly associated with suicide attempts among males were disruptiveness (OR 8.78, 95% CI 2.77–27.84) and hopelessness (OR 1.74, 95% CI 1.04–2.94).

Personal Among females, a previous abortion significantly increased the risk of suicide attempts (OR 1.3, 95% CI 1.09–1.55).

Community Male adolescents and young adults with access to means (e.g., firearms, pesticides, toxic gas) had a significant OR for suicide attempts compared with those who did not (OR 1.6, 95% CI 1.04–2.45). Exposure to the suicidal behavior of a friend (OR 1.65, 1.07–2.56) was significantly associated only in males.

Suicide death

Individual negative life events and family adversity For both genders, any negative life event (e.g., death of a parent, losing boy/girlfriend) was a common risk factor for suicide death (females: OR 1.99, 95% CI 1.08–3.68; males: OR 2.56, 95% CI 1.65–3.97). Other factors were childhood maltreatment (females: OR 11.20, 95% CI 1.71–73.21; males: OR 33.77, 95% CI 6.43–177.22) and previous suicidal behavior in the family (females: OR 5.68, 95% CI 1.51–21.38; males: OR 7.03, 95% CI 2.79–17.71).

Psychiatric and psychological Among both genders, the risk of suicide death was increased by a history of any mental disorder or abuse (females: OR 3.64, 95% CI 1.11–11.18; males: OR 4.92, 95% CI 3.52–6.87). Among males, significant associations were found with conduct disorder (OR 5.02, 95% CI 1.91–13.15), antisocial disorder (OR 4.19, 95% CI 2.31–7.61), and drug abuse (OR 5.26, 95% CI 5.26; 2.27–12.19).

Community Among males, the risk of suicide was increased by access to means (OR 4.00, 95% CI 3.69–4.34). Among females, the risk was also increased, but not significantly so.

For both genders, nonsignificant associations were observed between the following risk and protective factors for suicide attempts: any negative life event, conflicts with the partner, attention deficit hyperactivity disorder, alcohol and drug use, conduct disorder, gambling disorder, nonsuicidal self-injuries, low self-esteem, any kind of support, and all the personal factors assessed except abortion. For suicide death, nonsignificant associations were found with having a dysfunctional family and a family history of mental disorders.

Discussion

We estimated the pooled risk of suicidal behaviors among adolescents and young adults and found that females had an almost twofold higher risk of suicide attempts than males, while males had an almost threefold higher risk of dying by suicide than females. Our meta-analysis has identified risk factors for both suicide attempts and death, which are common to male and female adolescents and young adults: exposure to any form of interpersonal violence and a history of mental or substance abuse disorder. Risk factors for suicide attempts included a history of previous suicidal thoughts and behaviors and a family history of mental disorders and abuse. For suicide death, a common risk factor was a family history of suicidal behavior. We also identified risk factors for suicide attempts in adolescents and young adults that were more specific for females or males, and for suicide death, which were specific for males only (Table 3). Finally, no significant associations were found between the protective factors assessed and suicide attempts and death.

Table 3 Significant meta-analyses results of gender risk factors of suicidal behavior among adolescents and young adults—results of the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)

Factor(s)	Severity[a]			
	Suicide death		Suicide attempt	
	Female	Male	Female	Male
Individual negative life events and family adversity				
Childhood maltreatment	**+++**	**+++**	++	++
Family previous suicidal behavior	**+++**	**+++**		++
Any negative life event[b]	+	++		
Bullying			**+++**	**++**
Family history of mental disorders and abuse			++	++
Community violence			+	+
Parental separation or divorce				+
Psychiatric and psychological				
Any mental disorder or abuse	++	++		
Drug abuse		**+++**		
Conduct disorder		**++**		
Antisocial disorder		++		
Major depressive disorder			++	+++
Personality disorder			+++	+++
Previous suicide attempts			+++	+++
Anxiety disorder			++	++
Alcohol abuse			++	++
Drug abuse			++	++
Previous suicidal ideation			++	++
Eating disorder			+++	
PTSD			++	
Dating violence			++	
Bipolar disorder			+	
Interpersonal difficulties			+	
Depressive symptoms			+	
Disruptiveness				**+++**
Hopelessness				+
Personal				
Abortion			+	
Community				
Suicidal behavior of a friend				+
Access to means		++		+

PTSD posttraumatic stress disorder

[a]Severity according to odds ratio values + > 1 to < 2, ++ ≥ 2 to < 5, +++ ≥ 5. [b]Death of a parent, parental divorce, losing boy/girlfriend, trauma exposure, major events

Gender as a risk factor for suicidal behaviors

Girls aged between 12 and 24 years have a higher lifetime prevalence (Evans et al. 2005; Kokkevi et al. 2012; Nock et al. 2013) and 12-month incidence (Evans et al. 2005; Afifi et al. 2007) of suicide attempts. The incidence and lethality of suicide attempts might be reduced among female youths by identifying high risk cases. Young women may be more likely to engage in help-seeking behaviors, to have a general readiness to talk about emotional problems (Beautrais 2002) and to frequently identify friends and professionals as sources of help (Rickwood

et al. 2005). Moreover, considering that there is a high prevalence of mental disorders among youth who die by suicide (Renaud et al. 2008), help-seeking behaviors and contact with the health care system may diminish the risk of suicide among girls (Rhodes 2013).

In line with previous studies (Canetto and Sakinofsky 1998; Beautrais 2002), our results show that male youths have a considerably higher risk than females of dying by suicide. Higher mortality among males might be explained by the use of more lethal means, such as firearms and hanging methods (Beautrais 2003; Rhodes et al. 2014b), while drug poisoning is more frequent in females (Beautrais 2003; Mergl et al. 2015). Young males may be less predisposed to help-seeking behaviors in an attempt to exhibit masculine behaviors (Rhodes et al. 2014a). This association may be moderated by intentionality, impulsiveness, and aggressiveness (Beautrais 2003). Furthermore, a male tendency to adopt avoidance strategies (Gould et al. 2004) might make it more difficult for them to cope with emotional and behavioral problems.

An additional explanation for gender differences in suicide deaths may be misclassification. Suicide deaths tend to be reported as accidental or underdetermined due to shame, stigma, or lack of evidence (Beautrais et al. 1996). However, in a Canadian study that reclassified accidental or underdetermined deaths and suspected suicides, the gender gap of suicide rates remained for youths aged 16–25 years (Gould et al. 2004).

Common and gender-specific risk factors for suicidal behaviors

Common risk factors

For suicide attempts, risk factors common to both genders include bullying, childhood maltreatment, community violence, previous suicidal thoughts and behaviors, any previous mental disorder or alcohol or drug abuse, and a family history of mental disorders and substance abuse. For suicide death, common risk factors include childhood maltreatment, any negative life events, and a family history of suicidal behavior.

Early exposure to traumatic life events, such as childhood maltreatment and bullying, implies complex processes that may increase vulnerability for suicidal behaviors, in both genders (Wilcox et al. 2009), including psychopathology (e.g., PTSD) (Wilcox et al. 2010) or maladaptive personality features (ÓBrien and Sher 2013). Specifically, exposure to any childhood physical and/or psychological abuse is associated with a lack of social support and risky health behaviors, which consequently are related to poorer mental health and well-being (Sheikh et al. 2016). However, it seems that childhood traumatic experiences favor the development of internalizing symptoms in adulthood due to dissatisfaction with social connections more than a real lack of external support (Sheikh 2018). Furthermore, our findings agree with the results of an extended study conducted in eight eastern European countries, showing that individuals with traumatic childhood experiences were at a significantly increased risk of health-harming behaviors including suicide attempts (Bellis et al. 2014). We found an association between PTSD and suicide attempts among females, and the single study with males showed a threefold risk, which was statistically nonsignificant, probably due to the scarcity of data. No data were found to estimate the association between PTSD and suicide death.

A history of previous suicidal thoughts and behaviors is one of the most frequent common risk factors for later suicide attempts (Borges et al. 2008; O'Connor et al. 2015) and death (Suokas et al. 2001; Wenzel et al. 2011), as well as the presence of any mental disorder (Cavanagh et al. 2003; Zubrick et al. 2016), and alcohol and drug abuse (Evans et al. 2004) for both genders. Suicidal ideation has been related to MDD; when this relationship was analyzed, the risk of suicide attempts was higher among female adolescents and young adults (Wittchen 1994), especially among younger girls (Bolger et al. 1989). This association may also be moderated by depressive symptoms. In males, a predisposition to suicidal behavior may be moderated by hopelessness traits, disruptiveness and conduct problems, and antisocial disorders (highly related to aggressiveness).

Finally, strong associations were found between suicidal behavior in youths and exposure to a history of mental disorders or substance abuse or previous suicidal behaviors in family members. Vulnerability in youths with a family history of mental disorders or suicidal behavior may be reflected in their tendencies to experience increased rates of mental or substance abuse disorders and suicidal behaviors (Mann et al. 1999).

Female-specific risk factors

Female adolescent and young adult victims of dating violence are at a higher risk of attempting suicide. This risk might be moderated by a higher predisposition to have internalizing symptoms and a higher exposure to psychological abuse (Temple et al. 2016). Dating violence might also be a mediator in the association between abortion and suicidal thoughts in youths, the magnitude of this association being related to the severity of the aggression (Ely et al. 2009), but there is no evidence of any mechanism. Nevertheless, there are no similar data in relation to suicidal behaviors.

Previous studies, including a systematic review, are in agreement with our meta-analysis results showing previous

abortion as risk factor for suicide attempts. This association may be moderated by mental disorders or substance use (Mota et al. 2010; Coleman 2011). Mental disorders could be related to poor social support or psychological factors that lead to unintended pregnancy; due to a feeling of inability to cope with pregnancy, women decide to have an abortion (Mota et al. 2010). Another possibility is that some vulnerability factors (e.g., poor social support) related to abortion and mental disorders mediate the association (Fergusson et al. 2006). Finally, interpersonal difficulties are associated with suicide attempts among female youths. This may be explained by their greater predisposition to emotional problems, increasing the risk (Kaess et al. 2011). It is clear that all the factors discussed are both interrelated and related to the occurrence of suicidal behaviors. Further research is needed to clarify the pathways and mechanisms.

Male-specific risk factors

According to our results, access to means was a relevant risk factor among male adolescents and young adults, for both suicide attempts and death. Male-specific risk factors for suicide attempts included parental separation or divorce. Our findings are consistent with evidence that living in single-parent families may increase the risk of suicide attempts in male youths. However, other reports suggest that females are also at risk (Chau et al. 2014; Dieserud et al. 2015) or that the risks are similar in both genders (Fergusson and Lynskey 1995; Kim and Kim 2008). In addition, disruptiveness, hopelessness, and previous suicidal behavior among family or friends increased the risk of suicide attempts among males. For suicide death, externalizing disorders and drug abuse conferred a significant risk.

Previous research has shown that male adolescents tend to have slightly more symptoms of externalizing problems, such as aggressive, delinquent (Kaess et al. 2011), and antisocial behavior (Marmorstein and Iacono 2005), which may act as mediators for suicidal behaviors. Further research is needed on this topic. In addition, similar to our data, some studies have found higher rates of suicide attempts among individuals exposed to suicidal behavior in the family and peers (Randall et al. 2015), showing the influence of the environment in youths.

Protective factors

No evidence on protective factors for suicidal behaviors was found in either males or females, probably due to the scarcity of published data. A previous study has shown that the risk of suicidal behavior in adolescents of both genders is reduced by family support (Tseng and Yang 2015) and is possibly increased by weak relationships with peers. In general, females have a higher perception of peer support than males (Kerr et al. 2006). Our meta-analyses results did not find a protective association between peer support and suicidal behaviors in both genders. However, the primary data used for the analyses reported peer support but not perception of it. In addition, peer support might not always be positive, since close relationships with peers involved in suicidal behaviors or at high risk of it do not act as a protective factor (Prinstein et al. 2010). Further investigation is needed for the assessment of protective factors and suicidal behaviors in young people.

Limitations

This review has some limitations. We used the most widely recommended databases for psychiatric research, including Web of Science and PsycINFO (Löhönen et al. 2010), but were not able to search all available databases. Similar to previous systematic reviews (Devries et al. 2013; Maxwell et al. 2015), articles included came from a broad search strategy. Important information about vulnerable populations (e.g., incarcerated, veteran or active duty populations) was not considered because the inclusion criteria excluded institutionalized populations. No assessment was made of the suicide risk related to sexual orientation and gender identity. However, data analyzing these issues were already published (Miranda-Mendizábal et al. 2017).

The NOS was used to assess the quality of the included studies, but there is limited evidence on its validity (Wells et al. 2013). Nevertheless, its use is recommended by the Cochrane Collaboration. Random effect models were used for meta-analyses. They provide a very conservative estimate of the combined data with wider confidence intervals, as may be seen in some of our results. In addition, they may also lead to statistical values that are less likely to be significant (Borenstein et al. 2009).

For the association of gender and suicide death, only one cohort study was found, including individuals discharged from emergency departments; however, reference individuals were randomly selected from the general population, fulfilling our inclusion criteria. The wide heterogeneity observed in the meta-analyses of risk and protective factors may be explained by (1) the inclusion of observational studies that may have design flaws or tend to distort the magnitude or direction of associations (Stroup et al. 2000); (2) the differences in the adjustment; and (3) the possible reporting bias of the included studies. In addition, there were not enough studies to conduct meta-analyses for some risk, and especially, protective factors, particularly for suicide death.

Implications for prevention

From a public health perspective, there is a need for the development and implementation of effective health policies and preventive strategies for suicidal behavior in adolescents and young adults, as well as for the early identification and reduction in the most prevalent risk factors. For example, reducing the different forms of interpersonal violence could help to diminish the prevalence of mental disorders and risky health and sexual behaviors (Wasserman et al. 2010). In addition, encouraging healthy behaviors (e.g., physical activity) may protect against some risk factors for suicide (Sheikh 2018). However, there is evidence that targeting individuals to change their behaviors will fail as long as the primary risk factors (e.g., childhood maltreatment) remain, because they would allow the appearance of new mediators (Sheikh et al. 2016).

Individual perception of social isolation may lead to impaired mental health and well-being. Strategies applying a more comprehensive approach (including community, school and family environment) (Fountoulakis et al. 2011) and increasing knowledge, to facilitate help-seeking behaviors, could be more effective (Riner and Saywell 2002). In addition, rather than implementing gender-specific prevention strategies, it is important for strategies to target and better address the most prevalent risk and protective factors to prevent suicidal behaviors.

Implications for research

Although gender differences in youth suicidal behavior have been identified, further research is needed. We encourage longitudinal research assessing the role of sociodemographic variables (e.g., socioeconomic status, ethnicity) in suicidal behavior among young persons. Additional research is also needed on academic (e.g., academic failure) and protective factors (e.g., resilience) in young females and males, as well as research on access to means, externalizing problems, and a family history of mental disorders and abuse among young females, and relationship problems, bipolar and eating disorders in young males. To reduce suicide mortality, information is needed on related pathways in both genders. Importantly, the development and implementation of preventive strategies should include gender preferences and context. To do so, youth preferences with respect to public health interventions should be assessed. Finally, as gender is one of the most important social determinants of health inequalities (Solar and Irwin 2010), efforts should be made to reduce the gender gap in health issues, particularly during adolescence and young adulthood, which are periods of special vulnerability.

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Compliance with ethical standards

Conflict of interest None.

Ethical Statement This study is a systematic review; ethics committee approval is not required.

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Affiliations

Andrea Miranda-Mendizabal[1,2] · Pere Castellví[1,3] · Oleguer Parés-Badell[1] · Itxaso Alayo[1,4] · José Almenara[5] · Iciar Alonso[6] · Maria Jesús Blasco[1,2,4] · Annabel Cebrià[7] · Andrea Gabilondo[8,9] · Margalida Gili[10,11] · Carolina Lagares[12] · José Antonio Piqueras[13] · Tiscar Rodríguez-Jiménez[13] · Jesús Rodríguez-Marín[13] · Miquel Roca[10,11] · Victoria Soto-Sanz[13] · Gemma Vilagut[1,4] · Jordi Alonso[1,2,4]

[1] Health Services Research Group, IMIM-Institut Hospital del Mar dInvestigacions Mèdiques, PRBB Building. Doctor Aiguader 88, 08003 Barcelona, Spain

[2] Department of Health and Experimental Sciences, Pompeu Fabra University (UPF), Barcelona, Spain

[3] Department of Psychology, Jaen University, Jaén, Spain

[4] CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain

[5] Preventive Medicine Area and Public Health, University of Cádiz, Cádiz, Spain

[6] Morales Meseguer Hospital, Murcia, Spain

[7] Department of Mental Health, Corporació Sanitaria Parc Taulí, Sabadell, Spain

[8] Outpatient Mental Health Care Network, Osakidetza-Basque Health Service, San Sebastian, Spain

[9] Mental Health and Psychiatric Care Research Unit, BioDonosti Health Research Institute, San Sebastian, Spain

[10] Institut Universitari d'Investigació en Ciències de la Salut (IUNICS-IDISPA), University of Balearic Islands, Palma de Mallorca, Spain

[11] Network of Preventive Activities and Health Promotion, University of Balearic Islands, Palma de Mallorca, Spain

[12] Department of Statistics and Operative Research, University of Cádiz, Cádiz, Spain

[13] Department of Health Psychology, Miguel Hernandez University of Elche, Elche, Spain

Article 2. *"Gender commonalities and differences in risk and protective factors of suicidal thoughts and behaviors: a cross-sectional study of Spanish university students"*

Miranda-Mendizabal A, Castellví P, Alayo I, Vilagut G, Blasco MJ, Torrent A, et al. Gender commonalities and differences in risk and protective factors of suicidal thoughts and behaviors: a cross-sectional study of Spanish university students. Depress. Anxiety. 2019. *Article accepted for publication.*

GENDER COMMONALITIES AND DIFFERENCES IN RISK AND PROTECTIVE FACTORS OF SUICIDAL THOUGHTS AND BEHAVIORS: A CROSS-SECTIONAL STUDY OF SPANISH UNIVERSITY STUDENTS

Gender and suicidal ideation in Spanish university students

Andrea Miranda-Mendizabal[1,2], Pere Castellví[3], Itxaso Alayo[1,4], Gemma Vilagut[1,4], Maria Jesús Blasco[1,4], Aina Torrent[5], Laura Ballester[1,4,6], José Almenara[7], Carolina Lagares[7], Miquel Roca[8], Albert Sesé[8], José Antonio Piqueras[9], Victoria Soto-Sanz[9], Jesús Rodríguez-Marín[9], Enrique Echeburúa[10], Andrea Gabilondo[11], Ana Isabel Cebrià[12], Ronny Bruffaerts[13], Randy P. Auerbach[14,15], Philippe Mortier[1], Ronald C. Kessler[16], Jordi Alonso[1,2,4] on behalf of the UNIVERSAL study group.

1 Health Services Research Group, IMIM-Institut Hospital del Mar d´Investigacions Mèdiques, Barcelona, Spain

2 Department of Health & Experimental Sciences, Pompeu Fabra University (UPF), Barcelona, Spain

3 Department of Psychology, University of Jaén, Jaén, Spain.

4 CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain.

5 Health and Life Sciences Faculty, Pompeu Fabra University (UPF), Barcelona, Spain

6 Girona University (UdG), Girona, Spain

7 University of Cadiz (UCA), Cádiz, Spain.

8 Institut Universitari d'Investigació en Ciències de la Salut (IUNICS-IDISPA), University of Balearic Islands (UIB), Palma de Mallorca, Spain.

9 Miguel Hernandez University of Elche (UMH), Alicante, Spain.

10 University of the Basque Country (UPV-EHU), Bilbao, Spain.

11 Outpatient Mental Health Care Network, Osakidetza-Basque Health Service. Biodonosti Health Research Institute, San Sebastian, Spain.

12 Department of Mental Health, Corporació Sanitaria Parc Taulí, Sabadell, Spain.

13 Universitair Psychiatrisch Centrum, KU Leuven (UPC-KUL), Leuven, Belgium.

14 Department of Psychiatry, Harvard Medical School, Boston, MA, USA.

15 Center for Depression, Anxiety and Stress Research, McLean Hospital, Belmont, MA, USA.

16 Department of Health Care Policy, Harvard Medical School, Boston, MA, USA.

Corresponding author: Dr. Jordi Alonso. IMIM-Institut Hospital del Mar d´Investigacions Mèdiques, PRBB Building. Doctor Aiguader 88. 08003 Barcelona, Spain.

Phone number: 0034 93 316 07 60; Fax: 00 34 93 316 07 97.

E-mail: jalonso@imim.es.

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ABSTRACT

Aim

To assess gender-differences in the association between risk/protective factors and suicidal thoughts and behaviors (STB); and whether there is any gender-interaction with those factors and STB; among Spanish university students.

Methods

Data from baseline online survey of UNIVERSAL project, a multicenter, observational study of first-year Spanish university students (18-24 years). We assessed STB; lifetime and 12-month negative life-events and family adversities; mental disorders; personal and community factors. Gender-specific regression models and gender-interactions were also analyzed.

Results

We included 2,105 students, 55.4% women. Twelve-month prevalence of suicidal ideation (SI) was 10%, plans 5.7%, attempts 0.6%. Statistically significant gender-interactions were found for lifetime anxiety disorder, hopelessness, violence between parents, chronic health conditions and family support. Lifetime mood disorder was a common risk factor of SI for both genders (Females: OR=5.5; 95%CI 3.3-9.3; Males: OR=4.4; 95%CI 2.0-9.7). For females, exposure to violence between parents (OR=3.5; 95%CI 1.7-7.2), anxiety disorder (OR=2.7; 95%CI 1.6-4.6), and alcohol/substance disorder (OR=2.1; 95%CI 1.1-4.3); and for males, physical childhood maltreatment (OR=3.6; 95%CI 1.4-9.2), deceased parents (OR=4.6; 95%CI 1.2-17.7), and hopelessness (OR=7.7; 95%CI 2.8-21.2), increased SI risk. Family support (OR=0.5; 95%CI 0.2-0.9) and peers/others support (OR=0.4; 95%CI 0.2-0.8) were associated to a lower SI risk only among females.

Conclusions

Only mood disorder was a common risk factor of SI for both genders, while important gender-differences were observed regarding the other factors assessed. Protective effect from family and peers/others support was observed only among females. Further research assessing underlying mechanisms and pathways of gender-differences is needed.

Keywords: gender, suicide/self-harm, mood disorders, anxiety/anxiety disorders, depression.

INTRODUCTION

Suicide is the second leading cause of death among 15- to 29-year-olds (World Health Organization, 2016). In Spain in 2015, suicide was the first cause of death among 15- to 19-year-old women and the second among 20- to 24-year-old men (Instituto Nacional de Estadísticas, 2015). More current data shows that suicide rates among 15- to 29-year-olds represent a 7.77% of the total suicide deaths in the country (Navarro-Gómez, 2017).

Prevalence estimates of suicidal thoughts and behaviors (STB) among university students are consistently high. Before ending university, over one-tenth of the students would seriously consider suicide and one-sixth would attempt suicide (Ashrafioun, Bonar, & Conner, 2016). Results from 19 universities from eight countries showed 17.2%, 8.8%, and 1.0% 12-month prevalence of suicidal ideation (SI), plans and attempts, respectively (Mortier et al., 2018). From those, Northern Ireland results raise attention: almost the double individuals (31% total; 24.3% males, 36.9% females) reported 12-month SI, with almost 1 in 5 students having made a suicide plan (O'Neill et al., 2018).

Mental disorders are highly prevalent among university students (Auerbach et al., 2016; Eskin et al., 2016; Pedrelli, Nyer, Yeung, Zulauf, & Wilens, 2015). Mood, anxiety, disruptive, alcohol/substance abuse disorders increase STB more frequently (Cash & Bridge, 2009; Mortier et al., 2018). Mental disorders also increase distress (Eskin et al., 2016) and substantial impairment in academic performance (Auerbach et al., 2016). Childhood and adolescent adversities, bullying, stressful life experiences and personal traits could also be related (Holt et al., 2015; Johnson et al., 2002; L. Wang et al., 2014; Werbart Törnblom, Werbart, & Rydelius, 2015). On the contrary, positive relationships with peers and family might be STB protective factors (Cash & Bridge, 2009; Thompson, Eggert, & Herting, 2000).

A "gender paradox" exists regarding suicidal behavior. Males have higher rates of completed suicide and lower rates of suicide attempt, compared to females. Likewise, males are three- to four-fold more likely to die by suicide than females (Eaton, Kann, & Jinchen, 2012; Werbart Törnblom et al., 2015). The association between suicide and masculinity may play a role in creating a genuine gender gap in suicide rates (Canetto & Sakinofsky, 1998). Males are more likely to resort to more lethal means in order to reduce the likelihood of surviving (Mergl et al., 2015; Värnik et al., 2008). Gender-differences between

internalizing (e.g. mood disorders) and externalizing (e.g. conduct disorders) disorders may also be related (Boyd et al., 2015). The few empirical data available about gender paradox in Spain suggest similar gender trends for STB (Navarro-Gómez, 2017).

Most of the evidence about STB risk and protective factors come from Anglo-Saxon countries; Spanish cross-national data is limited. Moreover, available evidence of gender-differences in STB risk and protective factors is not specific for university students (Miranda-Mendizabal et al., 2019). This study aims to determine the association between risk and protective factors and STB stratified by gender, and to assess whether there is any interaction between those factors and gender with STB among Spanish university students. Results from the present study will advance the understanding of the epidemiological gender-differences of STB among university students.

METHODS

Study design and setting

Data came from baseline survey (October 2014 to October 2015) of the UNIVERSAL (University and Mental Health) project, an ongoing, multicenter and observational study of first-year Spanish university students. This project is part of the World Mental Health International College Student Initiative (WMH-ICS) (http://www.hcp.med.harvard.edu/wmh/college_student_survey.php). More project details can be found elsewhere (Blasco et al., 2016).

Sample was recruited from five Spanish public universities: Cadiz University (UCA), Balearic Islands University (UIB), Basque Country University (UPV-EHU), Pompeu Fabra University (UPF) and Miguel Hernández University (UMH), representing about 8% of the undergraduate enrolment capacity annually offered in the country. Inclusion criteria were: a) students aged 18 to 24 (subjects under 18 at the start of the academic year were eligible when they turned 18); and b) being enrolled in the first university year for the first time. Students not accepting the study's informed consent were excluded. Based on eligibility criteria, 16,332 students were suitable to participate **(Figure 1)**. Participants underwent an online survey via a secure web-based platform designed for the study.

Sample recruitment was performed in two stages. First, all first-year undergraduates were invited to participate in baseline survey (e.g., census sampling). Invitation methods across the universities included: campus advertising campaigns (e.g., information stands, university website) and up to four personal e-mail invitation letters from the university authorities. Second, a random subsample of non-respondents to the first stage was contacted by e-mail including an economic incentive of 25 € to complete the survey ("endgame strategy"). In UPV-EHU, only stage one was carried out. Protocol of the study was approved by Parc de Salut MAR-Clinical Research Ethics Committee *(Reference number 2013/525/I).*

Variables

Suicidal thoughts and behaviors (STB)

STB were assessed through ideation (*"Have you ever had thoughts of killing yourself?"*); possibly accompanied by plans (*"Did you ever think about how you might kill yourself or work out a plan of how to kill yourself?")* or attempts (*"Did you ever have a suicide attempt (i.e., purposefully hurt yourself with at least some intent to die)?"*); from modified versions of the Self-Injurious Thoughts and Behaviors Interview (SITBI) (Nock, Holmberg, Photos, & Michel, 2007) and Columbia-Suicide Severity Rating Scale (C-SSRS) (Posner, Oquendo, Gould, Stanley, & Davies, 2007).

Negative life events and family adversity

Childhood maltreatment items, prior to the age of 17, included emotional maltreatment (*e.g. "Someone in your family repeatedly said hurtful or insulting things to you"),* physical abuse (*e.g. "Someone in your family hit you so hard that it left bruises or marks")*, sexual abuse (*"Someone in your family touched you or made you touch them in a sexual way against your will")*, and neglect (*e.g. "You were seriously neglected at home").* Four items assessed physical, verbal and cyberbullying victimization: *"How often were you bullied at school: physically/verbally by someone who purposefully ignored you, excluded you, or spread rumors about you behind your back?"* and *"How often were you bullied over internet or by text messaging?"* Dating violence was evaluated with *"How often were you in a romantic relationship where your partner repeatedly hit you/said hurtful or insulting things to you?"* Family adversity included deceased parents, parental separation or divorce, psychopathology or criminal activities, any parent attempted or died by suicide, and violence between parents. Items were adapted from the CIDI 3.0

(Kessler & Ustün, 2004), the Adverse Childhood Experiences Scale (CES) (Felitti et al., 1998) and the Bully Survey (BS) (Swearer & Cary, 2003).

Stressful events experienced in the past 12 months

These included death of a friend/family member, life-threatening illness or injury of a friend/family member, stressors related to a romantic partner (breakup or cheating), betrayal, arguments or breakup with friends/family member, interpersonal conflicts (fights with romantic partner/family member/someone else you know/stranger), life-threatening accidents, serious physical assault, sexual assault or rape, trouble with police or serious legal problems and others stressful experiences. Items were adapted from the Life Events Questionnaire (Brugha & Cragg, 1990), the Deployment Risk and Resilience Inventory Survey (Vogt, Proctor, King, King, & Vasterling, 2008) and the Department of Defense Survey of Health-Related Behaviors among active duty military personnel (Bray et al., 2009).

Individual factors

Probable lifetime mood disorder (major depressive or bipolar disorder) and anxiety disorder (panic or generalized anxiety disorder) were evaluated using CIDI 3.0 (Kessler & Ustün, 2004) and Epi-Q Screening Survey (EPIQ-SS) (Kessler et al., 2010). Probable lifetime alcohol or substance disorder (abuse or dependence) was screened through a modified version of the Alcohol Use Disorders Identification Test, 10-item version (AUDIT-10) (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) and items from the CIDI 3.0 (Kessler & Ustün, 2004). Hopelessness was evaluated with selected items from Beck Hopelessness Scale (BHS) (Beck, Weissman, Lester, & Trexler, 1974). Students were asked whether they had epilepsy, seizure disorder or any chronic condition (e.g. asthma, diabetes, migraine). Physical impairment (e.g., vision, hearing, movement) was also assessed.

Community factors

Access to means was assessed with *"In the past 12 months, how many times did you carry a weapon such as a gun, knife, or club?"* Positive relationships, such as family support, peers/others support and school connectedness, were evaluated using 13 adapted items from CIDI 3.0 (Kessler & Ustün, 2004), the Psychological Sense of School Membership Scale (Goodenow, 1993), the Adverse Childhood Experience Scale (Felitti et al., 1998), and the Childhood Trauma Questionnaire (Bernstein, Ahluvalia, Pogge, &

Handelsman, 1997). Scales' scores were categorized into tertiles (high, middle or low) for the analysis after having checked that the linearity assumption of the logit in the continuous variables was not fulfilled. The least positive relationship category was the reference.

Socio-demographics and educational

These factors included gender, center, and academic field, country of birth, parents' studies and living location at first term (parents' home or others).

Analysis

Missing values were imputed with multiple imputation (MI) (n = 5 imputations) using a fully conditional specification method. Pooled estimates from multiple imputations and MI-based standard errors taking into account within imputation and between imputation variances were obtained (Van Buuren, 2012). Inverse-probability weighting was applied to hard-to-reach respondents that were randomly selected in the second sampling stage (endgame strategy weights). Post-stratification weighting was used to adjust for differences between respondents and population distribution of sex, country of birth, academic field and university. Descriptive analyses were performed. Twelve-month prevalence of ideation, plan and attempt, stratified by gender, was estimated.

Risk and protective factors were classified on a modification of the socio-ecological model from the WHO (World Health Organization, 2014). As the model states, categories are not mutually exclusive, and factors can contribute to STB directly and indirectly by interrelating between them. Understanding the categories moving from systemic to individual represents a more useful approach. While previous analyses of UNIVERSAL project used a distal/proximal-factor epidemiological model (Blasco et al., 2019), a gender approach of suicidal risk does not correspond to a linear model and WHO socio-ecological model may be more adequate and complementary.

Bivariate analyses were performed to examine the associations of selected candidate risk and protective factors and 12-month STB. Crude ORs and 95% Confidence Intervals (CI) were estimated and differences across subgroups (e.g., parent deceased yes vs. no) were evaluated using MI-based Wald statistic. Gender-differences in the associations between candidate predictors and 12-month STB were assessed using multiple logistic regression models including, one at a time, a gender-interaction term with

each factor. Based on those results, gender-stratified multiple logistic regression models of 12-month STB were built adjusting by center, academic field, parents' university studies and living at first term. Group Lasso regularization was applied for the selection of variables to be included in the final multivariable models. Analyses excluded variables that showed low numbers within cells. Statistical significance was evaluated with a two-sided F-test based on multiple imputations and level of significance of 0.05. SAS software version 9.4 was used. Although we aimed to evaluate STB, due to low prevalence of suicide plan and attempts, we were not able to calculate its risk estimates. Only estimates of SI are presented.

RESULTS

A total sample of 2,105 students were included, with more than half being female (55.4%, weighted restored proportion of 72.4%). Suicidal ideation (SI) and suicide plans showed a higher likelihood among females (Females: 10.5% SI; 6.4% plans. Males: 9.2% SI; 4.8% plans), while suicide attempts were more frequent among males (Females: 0.5%. Males: 0.9%).

Some negative life events, recent stressful experiences and family adversities, among females and males, were as follows: dating violence (Females 8.9%; Males 3.2%); parental psychopathology (33.5%; 28%) and stressors related to romantic partner (31.5%; 23.8%). Mood (28.8%; 18.1%) and anxiety (25.8%; 12.7%) disorders were almost twice more frequent among females. Males reported a higher alcohol or substance abuse disorder than females (Females 7.5%; Males 13.4%), as well as physical maltreatment (8.8%; 11.3%), physical bully victimization (4%; 9.5%) and seriously physically assault (2.6%; 8.1%). In contrast, females showed higher family support (39%; 30.5%) and peers/others support (30.1%; 25.9%) **(Table 1)**.

-- Insert Table 1 --

Table 2 shows bivariate associations of risk and protective factors with 12-month SI, stratified by gender. Common risk factors of SI for both genders included: mood disorders, childhood maltreatment and verbal bully victimization. Among stressful experiences in the last 12 months, common risk factors for both genders were betrayal, arguments or breakup with friends or family members (Females: OR 2.4; 95%CI 1.6-3.6; *p-value*<.01. Males: OR 3.5; 95%CI 2.1-5.6; *p-value*<.01), interpersonal conflicts (Females: OR

2.1; 95%CI 1.2-3.6; *p-value*<.01. Males: OR 1.8; 95%CI 1.1-2.9; *p-value*=.02) and parental psychopathology (Females: OR 2.2; 95%CI 1.5-3.2; *p-value*<.01. Males: OR 3.4; 95%CI 2.1-5.3; *p-value*<.01). For males only, SI was associated with parents' university studies (OR 2.4; 95% 1.3-4.3; *p-value*=.01), and hopelessness (OR 12.7; 95%CI 6.1-26.3; *p-value*<.01). Positive relationships (high family, peers support and high school connectedness) were significantly associated to a lower SI risk for both genders.

-- Insert Table 2 –

Table 3 shows gender-specific risk and protective factors associated with 12-month SI adjusting for socio-demographic variables. Mood disorder predicted 12-month SI for both genders (Females: OR 5.5; 95%CI 3.3-9.3; *p-value*<.01; Males: OR 4.4; 95%CI 2.0-9.7; *p-value*<.01), with no gender-interaction. Females exposed to violence between parents had higher odds of 12-month SI (OR 3.5; 95%CI 1.7-7.2; *p-value*<.01), whereas unexpected protective effect was seen for males (OR 0.3; 95%CI 0.1-0.9; *p-value*=.03) with significant gender-interaction (*p-value*<.01). Anxiety disorder (OR 2.7; 95%CI 1.6-4.6; *p-value*<.01) and alcohol or substance disorder (OR 2.1; 95%CI 1.1-4.3; *p-value*=.04) also increased SI risk among females, gender-interaction was observed for anxiety disorder (*p-value*<.01). Exposure to physical childhood maltreatment (OR 3.6; 95%CI 1.4-9.2; *p-value*<.01), death of any of the parents (OR 4.6 95%CI 1.2-17.7; *p-value*=.03), parental psychopathology (OR 2.4; 95%CI 1.1-5.1; *p-value*=.03) and hopelessness (Agree strongly/moderate OR 7.7; 95%CI 2.8-21.2; *p-value*<.01) were predictors of 12-month SI in males. Except for hopelessness (*p-value*=.02), these gender-interactions were not significant. Family support (High: OR 0.5; 95%CI 0.2-0.9; Middle: OR 0.4; 95%CI 0.2-0.7; *p-value*<.01) and peers/others support (Middle: OR 0.4; 95%CI 0.2-0.8; *p-value*=.01) were protective factors only for females. Chronic health conditions reduced SI risk among males (OR 0.3; 95%CI 0.1-0.8; *p-value*=.02) with significant gender-interaction (*p*-value=.04).

-- Insert Table 3 –

DISCUSSION

Main findings

The present study assessed gender-differences in suicidal ideation (SI) and in SI risk and protective factors among Spanish university students. Females presented SI and plans more often than males, while suicide attempts were more prevalent among males, which was consistent with previous reports (Cash & Bridge, 2009; Eaton et al., 2012). Mood disorders were the only common risk factor of SI for both genders. Others risk factors assessed for the whole sample were specific either for females or males only. Among females, anxiety disorder, alcohol or substance disorder and violence between parents were major risk factors, with significant gender-interaction for anxiety and violence between parents. Hopelessness, physical childhood maltreatment, deceased parents and parental psychopathology were male-specific risk factors, with significant gender-interaction for hopelessness. Family and peers/others support were SI protective factors for females, with gender-interaction for family support. Surprisingly, violence between parents and chronic health conditions decreased SI risk among males. A comparative cross-gender summary of the magnitude of the association between significant risk and protective factors is presented in **Table 4**.

-- Insert Table 4 –

Strengths and limitations

This is the first original study systematically assessing gender-differences and interaction in a wide range of SI risk and protective factors among Spanish university students. Moreover, being part of the World Mental Health International College Survey (WMH-ICS) facilitates future comparisons and analyses.

Several limitations of this study deserve attention. First, although a convenience sample of universities was included, potentially limiting generalizability of our study's findings, geographical dispersion over Spain was considered. In fact, population's characteristics of the participating universities are similar to that of the overall Spanish university students. Also, low response rate and high proportion of females on the final respondents could limit representativeness. However, population-based adjustments through post-stratification and inverse probability weighting were applied to restore it (Brick, 2013). Second, the low number of individuals in some of the target factors limited the possibility to compare their association

with SI for females and males when these variables were included in the models. Third, although our goal was to evaluate STB, low frequencies of suicide plans and attempts did not allow us to estimate multivariable logistic regression models for these outcomes. Therefore, only SI results are reported. However, for both genders, SI is one of the main predictors of suicidal behaviors; its assessment and prevention are of high concern. Moreover, we identified significant gender-interactions with some SI risk factors. Nevertheless, studies with larger samples, including higher number of males, are necessary to obtain a more reliable assessment of STB gender-differences. Fourth, results are based on self-reported data, without a clinical interview. It is unknown to what extent these two sources coincide but we addressed this limitation by undergoing a clinical re-appraisal study to control the validity of the research, which indicates a good concordance with these results (Ballester et al., 2019). Fifth, analyses according to sexual orientation were not performed and transsexual individuals were excluded. We are aware there are important suicidal risk differences among sexual minorities and we have reported some of them in a recent systematic review of the literature (Miranda-Mendizábal et al., 2017). To assess these issues, a specific paper based on the UNIVERSAL project survey will be performed. Finally, associations found cannot be considered as causal due to the cross-sectional nature of the data. Longitudinal studies are needed to determine causality.

Comparisons with other studies

Mood disorders are one of the most prevalent mental disorders among university students (Auerbach et al., 2016). Our results indicated that lifetime major depression and bipolar disorders are the only risk factors for SI common for both genders, accordingly with previous literature (Skogman, Alsén, & Öjehagen, 2004). Alcohol and substance disorder and anxiety disorder were strongly associated to SI only among females, with significant gender-interaction for the latter. Previous findings showed strong correlation between anxiety and SI among university students (O'Neill et al., 2018) and specifically among females (Goel et al., 2018). Probable gender-differences in the association between anxiety and SI might be implied based on interaction results. Our findings about the association between alcohol/substance disorder and SI among females are novel. Previous research has shown no increased risk of SI associated to alcohol/substance abuse among university students. However, those analyses were not specific for either male or female students. Anxiety is strongly associated with severe impairment (e.g. university-related problems) (Alonso et al., 2018). Meanwhile, the effects of alcohol/substance

use/abuse include failure in developmental tasks (e.g. healthy interaction with peers) and in daily obligations (e.g., attending school); and impair users' judgment (Mann, 2003; P.-W. Wang & Yen, 2017).

A gender-interaction was observed for hopelessness, and increased risk of SI was observed only for males. Previous research has consistently found that hopelessness increased SI risk (Lane & Miranda, 2018) or mediates the relationship of some other risk factors with SI (Abdollahi, Abu Talib, Siti Nor, & Zanariah, 2016; Lamis, Ballard, May, & Dvorak, 2016). However, there is lack of evidence about the association between hopelessness and STB according to gender among university students, showing the need of further studies.

Protective effect from family and peers/others support for SI among females was observed, being consistent with previous literature (Cash & Bridge, 2009; Macalli et al., 2018; Miller, Esposito-Smythers, & Leichtweis, 2015). Higher levels of support exert its protective effect by increasing self-efficacy or reducing stress (Arria et al., 2009; Thompson et al., 2000). Unexpected results observed in the association between violence between parents and chronic health conditions or physical impairment with SI are probably due to low numbers in these and some other variables included in the model. Further analyses that include wider samples and higher number of males are needed to draw robust conclusions.

Implications for prevention and future research

Our findings contribute substantially to the existing literature on gender-differences in SI risk and protective factors. A profound knowledge of SI gender-risk factors might help increasing awareness about students who could be at serious risk. Results showed gender-interactions with some mental disorders and psychological factors; which have a profound impact on students' physical, emotional, cognitive and interpersonal functioning, affecting their academic performance, retention and graduation rates (Kitzrow, 2009).

Students' mental health should be a priority for universities. A prompt detection of high-risk suicidal cases may reduce suicide mortality (Paschall & Bersamin, 2018). Gatekeeper prevention interventions are an example of intervention at university campuses to improve knowledge, skills and self-efficacy regarding suicide intervention to identify and potentially help suicidal students. There is little evidence about interventions on treatment referrals for students with STB, and studies do not address the

effectiveness of the treatment in STB (Wolitzky-Taylor, LeBeau, Perez, Gong-Guy, & Fong, 2019). A combination of individual strategies building personal skills and setting-based approach to improve the overall university setting has also been recommended (Fernandez et al., 2016). Ensuring self-regulation and coping strategies prior to the onset of university stressful life events might be helpful (O'Neill et al., 2018). Although suicide prevention in universities has increased, there is still room for improvement. Research addressing effectiveness of interventions to reduce the frequency and intensity of STB, or to change help-seeking behavior and linkage to treatment, as well as secondary and tertiary STB prevention, is needed.

Gender-differences when engaging into preventive strategies also should be taken into account. Females are more willing to communicate and to use prevention centers (Klimes-Dougan, Yuan, Lee, & Houri, 2009). Accordingly, the benefit from school-based programs (Kalafat & Gagliano, 1996) and screening at primary care settings (Rutz, von Knorring, & Wålinder, 1992) is evident. Males are not prone to be actively involved in suicide awareness programs (Shaffer, Vieland, & Garland, 1990). School-wide screening (Garlow., 2008) and public campaigns (Daigle et al., 2006) may facilitate STB identification among them.

Further research is needed in several areas. In this study, no attempt has been made to interpret the causal associations between the evaluated factors. Future longitudinal research to clarify the mechanisms underlying gender-differences, mediator variables and possible pathways of STB development is required. Tests for analyzing significant interactions/effects or techniques for more accurate baseline screening algorithms are also needed. Finally, improving quantity and quality of research about preventive strategies of STB in university settings is desirable.

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Table 1. Socio-demographic, individual, community risk, and protective factors of the students included in the analysis (absolute numbers and weighted proportions). The UNIVERSAL (University and Mental Health) project

		TOTAL n=2,105		FEMALE n=1,525		MALE n=580	
		n	%	n	%	n	%
SOCIO-DEMOGRAPHICS AND EDUCATIONAL							
Centre	Balearic Islands University (UIB)	300	12.4	238	13.1	62	11.5
	Basque Country University (UPV-EHU)	636	43.8	449	42.1	187	45.8
	Cadiz University (UCA)	297	19.7	208	20.1	89	19.2
	Miguel Hernández University (UMH)	291	10.5	185	9.5	106	11.7
	Pompeu Fabra University (UPF)	581	13.6	445	15.1	136	11.7
Academic Field	Arts and Humanities	240	9.8	211	12	29	7
	Engineering and Architecture	290	18.6	121	8	169	31.7
	Health Sciences	541	15.6	425	20	116	10.1
	Science	202	8.4	127	8	75	8.9
	Social and Legal Sciences	832	47.6	641	51.9	191	42.3
Country of birth	Spain	1951	94.8	1411	95.1	540	94.4
	Other	154	5.2	114	4.9	40	5.6
Parent´s studies	At least one	950	42.8	676	41.4	275	44.5
	Neither	1155	57.2	849	58.6	305	55.5
Living at first term	Parents home	1185	56.2	842	52.5	343	60.6
	Other	920	43.8	683	47.5	237	39.4
NEGATIVE LIFE EVENTS AND FAMILY ADVERSITY							
Childhood maltreatment	Emotional	470	20.8	348	21.6	122	19.7
	Physical	218	9.9	148	8.8	70	11.3
	Sexual	35	1.7	28	2.4	8	0.8
	Neglect	173	7.5	121	7.3	52	7.9
	Any	596	27.2	429	26.6	167	28
Bully victimization	Physical	131	6.4	70	4	60	9.5
	Verbal	654	30.8	471	29.6	184	32.2
	Cyber	69	3	58	3.2	11	2.7
	Any	670	31.5	483	30.2	187	33.1
Dating violence	Yes	169	6.4	146	8.9	23	3.2
Family adversity	Any parents deceased	78	3.8	56	3.7	21	3.9
	Parents separation or divorce	367	13.8	286	16.3	82	10.7
	Parental psychopathology	707	31	521	33.5	186	28
	Attempted or died by suicide	62	2.6	40	2.5	22	2.7
	Violence between parents	217	9.5	152	9.1	65	10
	Parental criminal activities	50	2.2	36	2	14	2.5
RECENT STRESSFUL EXPERIENCES (12-MONTH)							
	Death, life-threatening illness or injury of a friend or family member	1106	51.6	819	55.1	287	47.3
	Stressors related to romantic partner (break-up or cheated)	633	28	478	31.5	155	23.8
	Betrayal, arguments or break up with friends or family member	959	45.8	745	50.6	215	40
	Interpersonal conflicts	218	13.5	121	8.5	97	19.8
	Life-threatening accident	90	5.3	49	2.6	41	8.6
	Seriously physically assaulted	81	5.1	40	2.6	41	8.1
	Sexually assaulted or raped	12	0.5	11	0.8	1	0.3

Table 1 *(continued)*

	Trouble with the police or serious legal problems	57	5.6	15	1.3	41	11
	Other stressful experience	151	6.6	118	6.3	32	6.9
	Any past year stressful experiences	1677	79.5	1240	82.6	437	75.7
INDIVIDUAL							
Mental disorders †	Mood disorder	598	24	465	28.8	133	18.1
	Anxiety disorder	509	19.9	418	25.8	91	12.7
	Alcohol or substance disorder	172	10.1	109	7.5	63	13.4
	Any mental disorder	867	37.1	675	41.4	192	31.7
Psychological							
Hopelessness	Agree strongly/moderate	297	14	229	16.3	68	11.2
	Neither agree or disagree	949	45.9	692	44.1	257	48.2
	Disagree strongly/moderate	859	40	604	39.6	255	40.6
Chronic health conditions or physical impairment		403	20.7	296	22.5	107	18.5
COMMUNITY							
Access to means	Yes	52	2.7	22	1.1	30	4.7
Positive Relationships ‡							
Family support	High	818	35.2	638	39	179	30.5
	Middle	707	34.8	486	34.7	221	34.9
	Low	581	30	401	26.2	180	34.6
Peers/others support	High	589	28.2	457	30.1	132	25.9
	Middle	849	36.7	633	38.3	216	34.8
	Low	667	35.1	435	31.6	231	39.4
School connectedness	High	617	29.1	453	28.6	164	29.7
	Middle	813	37.7	579	37.8	233	37.6
	Low	675	33.2	493	33.6	183	32.7

†**Mood** includes Major Depression or Bipolar; **Anxiety** includes Panic Disorder or Generalized Anxiety Disorder; **Alcohol or substance** includes abuse or dependence.

‡ **Family support** lowest tertile [1-3.75], middle tertile [4-4.5], highest tertile [4.75-5]. **Peers/others support** lowest tertile [1-2.75], middle tertile [3-3.5], highest tertile [3.75-5]. **School connectedness** lowest tertile [1.17-3.33], middle tertile [3.5-4.17], highest tertile [4.33-5].

Table 2. Bivariate associations between risk and protective factors with 12-month suicidal ideation among Spanish university students, stratified by sex. The UNIVERSAL (University and Mental Health) project.

		FEMALE n=1,525			MALE n=580		
		OR	**95%CI**	***p-value****	**OR**	**95%CI**	***p-value****
SOCIO-DEMOGRAPHICS AND EDUCATIONAL							
Country of birth (ref = Spain)	Other	1.6	0.8-3.4	.19	0.6	0.1-3.2	.51
Parents University Studies (ref = Neither)	At least one	1.0	0.7-1.4	.83	2.4	1.3-4.3	**.01**
Living at first term (ref = Parents home)	Other	0.6	0.4-0.8	**<.01**	1.0	0.6-1.6	.95
NEGATIVE LIFE EVENTS AND FAMILY ADVERSITY †							
Childhood maltreatment	Emotional	3.1	2.1-4.6	**<.01**	2.9	1.8-4.8	**<.01**
	Physical	2.4	1.4-4.1	**<.01**	3.8	2.2-6.4	**<.01**
	Sexual	1.7	0.5-5.7	.38		Insufficient data	
	Neglect	2.6	1.5-4.7	**<.01**	4.1	2.3-7.3	**<.01**
	Any	2.9	2.0-4.3	**<.01**	3.7	2.3-5.9	**<.01**
Bully victimization	Physical	2.6	1.3-5.4	**<.01**	2.0	1.0-3.7	.04
	Verbal	2.3	1.6-3.3	**<.01**	2.9	1.9-4.7	**<.01**
	Cyber	2.2	0.9-5.0	.07	0.6	0.1-4.6	.60
	Any	2.2	1.5-3.3	**<.01**	2.8	1.8-4.5	**<.01**
Dating violence	Yes	2.1	1.2-3.7	**<.01**	6.3	2.8-13.9	**<.01**
Family adversity	Deceased parents	1.7	0.7-3.9	.23	2.5	1.0-5.8	**.04**
	Parents separation or divorce	1.3	0.8-2.1	.24	1.3	0.7-2.6	.37
	Parental psychopathology	2.2	1.5-3.2	**<.01**	3.4	2.1-5.3	**<.01**
	Attempted or died by suicide	0.6	0.2-2.7	.55	1.0	0.1-6.9	.99
	Violence between parents	4.4	2.8-7.1	**<.01**	1.7	0.8-3.4	.15
	Parental criminal activities	1.4	0.4-5.2	.58	1.2	0.2-7.3	.87
RECENT STRESSFUL EXPERIENCES (12-MONTH)							
	Death, life-threatening illness or injury of a friend or family member	1.3	0.9-1.9	.19	0.8	0.5-1.3	.48
	Stressors related to romantic partner (break-up or cheated)	1.4	0.9-2.0	.11	1.9	1.1-3.0	**.01**
	Betrayal, arguments or break up with friends or family member	2.4	1.6-3.6	**<.01**	3.5	2.1-5.6	**<.01**
	Interpersonal conflicts	2.1	1.2-3.6	**<.01**	1.8	1.1-2.9	**.02**
	Life-threatening accident	0.7	0.2-2.8	.66	0.3	0.1-1.1	.08
	Seriously physically assaulted	2.2	0.8-5.6	.11	1.4	0.7-3.0	.31
	Sexually assaulted or raped	3.2	0.7-14.5	.12		Insufficient data	
	Trouble with the police or serious legal problems	0.4	0-4.8	.46	1.6	0.9-3.0	.13
	Other stressful experience	1.4	0.6-3.1	.46	1.3	0.5-3.1	.61
	Any past year stressful experiences	2.3	1.2-4.3	**.01**	7.3	2.7-20.2	**<.01**

Table 2 *(continued)*

INDIVIDUAL							
Mental disorders † ‡	Mood disorder	9.7	6.3-15	**<.01**	7.3	4.6-11.8	**<.01**
	Anxiety disorder	5.6	3.8-8.4	**<.01**	2.0	1.1-3.5	**.02**
	Alcohol or substance disorder	2.3	1.3-4.0	**<.01**	2.2	1.3-3.9	**<.01**
	Any mental disorder	15.6	8.5-28.8	**<.01**	3.9	2.4-6.2	**<.01**
Psychological							
Hopelessness (ref = Disagree strongly/moderate)	Agree strongly/moderate	3.4	2.1-5.6	**<.01**	12.7	6.1-26.3	**<.01**
	Neither agree or disagree	1.2	0.8-1.9		3.4	1.8-6.6	
Chronic health conditions or physical impairment †		1.2	0.7-1.8	.51	0.4	0.2-0.9	**.03**
COMMUNITY							
Access to means †	Yes	4.1	1.2-13.4	**0.02**	4.5	2.3-9.1	**<0.01**
Positive Relationships §							
Family support (ref = Low)	High	0.3	0.2-0.4	**<0.01**	0.1	0-0.3	**<0.01**
	Middle	0.3	0.2-0.5		1.2	0.7-1.9	
Peers/others support (ref = Low)	High	0.5	0.3-0.7	**<0.01**	0.1	0.0-0.4	**<0.01**
	Middle	0.3	0.2-0.5		0.9	0.5-1.4	
School connectedness (ref = Low)	High	0.4	0.2-0.6	**<0.01**	0.1	0.1-0.3	**<0.01**
	Middle	0.4	0.2-0.6		0.5	0.3-0.9	

OR odds ratio; **95%CI** 95% confidence interval; *p-values for F-test to evaluate significance of each categorical predictor based on multiple imputation**.** p-values <0.05 highlighted in bold. .

† **Reference category:** no.

‡ **Mood** includes Major Depression or Bipolar; **Anxiety** includes Panic Disorder or Generalized Anxiety Disorder; **Alcohol or substance** includes abuse or dependence.

§**Family support** lowest tertile [1-3.75], middle tertile [4-4.5], highest tertile [4.75-5]. **Peers/others support** lowest tertile [1-2.75], middle tertile [3-3.5], highest tertile [3.75-5]. **School connectedness** lowest tertile [1.17-3.33], middle tertile [3.5-4.17], highest tertile [4.33-5].

Table 3. Results of the multivariable models of gender-specific risk and protective factors of 12-month suicidal ideation among Spanish university students. The UNIVERSAL (University and Mental Health) project.

		FEMALE			MALE			*p-value* for intxn**
		OR	**95%CI**	***p-value****	**OR**	**95%CI**	***p-value****	
NEGATIVE LIFE EVENTS AND FAMILY ADVERSITY †								
Childhood maltreatment	Emotional	1.2	0.7-2.2	.49	1	0.4-2.4	.94	.56
	Physical	0.7	0.3-1.6	.39	3.6	1.4-9.2	**<.01**	.48
	Neglect	---	----	---	1.8	0.6-4.9	.27	.42
	Verbal	1.0	0.6-1.7	.86	1.1	0.5-2.5	.73	.72
Dating violence	Yes	1.5	0.7-3.0	.28	4.0	0.9-18.1	.08	.41
Family adversity	Deceased parents	---	----	---	4.6	1.2-17.7	**.03**	.54
	Parental psychopathology	1.1	0.6-1.8	.79	2.4	1.1-5.1	**.03**	.40
	Violence between parents	3.5	1.7-7.2	**<.01**	0.3	0.1-0.9	**.03**	**<.01**
RECENT STRESSFUL EXPERIENCES (12-MONTH)								
	Life-threatening illness or injury of a friend or family member	---	----	---	0.5	0.3-1.0	**.04**	.35
	Stressors related to romantic partner (break-up or cheated)	---	----	---	2.0	1.0-4.0	.05	.13
	Betrayal, arguments or break up with friends or family member	1.2	0.7-2.0	.49	1.2	0.6-2.5	.57	.68
	Interpersonal conflicts	1.6	0.8-3.2	.20	1.3	0.6-2.8	.49	.95
	Seriously physically assaulted	---	----	---	1.4	0.5-3.8	.57	.85
	Trouble with the police or serious legal problems	---	----	---	1.9	0.8-4.7	.17	.21
	Other stressful experience	0.7	0.3-2.0	.55	0.4	0.1-1.7	.23	.16
INDIVIDUAL								
Mental disorders † ‡	Mood disorder	5.5	3.3-9.3	**<.01**	4.4	2.0-9.7	**<.01**	.13
	Anxiety disorder	2.7	1.6-4.6	**<.01**	1.0	0.4-2.6	.94	**<.01**
	Alcohol or substance disorder	2.1	1.1-4.3	**.04**	0.5	0.2-1.6	.27	.51
Psychological								
Hopelessness (ref = Disagree strongly/moderate)	Agree strongly/moderate	1.4	0.7-2.7	.31	7.7	2.8-21.2	**<.01**	**.02**
	Neither agree or disagree	0.9	0.5-1.6		2.9	1.2-6.8		
Chronic health conditions or physical impairment †	Yes	---	----		0.3	0.1-0.8	**.02**	**.04**
COMMUNITY								
Access to means †	Yes	---	----		1.6	0.5-5.3	.47	.48
Positive Relationships §								
Family support (ref = Low)	High	0.5	0.2-0.9	**<.01**	0.2	0.1-1.0	**<.01**	**<.01**
	Middle	0.4	0.2-0.7		2.1	0.9-4.5		
Peers/others support (ref = Low)	High	0.6	0.3-1.1	**.01**	0.2	0.0-1.3	.11	.13
	Middle	0.4	0.2-0.8		0.5	0.2-1.1		

Table 3 *(continued)*

School connectedness (ref = Low)	High	0.8	0.4-1.5	.46	0.7	0.2-2.4	.39	.40
	Middle	0.7	0.4-1.2		0.6	0.3-1.2		

Adjusted by: Center, academic field, parents' university studies and living at first term; *p-value* <0.05 highlighted in bold.
*****p-value for F-test to evaluate significance of each variable based on multiple imputation. ******p-value for F-test of the interactions between gender with each of the assessed factors based on multiple imputation.
† **Reference category:** no.
‡ **Mood** includes Major Depression or Bipolar; **Anxiety** includes Panic Disorder or Generalized Anxiety Disorder; **Alcohol or substance** includes abuse or dependence.
§ Family support lowest tertile [1-3.75], middle tertile [4-4.5], highest tertile [4.75-5]. **Peers/others support** lowest tertile [1-2.75], middle tertile [3-3.5], highest tertile [3.75-5]. **School connectedness** lowest tertile [1.17-3.33], middle tertile [3.5-4.17], highest tertile [4.33-5].

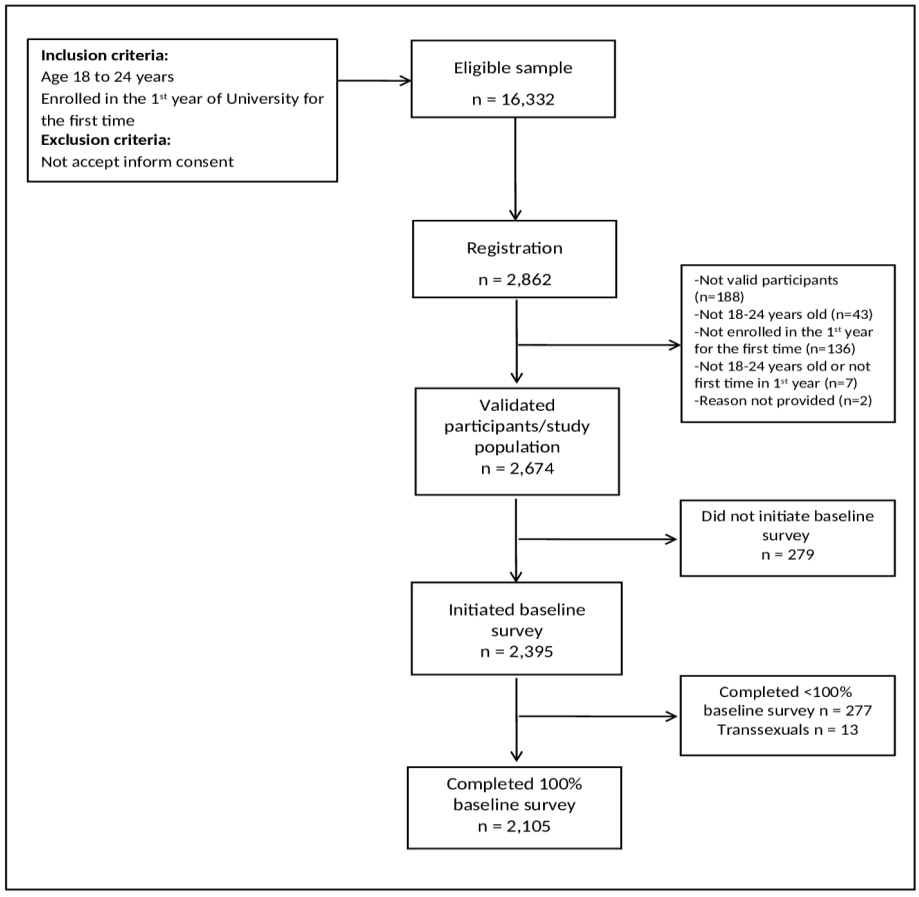
Table 4. Summary of common and gender-specific risk and protective factors of suicidal ideation among Spanish university students. The UNIVERSAL (University and Mental Health) project.

		FEMALE	MALE
NEGATIVE LIFE EVENTS AND FAMILY ADVERSITY			
Childhood maltreatment	Physical	NS	++
Dating violence	Yes	NS	++
Family adversity	Deceased parents	NS	++
	Parental psychopathology	NS	++
	Violence between parents	++	NS
INDIVIDUAL			
Mental disorders †	Mood disorder	+++	++
	Anxiety disorder	++	NS
	Alcohol or substance disorder	++	NS
Psychological			
Hopelessness (ref=Disagree strongly/moderate)	Agree strongly/moderate	NS	+++
COMMUNITY			
Positive Relationships			
Family support (ref=low)	High, Middle	**	NS
Peers/others support (ref=low)	Middle	**	NS

Based on logistic model results of the magnitude of the ORs: + >1 to <2, ++ ≥2 to <5, +++ ≥5; ** < 1.
NS no statistically significant.

† **Mood** includes Major Depression or Bipolar; **Anxiety** includes Panic Disorder or Generalized Anxiety Disorder; **Alcohol or substance** includes abuse or dependence.

Figure 1. Flow diagram of the number of individuals at each participation stage. The UNIVERSAL (University and Mental Health) project.



Article 3. *"Sexual orientation and suicidal behaviour in adolescents and young adults: systematic review and meta-analysis"*

Miranda-Mendizábal A, Castellví P, Parés-Badell O, Almenara J, Alonso I, Blasco MJ, et al. Sexual orientation and suicidal behaviour in adolescents and young adults: systematic review and meta-analysis. Br J Psychiatry. 2017;211:77–87.

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Supplementary material for this article can be found in ANNEX 3 (page 227).

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Review article

Sexual orientation and suicidal behaviour in adolescents and young adults: systematic review and meta-analysis

A. Miranda-Mendizábal,* P. Castellví,* O. Parés-Badell, J. Almenara, I. Alonso, M. J. Blasco, A. Cebrià, A. Gabilondo, M. Gili, C. Lagares, J. A. Piqueras, M. Roca, J. Rodríguez-Marín, T. Rodríguez, V. Soto-Sanz, G. Vilagut and J. Alonso

Background
Research suggests that lesbian, gay and bisexual (LGB) adolescents have a higher risk of suicidal behaviours than their heterosexual peers, but little is known about specific risk factors.

Aims
To assess sexual orientation as a risk factor for suicidal behaviours, and to identify other risk factors among LGB adolescents and young adults.

Method
A systematic search was made of six databases up to June 2015, including a grey literature search. Population-based longitudinal studies considering non-clinical populations aged 12–26 years and assessing being LGB as a risk factor for suicidal behaviour compared with being heterosexual, or evaluating risk factors for suicidal behaviour within LGB populations, were included. Random effect models were used in meta-analysis.

Results
Sexual orientation was significantly associated with suicide attempts in adolescents and youths (OR = 2.26, 95% CI 1.60–3.20). Gay or bisexual men were more likely to report suicide attempts compared with heterosexual men (OR = 2.21, 95% CI 1.21–4.04). Based on two studies, a non-significant positive association was found between depression and suicide attempts in LGB groups.

Conclusions
Sexual orientation is associated with a higher risk of suicide attempt in young people. Further research is needed to assess completed suicide, and specific risk factors affecting the LGB population.

Declaration of interest
None.

Suicide is one of the leading causes of death and it represents a serious public health concern. Over the past 45 years worldwide suicide rates have increased by 60%, the population of adolescents and youths registering the highest increase,[1] making suicide the second cause of death in the group aged 15–29 years.[2] There are few cases of attempted suicide before puberty, but a substantial increase occurs when individuals reach adolescence and young adulthood, especially between the ages of 19 and 23 years. In recent years studies have shown that lesbian, gay and bisexual (LGB) adolescents and youths have higher rates of suicidal ideation and suicide attempts than their heterosexual peers.[3–5] It has been suggested that risk factors for suicidal behaviours differ between heterosexual and LGB groups, owing to the interaction of these markers with sexual orientation.[6] Lesbian, gay and bisexual adolescents and youths are exposed to greater stigma, discrimination and victimisation within their families and romantic relationships compared with their heterosexual peers.[7] Exposure to these factors may predispose these individuals to more mental health problems and suicide attempts.[8,9] Minority stress theory, conceptualised as the burden of the perception of being different from others,[10] may explain the higher levels of health risk behaviours in LGB youth, and is related to greater stigmatisation, marginalisation and a hostile social environment.[11] In 2011 Marshal *et al* published a meta-analysis evaluating mental health in young LGB participants.[12] Their results showed an estimated overall effect size for the association between sexual orientation and suicidality of OR = 2.92 (95% CI 2.11–4.03). However, that review was limited in several ways: first, suicide attempts were analysed as a single overall variable labelled 'suicidality', which included suicidal ideation, suicidal plan and suicide attempt without stratified analysis; second, the population age range was 18–25 years, lacking information on adolescents; third, the majority of the articles included in their meta-analysis were cross-sectional (only one was a cohort study); and finally only studies up to 2009 were taken into account.

For our review we adopted a more general and robust approach: suicide attempts and suicide were separated for the analyses, in order to assess associations that could be specific for these outcomes, and age range inclusion criteria were enhanced, rendering our results applicable to a wider population, consistent with international recommendations.[13] Research published up to June 2015 was included, adding relevant recent information. More importantly, we assessed specific risk factors for suicidal behaviours and suicide death in the LGB population, thus contributing to filling a gap in knowledge about sexual minority groups in the adolescent and young adult populations, which have been little studied. An important characteristic of our review is that we included longitudinal studies only (either prospective cohorts or case–control studies). In fact, all except one of the articles analysed here were based on prospective cohort data. This ensured that exposure to the factors assessed preceded the outcome, making the evidence generated more relevant to establishing the temporal order of events, as well as minimising bias, improving the quality of included data and allowing us to establish valid and robust conclusions.[14,15] There is still a need to improve understanding of suicidal behaviours of adolescent and young adult LGB populations, as well as to quantify more accurately the risk and protective factors for suicide. There is also a need to develop evidence-based public health strategies to reduce the prevalence of suicide attempts and suicide deaths

*These authors contributed equally to the work.

among this high-risk population. We therefore undertook a systematic review of the literature, aiming to assess the extent to which sexual orientation is a risk factor for suicide attempts and suicide, and to identify risk factors for suicide attempts and suicide among LGB adolescents and young adults. The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42013005775).[16]

Method

Recommendations from the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for systematic reviews,[17] in relation to handling and reporting of results, were taken into account. Our initial search strategy was broad in scope and inclusive, with no restriction as to population or age, in order to identify predictors of suicidal-related behaviours. Text words, titles and MeSH terms were used as search terms, including suicide, suicidal behaviour, suicide attempt, suicidality, risk factor, causality, association, protective factor, incidence, longitudinal study, observational study, cohort study, case control study, prospective study, retrospective study, follow-up, and others, resulting initially in 23 682 references after duplicates were removed. Detailed information about all the keywords used for inclusion and exclusion, and search terms used to identify suicide attempt, suicidal behaviour, population and study design are provided in online supplement DS1. The following databases were first searched up to October 2013 and updated June 2015 in order to include the most accurate data: Cochrane Library, Medline, PsycINFO, EMBASE and Web of Science. We searched grey literature using the OpenGrey European database, and reference lists from previous reviews and books were examined. No restriction of language or year of publication was applied. Corresponding authors for articles written in languages other than Spanish and English were contacted. For the broad-scope review, studies were included if they met all of the following criteria:

(a) reported suicide attempt or suicide as a dependent variable;

(b) assessed at least one risk factor for any of these outcomes;

(c) the study population age ranged between 12 years and 26 years, both inclusive;

(d) were population-based longitudinal studies (non-clinical and non-institutional sample cohorts) or case–control studies where the control group was of the same age range (non-clinical and non-institutional).

Using an expert consensus reported previously, suicide was defined as any act done with the intention of taking one's own life, whereas suicide attempt was defined as any act of self-injury with intention to die.[18] Other suicide-related behaviours such as suicide ideation were excluded. Using these criteria we identified 197 studies for qualitative synthesis from the broader review. To these studies we applied the following specific selection criteria: first, studies that assessed LGB orientation as a risk factor for suicide attempts or suicide compared with a heterosexual peer group of the same age range; and second, studies that evaluated risk factors for suicide attempt or suicide within LGB populations. Studies assessing only the transsexual population were excluded, owing to certain conceptual differences. It has been reported that sexual orientation is a multidimensional concept referring to an enduring pattern of emotional, romantic and/or sexual attraction to males, females or both genders,[10] whereas gender identity is one's own sense or conviction of maleness or femaleness.[19] Moreover, transsexual individuals are considered to constitute a clinical population because transsexualism is classified as a type of gender identity disorder,[20] and although this is a controversial issue, we are convinced that risk and protective factors may have different mechanisms of action and deserve further and specific research. Furthermore, during data synthesis, information corresponding to the transsexual population was not included.

Study selection

A multidisciplinary team of psychiatrists, psychologists, statisticians, epidemiologists and public health professionals was established to perform the review. Five groups of independent peer reviewers assessed all references. During the title review terms listed in online supplement DS1 were used, and discrepancies between reviewers were included. During the title and abstract review phases, reviewers were masked to the article's author, journal and year of publication to minimise selection bias. A third independent reviewer resolved any discrepancies during abstract and full-text review.

Data extraction

We adapted a Cochrane Collaboration data collection form for this review. Each reviewer extracted data and an independent reviewer examined the data entered in the form, checking that the information was entered properly and attempting to complete any missing data. In case of discrepancies, consensus among reviewers was established. For each article the following data were extracted: sample size; number of LGB participants included; age range; mean age; country of recruitment; study design; type of outcome (suicide death or attempt); type of sample recruited; and ethics committee approval. From cohort studies additional data were extracted: weeks of follow-up; number of suicide attempts during follow-up; and number of suicides during follow-up. Information about risk factors was obtained as odds ratios and 95% confidence intervals; multivariate analysis prevailed over bivariate analysis. If available, stratified analysis was taken into consideration.

Quality of studies

The Newcastle–Ottawa Scale (NOS) was used for assessing the quality of non-randomised studies.[21] This uses a 'star' system, in which a study is evaluated on three broad perspectives: the selection of the study groups, the comparability of the groups and the ascertainment of either the exposure or outcome of interest for case–control or cohort studies respectively. The scale consists of eight questions with different responses; the response indicating the highest quality is given a star. The highest-quality studies are awarded up to nine stars.

Statistical analysis

Suicide attempt and suicide were analysed comparing LGB and heterosexual groups. Additional analyses assessing specific risk factors of suicidal attempt and suicide within the LGB group were carried out. In the case of multiple publications of the same sample and predictive factors, results from the largest sample and longest follow-up were selected. Meta-analyses were performed for each variable for which there was a minimum of two studies with usable data; adjusted OR with 95% CI were used when these data were provided in the articles; if not, unadjusted ORs were taken into account. Population attributable risk (PAR) was also calculated using the formula:

$$\mathrm{PAR} = \frac{P(RR-1)}{(1+P(RR-1)}$$

where P is the prevalence of being LGB obtained through data from some of the cohort studies included in meta-analysis,[22–27]

and RR is the relative risk of suicide attempt in LGB *v.* heterosexual groups based on data from the cohort studies included. To convert the OR to RR the following formula was used:

$$RR = \frac{OR}{(1 - P_0) + P_0 OR}$$

where OR is the odds ratio of suicide attempt in LGB *v.* heterosexual groups and P_0 is the prevalence of suicide attempts in the heterosexual group,[28] calculated through meta-analysis using data from four of the included articles.[22–25] Stata software version 13 was used to conduct the meta-analysis.

Random effect methods were used for the meta-analysis. Statistical heterogeneity was assessed by visual inspection of forest plots, by Galbraith plots, by chi-squared tests to calculate *P* value and by Higgins' test (I^2), which describes the percentage of observed heterogeneity that would not be expected by chance. If *P* was less than 0.10 heterogeneity was considered to be significant, and moderate if I^2 was 30–50% and severe if I^2 exceeded 50%.[29] Small study effects (including publication bias) were assessed through visual inspection of funnel plots and Harbord's modification of Egger's test, which has been recommended for binary outcomes with effects measured as odds ratios.[30] For fewer than three studies the Begg test was used. Sensitivity analyses were performed for cohort studies according to two criteria: first, length of follow-up corresponding to outcome assessment in the NOS score (less than 6 years), considering that the incidence of suicidal attempts and suicide is very low in non-clinical samples; and second, the country of origin of the samples, classified as USA *v.* non-USA. Because only three samples came from countries other than the USA, these could be a source of heterogeneity since there could be differences between countries in terms of social acceptance and stigma about sexual orientation.

Results

After duplicates were removed, 23 682 articles were retrieved. After reviewing titles and abstracts the full text of 1575 potentially eligible articles were reviewed and 1561 were excluded for the following reasons: 397 were not population-based cohorts or case–control studies in which the control group was non-clinical; 436 did not involve participants aged 12–26 years; 183 did not concern LGB people or assess sexual orientation as a risk factor; 350 did not treat suicide or suicide attempt as a dependent variable; and 95 did not assess any risk factor (Fig. 1). After these exclusions a total of 14 articles were identified, including five articles that had not been reviewed by Marshal *et al*,[12] even though the papers were published before 2009 and met their inclusion criteria. Of the final set of articles, ten assessed sexual orientation as a risk factor of suicide attempts or suicide,[22–24,26,27,31–35] three assessed specific risk factors of these outcomes among LGB,[36–38] and one assessed both sexual orientation as a risk factor and specific risk factors among LGB.[25]

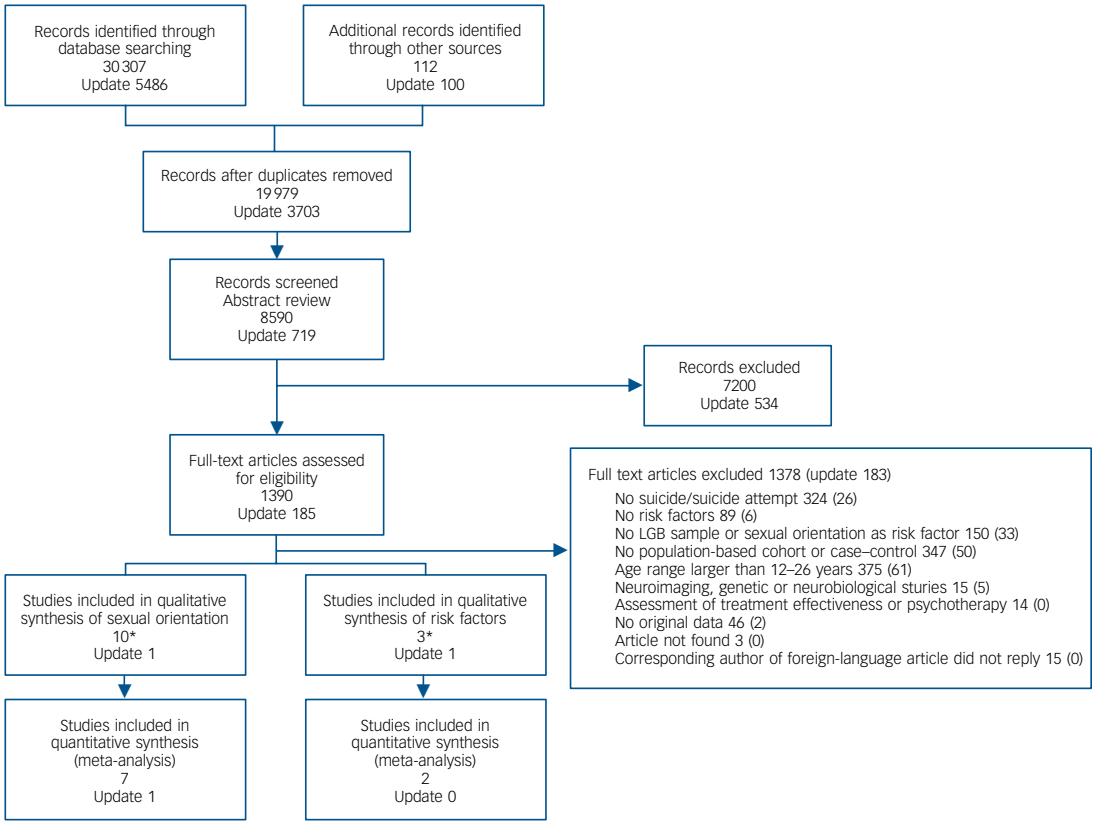

Fig. 1 Study selection. Studies in the qualitative synthesis included that by *Silenzio *et al* which assessed both sexual orientation as a risk factor, and risk factors in the lesbian, gay and bisexual population.[25]

Sexual orientation as risk factor

Eleven studies assessed LGB orientation as a risk factor for suicide attempt or suicide compared with heterosexual groups. These articles were published between 1995 and 2014, in four different countries: six from the USA, three from New Zealand, and one each from Norway and the UK (Table 1). Participation rates ranged from 30% to 100%.[24,35] These studies contained data on 1634 LGB and 22 117 heterosexual individuals and all of them included both male and female participants. Three studies were based on the general population, five recruited from high schools, one from a university and one among homeless adolescents. Based on data from seven of these articles, the prevalence of suicide attempts ranged from 1.5% to 3.5% in heterosexual adolescents and from 6% to 70% in LGB respondents. Ten studies assessed suicide attempt using a cohort design,[22–27,31–33,35] resulting in a total population of 23 484, but only one study assessed suicide using a case–control design (cases $n = 120$, controls $n = 147$); Table 1.[34]

Quality of studies

Of the 11 studies that assessed sexual orientation as a risk factor, no difference in quality was seen in selection domains in the cohort studies; in terms of comparability criteria eight articles were awarded two stars because relevant confounding factors were taken into consideration in the adjustment.[22,24–27,31,32,37] However, different covariables were taken into account: one study considered demographic, psychosocial, history of mental illness, and formal and informal help-seeking variables;[27] another included antecedents of suicidal behaviour;[24] and yet another took into account variables related to parental characteristics.[22] More detailed information is presented in Table 1. Regarding outcome domains, none of the studies achieved a star for ascertainment of outcome because data were self-reported by the participants and no confirmatory check of medical records was performed. The most significant difference was in length of follow-up, which was adequate only in five studies (Tables 2 and 3).[22–24,26,31]

Sexual orientation and suicide attempts

Three of the included studies reported a statistically significant higher risk for suicide attempt in LGB adolescents compared with a heterosexual group (adjusted OR 2.96–6.20),[22,25,27] whereas three studies showed a non-significant increment of risk.[26,32,35] Two articles presented rates of recent suicide attempts, values ranging from 5.4% to 17.6% for males and 2.1% to 15.5% for females.[31,33] There were differences in terms of how sexual orientation was classified. Two studies used five categories: 100% heterosexual, mostly heterosexual, bisexual, mostly homosexual and 100% homosexual;[27,33] four articles used only three categories: opposite-sex attraction only or heterosexual, minor same-sex attraction or bisexual, and persistent major same-sex attraction or homosexual;[22,23,25,31] and the other studies used a single item to assess sexual orientation in two categories: LGB and non-LGB.[24,26,32,35]

Eight studies were included in the meta-analysis. Adjusted OR and 95% CI from results of each article were used. A single OR value for the whole population was not provided in two studies: Skegg *et al* presented values stratified by gender,[23] and Whitlock *et al* reported OR for three sexual orientation categories,[27] resulting in eleven samples included for meta-analysis. Three studies were excluded because data were either non-extractable or in a format that did not permit comparisons with the other studies. Random effect models were used because severe heterogeneity was observed ($I^2 = 60\%$, $P = 0.005$). The overall pooled estimate in meta-analysis of cohort studies of suicide attempt showed a significantly higher risk for LGB youths when compared with heterosexual youths (OR = 2.32, 95% CI 1.59–3.39). Two studies appeared to be sources of heterogeneity: one assessed sexual orientation through three different categories,[27] whereas in the other the LGB sample size was only 28 but there were 979 in the heterosexual group.[22] Furthermore, on the Galbraith plot, these two studies were outliers. After exclusion of these two studies the new OR was 2.26 (95% CI 1.60–3.20; $I^2 = 35\%$, $P = 0.161$). Visual inspection of the funnel plot does not suggest any publication bias, as small studies tend to lead to lower estimates of the effect than larger studies (Fig. 2). Although the Harbord test was not significant ($P = 0.4$) it is important to note that these results should be interpreted with caution, since the small number of studies means there is insufficient power to distinguish chance from real asymmetry.

Sensitivity analyses

Taking into consideration only the studies that did not appear as possible sources of heterogeneity, sensitivity analyses were carried out according to length of follow-up and country of origin of the samples. Removing three studies with insufficient length of follow-up, results were not altered substantially with respect to the association between sexual orientation and suicide attempt (OR = 2.59, 95% CI 1.58–4.26), whereas heterogeneity decreased compared with the first meta-analysis ($I^2 = 45\%$, $P = 0.122$). Possible explanations for observed heterogeneity could be the differences among covariables used for the adjustment, and gender differences because one study reported results for female participants,[24] another for males and females,[23] and two studies presented a single value for both genders together.[25,26] Similar results were obtained when samples from the USA were taken into account in the analyses, i.e. an increased risk in LGB youths (OR = 1.98, 95% CI 1.42–2.75) with no heterogeneity ($P = 0.488$).

Gender stratification

According to one study the lifetime prevalence of suicide attempts in gay and bisexual men was 4.8%, but 12.6% in lesbian and bisexual women in the same sample.[23] Only two cohort studies assessed sexual orientation as a risk factor of suicide attempts stratified according to gender,[23,32] and one study presented results only for women.[24] One of these articles found a significantly increased risk for lifetime suicide attempts in gay and bisexual men compared with heterosexual men (OR = 3.2, 95% CI 1.4–7.2).[23] Similar results were found for the risk of lifetime suicide attempts among lesbian and bisexual women; one study reported a risk almost five times higher (OR = 4.96, 95% CI 2.29–10.62).[24] In the other studies results in men showed that homosexual orientation was not associated with higher risk (OR = 1.71, 95% CI 0.92–3.17);[32] findings were similar in women: OR = 1.4 (95% CI 0.7–2.7),[23] and OR = 1.25 (95% CI 0.80–1.96).[32]

Meta-analysis found an increased risk of suicide attempts in gay or bisexual men compared with heterosexual men (OR = 2.21, 95% CI 1.21–4.04) (online Fig. DS1(a)). The Galbraith plot showed that the studies fell within confidence limits (online Fig. DS1(b)) and no publication bias was observed (Begg test, $P = 0.317$) (online Fig. DS1(c)). Being a lesbian or bisexual woman was associated with higher risk of suicide attempts, but this was not significant (OR = 1.97, 95% CI 0.90–4.30) (online Fig. DS2(a)) and severe heterogeneity was observed ($I^2 = 79\%$, $P = 0.008$). In the Galbraith plot one study appeared as a cause of variability (online Fig. DS2(b));[24] after excluding this study the OR was 1.29 (95% CI 0.89–1.88). As in the analyses for

Table 1 Characteristics of included articles

Study	Country	Study design	Follow-up	Sample at baseline (% women)	Sample at the end of follow-up (% attrition)	Percentage of LGB in final sample	Population	Outcome	Age (years)		Covariates used for adjustment	Ethics committee approval
									Range	Mean (s.d.)		
Fergusson et al (1999)[22]	New Zealand	Cohort	25 years	1265 (50)	1007	2.7	General	Suicide attempt	14–21	NR	Parental change, parental criminality	Yes
Noell et al (2001)[33]	USA	Cohort	6 months	536	532 (0.8)	44.7	Homeless	Suicide attempt	13–20	18.2 (1.7)	None	Yes
Skegg et al (2003)[23]	New Zealand	Cohort	26 years	1019	942 (7.5)	18.2	General	Suicide attempt	NR	NR	None	Yes
Wichstrom & Hegna (2003)[24]	Norway	Cohort	5 years	9679	2924 (69.7)	6.5	High school	Suicide attempt	12–20	14.9 (1.7)	Previous suicide attempt, depression	Yes
Bearman & Moody (2004)[32]	USA	Cohort	1 year	20 745	13 465 (35)	NR	High school	Suicide attempt	NR	NR	School clustering, grade range, school size, ethnic mix, region, urbanisation	NR
Fergusson et al (2005)[31]	New Zealand	Cohort	25 years	1265 (50)	967 (23.5)	11.9	General	Suicide attempt	21–25	NR	Gender, childhood sexual abuse, childhood physical abuse, parental illicit drug use, novelty-seeking, parental criminality, parental attachment	Yes
D'Augelli et al (2005)[36]	USA	Cohort	2 years	528	361 (31.6)	100	LGB	Suicide attempt	15–19	NR	None	Yes
Silenzio et al (2007)[25]	USA	Cohort	9 months	14 322	13 834 (3.5)	3.1	High school	Suicide attempt	18–26	NR	Gender, age, ethnicity	Yes
Young et al (2011)[26]	UK	Cohort	8 years	2586	2157 (16.5)	4.2[a]	High school	Suicide attempt	NR	NR	Gender, gender non-conformity, social class, family structure, same-sex partner, religion, parental control, area deprivation	Yes
Fried et al (2012)[35]	USA	Cohort	2 years	1728	1728	4.3	High school	Suicide attempt	16-18	NI	Cognitive development, smoking, failing grades, ethnicity, sexual abuse, depression, counselling, number of risk factors	Yes
Mustanski & Liu (2013)[37]	USA	Cohort	4 years	248	237 (4.4)	100	LGB	Suicide attempt	16–20	18.7 (1.3)	Previous suicide attempt, depression, hopelessness	Yes
Whitlock et al (2013)[27]	USA	Cohort	3 years	2320	1466 (36.8)	24.5	University	Suicide attempt	NR	NR	Gender, age, ethnicity, father's education level, sexual orientation, life orientation, acceptance of emotion, sense of meaning life, perceived social isolation	Yes
Burns et al (2015)[38]	USA	Cohort	2 years	450 (0)	449	100	LGB	Suicide attempt	16–20	18.9 (1.3)	Ethnicity, age, sexual orientation	Yes
Shaffer et al (1995)[34]	USA	Case–control	NA	267 (21)	NA	1.1	General	Suicide	NR	NR	NA	Yes

LGB, lesbian, gay or bisexual; NA, not applicable; NR, not reported.
a. Calculated from a sample of 1091 individuals.

Table 2 Quality assessment of included cohort studies

Study	Selection			Comparability		Outcome			
	Representativeness of exposed cohort[a]	Selection of non-exposed cohort[a]	Ascertainment of exposure[a]	Demonstration outcome of interest not present at start of study[a]	Comparability cohorts on the basis of design or analysis[b]	Ascertainment of outcome[a]	Adequate length of follow up[a]	Adequacy of follow up[a]	Total stars[c]
Fergusson et al (1999)[22]	*	*	*	*	**	-	*	*	8
Noell et al (2001)[33]	*	*	*	*	*	-	-	*	6
Skegg et al (2003)[23]	*	*	*	*	*	-	*	*	7
Wichstrom & Hegna (2003)[24]	*	*	*	*	**	-	*	-	7
Bearman & Moody (2004)[32]	*	*	*	*	**	-	-	*	7
Fergusson et al (2005)[31]	*	*	*	*	**	-	*	*	8
D'Augelli et al (2005)[36]	*	*	*	*	*	-	-	*	6
Silenzio et al (2007)[25]	*	*	*	*	**	-	-	*	7
Young et al (2011)[26]	*	*	*	*	**	-	*	*	8
Fried et al (2012)[35]	*	*	*	*	**	-	-	*	7
Mustanski & Liu (2013)[37]	*	*	*	*	**	-	-	*	7
Whitlock et al (2013)[27]	*	*	*	*	**	-	-	-	6
Burns et al (2015)[38]	*	*	*	*	*	-	-	*	6

a. A maximum of one star can be allotted in this category.
b. A maximum of two stars can be allotted in this category.
c. Highest-quality studies are awarded up to nine stars (–, no star awarded).

men, no publication bias was observed (Begg test, $P = 0.117$) (online Fig. DS2(c)). Meta-analysis comparing gay with heterosexual men showed significantly increased risk (OR = 8.36, 95% CI 1.88–37.11) (online Fig. DS3(a)); a similar situation occurred when bisexual men were compared with heterosexual men (OR = 2.44, 95% CI 1.16–5.16) (online Fig. DS(3)b). The results obtained in meta-analysis of lesbian *v.* heterosexual women demonstrated increased risk of suicide attempt (OR = 4.31, 95% CI 1.89–9.86) (online Fig. DS3(c)); and also in bisexual *v.* heterosexual women, although not significant (OR = 1.56, 95% CI 0.66–3.69) (online Fig. DS3(d)).

Sexual orientation and suicide

Only one case–control psychological autopsy study evaluated completed suicide. The objective was to assess risk profiles of all people who died by suicide under 20 years of age, through interviews with their parents (or other caregiver at the time of the death), a sibling or a friend – in one case a schoolteacher who had known about the person's behaviour was interviewed. Cases were suicide deaths, controls were a random sample from telephone subscribers in the study area. Out of 120 cases that were completely investigated 79% of the individuals were male, of whom 3 were gay. No one in the control group reported any homosexual experience. Even though no odds ratio value was reported, it was stated that the difference was not significant ($P = 0.088$). None of the women who died by suicide was lesbian.[34]

Population attributable risk

Using different values of the prevalence of being LGB corresponding to different scenarios (8%, range 4–13) and assuming the relationship between sexual orientation and suicide attempt is causal and not confounded (RR = 2.15, 95% CI 1.56–2.94), calculations suggest that 8% (range 4–13) of suicide attempts in adolescents and young adults could be attributed to sexual orientation (see online Table DS1).

Risk factors

Four studies that assessed specific risk factors for suicide attempts among the LGB population were identified (but none assessing suicide). These studies took place in the USA and were published in 2005 and 2015.[25,36–38] Participation rates ranged between almost 70% to 99.7%.[36,38] All of them used a cohort design and together contained data on 1476 LGB people, with representation of both genders (Table 1).

Quality of studies

According to our quality assessment, no difference was seen in selection domains between the four studies. Sample sizes ranged from $n = 20$ to $n = 449$; one study analysed data from a nationally representative sample of adolescents and young adults,[25] whereas the other three studies recruited participants from different US cities.[36–38] In the comparability domain, two studies achieved two stars because important confounders were taken into account in the design and/or the analysis. Two studies considered age and ethnicity as covariables for the analysis,[25,37,38] whereas Burns *et al* also included sexual orientation.[38] The other study considered only age during the recruitment.[36] For the ascertainment of the outcome, none of the studies had a star because suicide attempts were self-reported by the participants and no reference to records had been done to confirm. In terms of length of follow-up, none of the studies achieved a star; however, in the category that assessed the adequacy of follow-up the four articles had the

Table 3 Quality assessment of case–control study

Study	Case definition[a]	Representativeness of cases[a]	Selection of controls[a]	Definition of controls[a]	Comparability of cases and controls[b]	Ascertainment of exposure[a]	Same method of ascertainment in both groups[a]	Non response rate[a]	Total stars[c]
Shaffer et al (1995)[34]	-	–	*	*	*	–	*	*	5

a. A maximum of one star can be allotted in this category.
b. A maximum of two stars can be allotted in this category.
c. Highest-quality studies are awarded up to nine stars (–, no star awarded).

highest rating because attrition during the study was not related to the exposure or the assessed outcome. In general, all these studies had high overall quality (see Table 2).

Data syntheses

D'Augelli *et al* evaluated an important number of risk factors for suicide attempts; results showed that 61 individuals of the entire sample ($n = 361$) of LGB youths made a suicide attempt.[36] Risk factors such as having been more open about being LGB with their families, more often called 'sissy' or 'tomboy' by parents, more gender atypical in childhood, having experienced parental psychological abuse and a family history of depression or suicidality all presented higher prevalence or median values. Mustanski & Liu reported that having a history of suicide attempts represented an increased risk of subsequent suicide attempt whereas hopelessness and depression were not significant.[37] The results obtained by Silenzio *et al* indicated that problem drinking, depression and problem drug use were not related to increased risk of suicide attempts in LGB respondents, contrary to findings in non-LGB participants.[25] Finally, results from the USA reported by Burns *et al* suggest that in some young LGB males from minority ethnic groups such as native Americans there is a 3-fold risk of suicide attempts compared with young White LGB men.[38] However, Black or Hispanic men do not seem to have higher risk. More details of the risk factors assessed are presented in online Table DS2. Meta-analysis of depression as a risk factor for suicide attempts in LGB adolescents showed increased risk (OR = 1.05, 95% CI 0.93–1.19; $I^2 = 38\%$, $P = 0.204$) (online Fig. DS4(a)), but the result was not significant. Using a Galbraith plot no heterogeneity was observed (online Fig. DS4(b)). No publication bias was found, according to the Begg test ($P = 0.317$) (online Fig. DS4(c)).

Discussion

Our systematic review shows that sexual orientation is significantly associated with suicide attempts, based on meta-analysis of longitudinal studies. Nevertheless, not enough studies were found to associate sexual orientation with suicide. Sexual minority men were more likely to make suicide attempts than

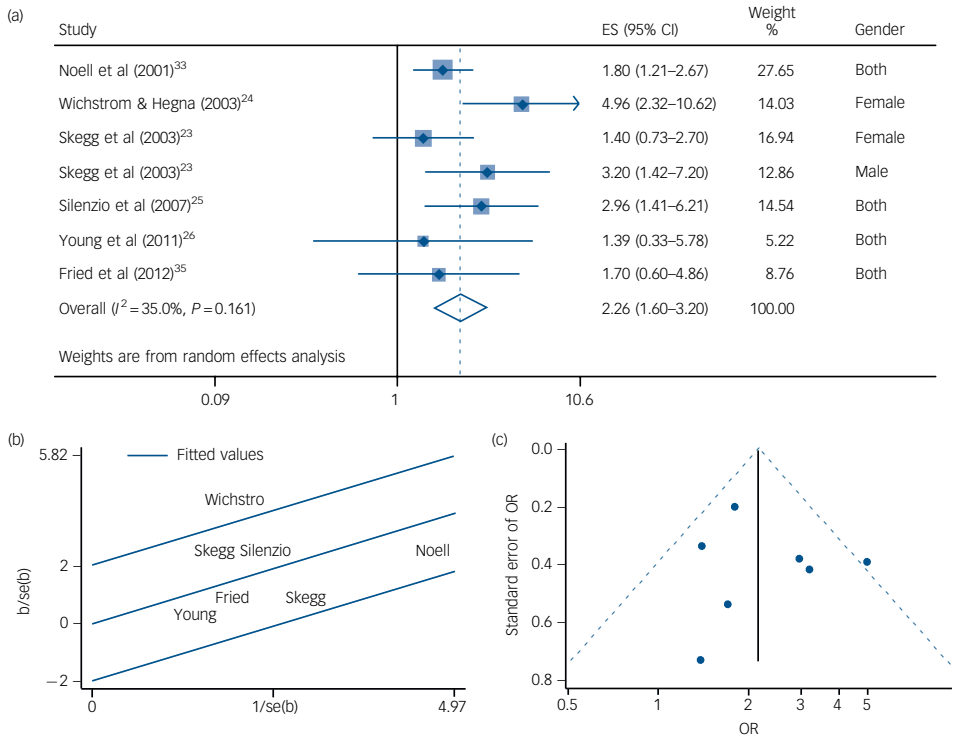

Fig. 2 Sexual orientation as risk factor for suicide attempts: (a) forest plot; (b) Galbraith plot; (c) funnel plot (Harbord test $P = 0.43$). ES, effect size.

heterosexual men. Among women, a similar association was found but it did not reach statistical significance, probably owing to the small number of studies assessed. Few studies were found evaluating risk factors for either suicide attempts or suicide among LGB populations. Further research assessing specific risk factors is needed.

Strengths and limitations

Our systematic review has several strengths: a broad-scope search in several databases and different languages was conducted, with peer review in the screening phase, independent review in the data extraction phase and use of methods for minimising bias; corresponding authors for articles written in languages other than Spanish and English were contacted for further information; a manual search and grey literature search were also carried out; and as far as we are aware no PAR calculation of sexual orientation as a risk factor for suicide attempts has been done in previous systematic reviews.

In relation to a previous systematic review,[12] our study extended the search strategy to three additional databases and a grey literature search was also performed; we used a wider age range as an inclusion criterion, considering adolescents, and also included studies published after 2009. This resulted in 13 additional studies, 5 of which were considered for meta-analysis, adding new, relevant and useful information for the assessment of causes and mechanisms, despite our having excluded other suicide-related outcomes, such as suicidal ideation and plan, and cross-sectional studies, which had been included in the previous review.[12] These additional articles added relevant and useful new information about the risk of sexual minority groups for future suicidal behaviours and death. Moreover, our results suggest the need for further assessment about the causes and mechanisms of suicidal behaviours and death among this population. A limitation is that our search strategy was not applied to the CINAHL and Sociological Abstracts databases. Additional papers might have been retrieved if these databases had been searched; however, we searched the databases most recommended for psychiatric research, including Web of Science and PsycINFO,[39] and also performed a manual search. Further, we searched grey literature only in OpenGrey, a European database; although it includes access to Greynet data (an international grey literature database) there is no certainty that our search was exhaustive. Overall, the use of the six particular databases in this study is in line with most strict systematic reviews and provides important coverage security. An additional limitation of our review is that the articles included came from a broader search strategy, as has been done in other systematic reviews.[40–42] However, in accordance with the initial inclusion criteria, both 'LGB population' and 'sexual orientation' as a risk factor were included in the search phase. Also, we included population-based studies in our review, which could have resulted in a higher heterogeneity. However, after excluding studies that seemed to be sources of heterogeneity, OR values became similar. Finally, we used the Newcastle–Ottawa Scale to assess the quality of the studies reviewed because it had been used in previous systematic reviews,[43–46] and also because it was designed for longitudinal studies. However, evidence about its validity is still limited.[21]

Comparison with other studies

Consistent with other reviews, sexual minority adolescents and youths were more likely to have made suicide attempts than their heterosexual peers. We estimated a 2-fold risk, which is similar to the risk ratios reported by King *et al*, which ranged from 1.96 to 2.76 in 12-month prevalence of suicide attempts, for LGB population of any age range.[47] Also, Marshal *et al* showed a risk of 2.92 in LGB young people aged from 18 to 25 years,[12] slightly higher than our results, probably because most of the included studies were cross-sectional and their OR values ranged from 1 to 10 (ours ranged from 1.30 to 5). These facts may lead to overestimation of the risk; however, this must be interpreted with caution. We estimated the risk of suicide attempts according to sexual orientation, stratifying by gender. Our results are consistent with previous original studies which stated that being a gay or bisexual male is associated with higher risk of suicide attempt than being a heterosexual male. Longitudinal studies have found that sexual orientation is an independent risk factor for suicide attempts among young males, more so than among females.[48] This finding could be related to results from other studies where elevated rates of suicide attempts in gay and bisexual adolescent men have been reported.[49–52] During adolescence models of gender, masculinity and femininity are reinforced; a possible explanation for observed data could be that during this stage of life these models may be affected by heteronormativity. It is important to note that gender definition covers aspects related to social categories and different life spheres, including sexual facets. Heterosexuality or homosexuality must be understood only as forms of sexual expression, since there are interrelations between non-sexual and sexual spheres.[53] In adolescents, the self-perception of failure to conform with this kind of model may affect different aspects of mental health.[54]

Among lesbian or bisexual women an increased risk of suicide attempt was found; however, it was not statistically significant, probably because few studies were identified. Our results also indicated that being bisexual is associated with higher risk of suicide attempt, but not in women; again, a possible reason could be the small number of studies. A previous systematic review summarised available research about bisexuality as a risk factor; it was associated with suicidal behaviour to a greater extent than heterosexuality.[55] There is no clear explanation or identification of specific risk factors acting among those with bisexual orientation. It seems therefore plausible that the same risks and mechanisms – such as more psychological distress and mental health problems (bisexuality and suicide) – act among all LGB categories.

Few studies were identified that evaluated risk factors for suicide attempts and suicide in LGB adolescents and youths. As a consequence, we could only perform a meta-analysis for the role of depression. According to our results depression does not seem to be related to suicide attempts in LGB population-based studies, in contrast to reports for the heterosexual population; however, these results should be interpreted with caution, because the lack of effect may be due to the insufficient number of included studies. Some authors suggest that minority stress theory may explain differences between the mechanisms of action of risk factors in the LGB population compared with the heterosexual population. This theory shows how specific external stressors such as victimisation, discrimination or stigma, or an internal stressor such as internalised homophobia, could increment suicide and suicidal behaviour risk. Discrimination involves anti-gay behaviour, including rejection, acts of physical violence and verbal assaults against gay men and other sexual minorities based on actual or assumed sexual orientation.[56] Internalised homophobia refers to internalised societal homophobic attitudes,[57] and includes negative attitudes toward homosexuality, displeasure with sexual orientation of others, disconnectedness from other LGB individuals, and discomfort with same-sex sexual activity.[58]

Negative 'coming out' reactions from family and friends, the experience of sexuality-oriented victimisation and having used drugs or alcohol to confront problems relating to their lesbian

or gay identity increase the risk of attempted suicide in adolescents who discover their same-sex preference early in adolescence.[59] Parental intolerance and rejection in response to the disclosure of an adolescent's sexual orientation, considered as forms of discrimination, are associated with specific risks, including depression, suicidal ideation, isolation, homelessness, prostitution, substance use, unprotected sex and sexually transmitted disease.[59–61] Finally, internalised homophobia was found to be significantly related to psychological distress: guilt, sex difficulties, suicide (ideation and/or behaviour) and AIDS-related traumatic stress response. Other factors such as stigma and experience of prejudice events were also significantly related to most of the measures of distress; however, internalised homophobia was reliably the most potent predictor. The interaction between these three factors causes psychological maladjustment, known as 'psychologically injurious effects'.[57]

Lesbian, gay and bisexual adolescents and young adults present significant differences compared with their heterosexual peers in relation to mechanisms by which risk factors act and are correlated. Risk factors such as depression, alcohol and drug misuse may be similar among LGB and heterosexual young people, but the mechanisms of action are completely different.

Generalisation of the findings

Some additional issues should be taken into consideration before generalising these results. First, the assessment of sexual orientation differed between included studies: one study assessed sexual orientation by asking if the person had ever had a sexual relation with another person of the same gender; this could be considered a sexual behaviour rather than sexual orientation.[62] It is important to differentiate sexual orientation from sexual behaviour. Sexual orientation is composed of emotional, romantic and/or sexual attraction, as well as an individual's sense of personal and social identity.[63] A person who has engaged in homosexual or bisexual behaviour should not necessarily be identified as lesbian, gay or bisexual. Second, we found important differences in the inclusion of confounding variables in multivariate models between the original studies. Some of them did not even adjust for any confounding variable, an important source of heterogeneity. Third, the length of follow-up in most of the cohort studies included was less than 5 years. Considering that the incidence of suicidal behaviour in the general population is low,[2] it is important to take latency into account because studies allowing for latent periods found higher incidence of the outcomes than those that ignored latency.[17] However, apparently this issue did not result in heterogeneity, as may be seen in the sensitivity analyses. Finally, although no publication bias was observed according to the Harbord test, we cannot firmly exclude it owing to the small number of studies analysed, well below the overall recommendation of a minimum of 10 studies for the assessment of asymmetry.[64] Even though the funnel plot should be interpreted with caution owing to the small sample size and the problems previously reported when applied to a binary outcome,[64] visual inspection of the graph suggests that if any, asymmetry would be in the sense of small studies tending to lead to lower estimates of the effect than larger studies, and thus publication bias does not seem to be explaining the asymmetry.[65]

Future research

Although a significant association between sexual orientation and suicide attempt has been established, research is needed in several areas. Sexual orientation and gender identity ought to be measured in a homogeneous way, or using the same definition by expert consensus, to allow comparisons between studies. Information about sexual orientation could be obtained from national surveys or registers, and there is a need for an appropriate method to determine the sexual orientation of people who have died by suicide. Longitudinal studies are needed to assess mediators such as victimisation, stigmatisation and discrimination to identify causal pathways between sexual orientation and suicidal behaviour. Public health prevention strategies ought to be developed that could reduce suicide attempts by around 9%, according to our PAR calculations, which indicated that sexual orientation is a major contributor to suicidal behaviour. Inclusion of LGB participants should be encouraged in research about effective public health strategies to reduce risk factors and suicidal behaviour among the LGB population, and research should be extended to other settings, such as developing countries. Sexual orientation is associated with increased risk of suicide attempts in LGB adolescents and young adults, and gay and bisexual men are more likely to make suicide attempts; this is probably the case in women as well but our results were inconclusive. Further research is needed to establish causality between sexual orientation and suicide, and specific risk factors among the LGB population. Public health strategies for prevention of mental disorders including suicidal behaviour must be considered among the LGB population, a high-risk group in which specific factors are acting.

A. Miranda-Mendizábal, MD, MPH, Health Services Research Group, Institut Hospital del Mar d'Investigacións Mèdiques (IMIM) and Department of Health and Experimental Sciences, Pompeu Fabra University (UPF), Barcelona; **P. Castellví**, PhD, Health Services Research Group, IMIM and Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Barcelona; **O. Parés-Badell**, MD, MPH, Health Services Research Group, IMIM, Barcelona; **J. Almenara**, MD, PhD, Faculty of Nursing and Physiotherapy, University of Cádiz; **I. Alonso**, PhD, Morales Meseguer Hospital, Murcia; **M. J. Blasco**, MSc, Health Services Research Group, IMIM, Department of Health and Experimental Sciences, UPF, and CIBERESP, Barcelona; **A. Cebrià**, PhD, Department of Mental Health, Corporació Sanitaria Parc Taulí, Sabadell; **A. Gabilondo**, MD, PhD, Outpatient Mental Health Care Network, Osakidetza-Basque Health Service, and Mental Health and Psychiatric Care Research Unit, BioDonosti Health Research Institute; **M. Gili**, PhD, Institut Universitari d'Investigació en Ciències de la Salut (IUNICS-IDISPA), University of Balearic Islands, Palma de Mallorca; **C. Lagares**, PhD, Department of Statistics and Operative Research, University of Cádiz; **J. A. Piqueras**, PhD, Department of Health Psychology, Miguel Hernandez University of Elche; **M. Roca**, MD, PhD, IUNICS-IDISPA and Network of Preventive Activities and Health Promotion, University of Balearic Islands, Palma de Mallorca; **J. Rodríguez-Marín**, PhD, **T. Rodríguez-Jiménez**, PhD, **V. Soto-Sanz**, BSc, Department of Health Psychology, Miguel Hernandez University of Elche; **G. Vilagut**, Health Services Research Group, IMIM, and CIBERESP, Barcelona; **Jordi Alonso**, MD, PhD, Health Services Research Group, IMIM, Department of Health and Experimental Sciences, UPF, and CIBERESP, Barcelona, Spain

Correspondence: Dr Jordi Alonso, IMIM-Institut Hospital del Mar d'Investigacions Mèdiques, PRBB Building, Doctor Aiguader 88, 08003 Barcelona, Spain. Email: jalonso@imim.es

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Article 4. *"Suicidal ideation risk among LGB Spanish university students: the role of childhood and adolescence adversities and mental disorders"*

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Supplementary material for this article can be found in ANNEX 4 (page 245).

SUICIDAL IDEATION RISK AMONG LGB SPANISH UNIVERSITY STUDENTS: THE ROLE OF CHILDHOOD AND ADOLESCENCE ADVERSITIES AND MENTAL DISORDERS

Andrea Miranda-Mendizabal[1,2], Pere Castellví[3,], Gemma Vilagut[1,4], Itxaso Alayo[1,4], José Almenara[5], Laura Ballester[1,4,6], Enrique Echeburúa[7], Andrea Gabilondo[8], Margalida Gili[9], Philippe Mortier[1], José Antonio Piqueras[10], Miquel Roca[9], Randy P. Auerbach[11,12], Ronny Bruffaerts[13], Ronald C. Kessler[14], Jordi Alonso[1,2,4] on behalf of the UNIVERSAL study group.

1 Health Services Research Group, IMIM-Institut Hospital del Mar d'Investigacions Mèdiques, Barcelona, Spain

2 Department of Health & Experimental Sciences, Pompeu Fabra University (UPF), Barcelona, Spain

3 Department of Medicine, Universitat Internacional de Catalunya (UIC), Barcelona, Spain

4 CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain.

5 University of Cádiz (UCA), Cádiz, Spain.

6 Girona University (UdG), Girona, Spain

7 University of the Basque Country (UPV-EHU), Bilbao, Spain.

8 Outpatient Mental Health Care Network, Osakidetza-Basque Health Service. Biodonosti Health Research Institute, San Sebastian, Spain.

9 Institut Universitari d'Investigació en Ciències de la Salut (IUNICS-IDISPA), University of Balearic Islands (UIB), Palma de Mallorca, Spain.

10 Miguel Hernandez University of Elche (UMH), Alicante, Spain.

11 Department of Psychiatry, Harvard Medical School, Boston, MA, USA.

12 Center for Depression, Anxiety and Stress Research, McLean Hospital, Belmont, MA, USA.

13 Universitair Psychiatrisch Centrum, KU Leuven (UPC-KUL), Leuven, Belgium.

14 Department of Health Care Policy, Harvard Medical School, Boston, MA, USA.

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ABSTRACT

Aims

To evaluate the role of childhood maltreatment and bullying on the relationship between sexual orientation, mental disorders and suicidal ideation (SI); and the role of mental disorders on the relationship between perceived sexual orientation discrimination and SI among LGB Spanish university students.

Methods

Data from baseline and 12-month follow-up online surveys of UNIVERSAL study, a cohort of Spanish freshmen students (18-24-year-olds), was used. Suicidal thoughts and behaviours (STB), mental disorders, childhood/adolescence adversities, sexual orientation and sexual orientation discrimination were assessed. Multiple logistic regression models estimated the risk for mental disorders and STB among LGBs. Path analysis estimated the effects of childhood/adolescence adversities in the relationship between sexual orientation and mental disorders, and SI; and the effect of mental disorders in the relationship between sexual orientation discrimination and SI.

Results

Statistically significant total effects of sexual orientation on mental disorders (β=0.179, SE=0.08) and on SI (β=0.415, SE=0.07) were observed. Indirect effects of childhood/adolescence adversities on the association between sexual orientation and mental disorders, and with SI, were significant. The ratio to the total effect of all mediation effects on the association between sexual orientation

and SI was 0.66. Mental disorders partially mediated the relationship between sexual orientation discrimination and SI (β=0.228, SE=0.12), ratio over the total effect 0.51.

Conclusions

Childhood/adolescence adversities and mental disorders mediate the association between sexual orientation and SI. Mental disorders partially mediate the association between sexual orientation discrimination and SI. Further research is needed to assess the mediators of the association between sexual orientation discrimination and SI.

INTRODUCTION

Suicide is the second leading cause of death among young adults [1]. Suicidal thoughts and behaviours (STB) are highly prevalent among sexual minority (LGB) young adults [2,3]. LGB youths have a two-fold risk for suicide attempt compared to heterosexuals, and risk remains high when stratifying by sex [4]. Data from 8 high-income countries showed that LGB freshmen have a three times higher risk for STB compared to their heterosexual counterparts [5].

LGB youths are highly exposed to childhood maltreatment (physical abuse, sexual abuse or neglect), with a prevalence ranging from 7.9% (physical neglect) to 12.7% (emotional abuse). These figures are higher than those found in comparable samples of heterosexuals [6]. Sterzing et al. found that poly-victimisation (e.g. 10 or more adverse events) is almost twice as much prevalent among sexual minority youths [7], involving multiple types of maltreatment [8–10]. Childhood maltreatment leads to a wide range of mental disorders (e.g. depression, anxiety, substance abuse, post-traumatic stress disorder) [11,12]. And childhood maltreatment has been consistently associated with an increased risk for suicidal ideation and suicide attempt [13–15], in particular, with the onset and persistence of STB during adolescence, even when controlling for lifetime mental disorders [16]. Thus, childhood maltreatment could mediate the relationship between mental disorders and STB.

LGB youths are also more exposed to stigma, discrimination and victimisation [17]. Bullying, including its physical form, is more frequent among LGB than

among heterosexual youths [18,19]. The minority stress model indicates the impact of external social conditions and structures (distal stressors) on individuals' stress processes, and of the proximal stressors such as the internalised experience of prejudice events (internalised homophobia) [20]. Both distal and proximal stressors create a social environment that substantially increases risk health behaviours and the risk for worse health outcomes [21–23] among LGB youths, including mental disorders [24–27] and STB [5,28–32]. Overlapping of risk characteristics (age, minority status) seems to increase the vulnerability for STB among LGB youths. There is a scarcity of similar data assessing mental health disparities among LGB university students.

In Spain, there is lack of data about mental health and the risk for STB among LGB youths, including university students. Health-related quality of life, including psychological aspects, has been evaluated among LGB individuals, but neither specifically among young adults nor university students [33]. The available data on university students only evaluate sexual behaviours related to sexual orientation [34]. In addition, there is neither data about minority stress risk factors nor information about childhood and adolescence adversities among LGB Spanish university students.

This study aims to estimate, among LGB Spanish university students, the prevalence of mental disorders (mood, anxiety, alcohol or substance abuse) and of suicidal thoughts and behaviours (STB) according to their sexual orientation. It also aims to evaluate the role of childhood/adolescence adversities up to the age of 17 (maltreatment, bullying) on the relationship between sexual orientation,

mental disorders and STB. Additionally, using the minority stress model as explanatory framework, we assess the role of mental disorders on the relationship between perceived sexual orientation discrimination and STB.

We hypothesised that the prevalence of lifetime and 12-month mental disorders and STB are higher among LGB Spanish university students compared to their heterosexual peers. We further hypothesised that childhood/adolescence adversities mediate the association between sexual orientation and mental disorders; and that the relationship between sexual orientation and STB is mediated by childhood/adolescence adversities and by mental disorders. Finally, the relationship between perceived sexual orientation discrimination and STB will be mediated by mental disorders.

METHODS

Study design

Longitudinal data from baseline (T1) (between October 2014 and October 2015) and 12-month follow-up (T2) online surveys from the "*University and Mental Health"* study (UNIVERSAL) were used. This study is part of the World Mental Health International College Student Initiative (WMH-ICS) [35]. Detailed description of the rationale and methods of the study are available in prior publication [36].

Sample and setting

A convenience sample of five public universities from different Spanish regions: Balearic Islands University (UIB), Basque Country University (UPV-EHU), Cádiz University (UCA), Miguel Hernández University (UMH) and Pompeu Fabra University (UPF). These universities represent about 8.2% from the total students' enrolment in public Spanish universities during 2014-15; while their overall distribution in terms of sex, age, study field and percentage of foreign students was similar to that of the overall population of students in public universities of Spain.

All freshmen students aged between 18 and 24 and enrolled in the participating universities for the first time were eligible to participate in the study (subjects under 18 years of age at the beginning of the academic year were eligible when they turned 18). Based on eligibility criteria, 16,332 students were suitable to participate.

Sample recruitment was performed in two stages. In the first stage, all eligible students were invited to participate of the study. Invitation methods across the universities included, for example: campus advertising campaigns (e.g., information stands, information in the classrooms, university web) and in some universities up to four personal e-mail invitation letters from the university authorities. Eligible students had to register to the survey and provide their informed consent before receiving a personalised link and password to access the baseline survey. In the second stage, a random subsample of non-respondents to the baseline survey was contacted by e-mail, including an economic incentive (25

€), to complete the survey ("endgame strategy"). In UPV-EHU, only first stage was carried out. Twelve months after completion of the baseline interview, respondents were contacted by e-mail with a link to complete the first follow-up survey. A raffle of academic materials (40 €) among all students who completed baseline and 12-month follow-up surveys was announced in recruitment campaigns. Protocol of the study was approved by the Parc de Salut MAR-Clinical Research Ethics Committee *(Reference number 2013/525/I).*

Variables

Suicidal thoughts and behaviours (STB)

At baseline (T1), lifetime suicidal thoughts and behaviours were assessed through: ideation *("Have you ever had thoughts of killing yourself?")*, plans *("Did you ever think about how you might kill yourself (e.g. taking pills, shooting yourself) or work out a plan of how to kill yourself?")* or attempts *("Did you ever make a suicide attempt (i.e., purposefully hurt yourself with at least some intent to die)?")*; from modified versions of the Self-Injurious Thoughts and Behaviors Interview (SITBI)[37] and Columbia-Suicide Severity Rating Scale (C-SSRS)[38]. At the 12-month follow-up (T2), respondents were presented an equivalent series of questions with the time frame adjusted.

Mental disorders

Probable cases of lifetime and 12-month mental health disorders were assessed, including mood disorder (major depressive or bipolar disorder), anxiety disorder

(panic or generalised anxiety disorder) and alcohol or substance disorder (abuse or dependence). The CIDI scale 3.0 [39] and a modified version of the Alcohol Use Disorders Identification Test, 10-item version (AUDIT-10) [40], were used for this purpose. A clinical re-appraisal study to control the validity of the research has been carried out, indicating a good concordance with the results of the self-reported data [41].

Sexual orientation

Items related to sexual orientation were developed based on recommendations of best practices [42]. For this study, answers to the question *"Which is your sexual orientation?"* were used, with the following response options: *"Heterosexual"*, *"Gay or lesbian"*, *"Bisexual"*, *"Asexual"*, *"I am not sure"*, *"Other (open answer)"* and *"I prefer not to answer"*.

Perceived sexual orientation discrimination

In the follow-up survey, homosexual and bisexual participants reported experiences with 9 discrimination events in the past 12 months from the Multiple Discrimination Scale (MDS), which assesses behavioural expressions of prejudice, including interpersonal discrimination (from close people, partners, strangers, others), institutional discrimination (verbal, housing, healthcare) and violent discrimination (physical, property) related to sexual orientation [43]. The scale items have been previously used and demonstrated to be valid and reliable [44]. In addition, some items have been previously used to assess other kinds of discrimination [45,46].

Childhood and adolescence adversities

Childhood maltreatment, prior to the age of 17, was assessed with 8-items including emotional maltreatment, physical abuse, sexual abuse and neglect (e.g. *"Someone in your family repeatedly said hurtful or insulting things to you"*, *"Someone in your family hit you so hard that it left bruises or marks"*). Four items assessed physical and verbal victimisation (*"How often were you bullied at school: physically/verbally by someone who purposefully ignored you, excluded you, or spread rumours about you behind your back?"*) and cyberbullying (*"How often were you bullied over internet or by text messaging?"*). Items were adapted from the CIDI 3.0 [39], the Adverse Childhood Experiences Scale (CES) [47] and the Bully Survey (BS) [48].

Socio-demographic

Gender, university, academic field, country of birth, parents' educational level and living location at first term (parents' home or others) were also evaluated and used here.

Analysis

Missing item-level data among respondents were imputed using multiple imputation (MI) by chained equations [49] with 43 imputed datasets, equivalent to the percentage of incomplete subjects [50], and 10 iterations per imputation. To correct the bias caused by lost to follow up missing values, inverse-probability weighting (IPW) [51,52] was applied, calculated as the inverse of the estimated probability of completing the follow-up survey on observed related covariates,

using a logistic regression model. Additionally, post-stratification weights were used to restore population distribution of sex, country of birth and academic field within each university, as well as population distributions across universities (further details available upon request).

Descriptive analyses were performed. Lifetime and 12-month prevalence of mental disorders: mood disorder, anxiety disorder and alcohol or substance disorder (abuse or dependence); and of suicidal ideation, plan and attempt, stratified by sexual orientation, were estimated. Multiple logistic regression models adjusted by age, gender, country of origin, university and academic field were estimated to assess the relationship between belonging to a sexual minority and the presence of mental disorders and STB. Adjusted odds ratios (aORs) and MI-based CIs were obtained. Categories with a very low number of observations (<10), which included transgender (n = 6) and asexual (n = 9), were excluded for the analysis. SAS software version 9.4 was used.

Path analysis was used to estimate, through simultaneous regression sub-models, the following relationships: 1) the relationship between sexual orientation and both mental disorders and suicidal ideation (SI), and the extent to which these relationships are mediated by childhood/adolescence adversities. Specifically, we will estimate the total effect of sexual orientation on mental disorders and on SI, the indirect effect of childhood/adolescence adversities on the relationship between sexual orientation and mental disorders, and SI, the simultaneous mediating effect of childhood/adolescence adversities and mental disorders on the relationship between sexual orientation and SI; and the direct effects of sexual

orientation on mental disorders and on SI not mediated by the remaining variables; 2) among homosexual and bisexual respondents, the relationship between perceived sexual orientation discrimination and SI, and the extent to which this relation is mediated by mental disorders. Specifically, the indirect effect of mental disorders on the relationship between perceived sexual orientation discrimination and SI, and the direct effect not mediated by mental disorders will be estimated.

The models were fitted using unweighted least squares estimator with categorical variables, with adjustment for mean and variance for robust model testing and standard error. Model fit was assessed by the comparative fit index (CFI), the Tucker-Lewis index (TLI) and the root-mean-square error of approximation (RMSEA). Indicators of acceptable model fit were considered to be >.90 for CFI and TLI and <.06 for RMSEA [53]. Statistical significance in all analyses was evaluated using two-sided MI-based tests with significance level α set at 0.05. The present study involved a relatively small sample due to both the hard-to-reach nature of the LGB population and low prevalence of the assessed outcomes. Therefore, even when we aimed to assess STB, only SI could be included in path analysis. Analyses were conducted in MPlus 8.1 (Muthén and Muthén, Los Angeles, CA). Path analyses controlled for sex, age and country of origin.

RESULTS

All the percentages presented below are weighted percentages.

A total sample of 1,224 students who responded the follow-up survey was included. Most of the students came from the Basque Country University (UPV-EHU) (43.8%) and studied Social or Legal Sciences (47.9%). Heterosexuals represented 83.6% of the weighted sample. Among the sexual minority groups, most of the students reported not being sure about their sexual orientation (representing 5.8% of the students' population), followed by bisexual (5%) and homosexual (gay/lesbian) (4.9%). Only 9 students reported being asexual or another sexual orientation not matching with the response options (0.7%). Seventy-eight percent of homosexual students were male, and more than half of both bisexual and unsure students were female. Prevalence of any childhood maltreatment ranged from 35.1% in homosexuals to 59.7% in asexual/other, while emotional maltreatment was the most common (from 22.2% in unsure to 56.3% in asexual/other). Twenty-four percent of heterosexual students reported some sort of childhood maltreatment. Most frequent form of bullying among LGB students was verbal form (from 27.2% in asexual/other to 69.9% in homosexuals). Detailed information about the distribution of the assessed variables is presented in **Table 1**.

-- Insert Table 1 --

Sixteen percent of homosexual students were insulted or made fun of by somebody due to their sexual orientation in the last 12 months; similarly happened to 7.1% of bisexual students. Almost 12% of homosexual and 14% of bisexual students were treated with hostility or coldness by strangers due to their sexual orientation. The 9.3% and 5.7% of homosexual and bisexual students,

respectively, were ignored, excluded or avoided by close people. Nobody reported discrimination in the health services **(Table S1)**.

Analysis of the risk for lifetime and 12-month mental disorders and STB for LGB students showed elevated odds of lifetime and 12-month mood disorder for bisexual students (Lifetime: aOR 4.7; 95%CI 2.6-8.3; 12-month: aOR 2.8; 95%CI 1.5-5.2) and unsure students (Lifetime: aOR 2.1; 95%CI 1.3-3.6; 12-month: aOR 2.2; 95%CI 1.3-4.0). The odds of both lifetime and 12-month alcohol or substance disorder was more than twice as higher among bisexual students compared to heterosexuals (Lifetime: aOR 2.7; 95%CI 1.6-4.7; 12-month: aOR 2.8; 95%CI 1.6-4.8). Odds of any lifetime mental disorder was higher among unsure (aOR 2.1; 95%CI 1.3-3.6) and bisexual (aOR 4.1; 95%CI 2.0-8.4) students. For the latter, 12-month probability of any mental disorder was also higher (aOR 3; 95%CI 1.7-5.4). The odds of lifetime suicidal ideation (SI) was between two or more than three times higher for LGB students (*Homosexual* aOR 2.4; 95%CI 1.3-4.4; *Bisexual* aOR 3.4; 95%CI 2.0-5.9; *Unsure* aOR 3.6; 95%CI 2.1-5.9). Similar results were seen for 12-month probability, but only for bisexual students (aOR 3.9; 95%CI 1.9-8.3) and unsure (aOR 2.8; 95%CI 1.3-6.0) students. Increased odds of lifetime suicide attempt were seen for homosexual (aOR 6.1; 95%CI 1.1-32.2) and unsure (aOR 5.1; 95%CI 1.2-20.7) students **(Table 2)**.

-- Insert Table 2 --

A path analysis model to assess the relationship between sexual orientation, mental disorders and SI, and the role of childhood/adolescence adversities (maltreatment, bullying) on these relationships, was carried out **(Figure 1)**. Model goodness of fit was adequate (CFI=0.975; TLI=0.944; RMSEA=0.023, σ =0.002). A statistically significant total effect was found of any sexual orientation on mental disorders (standardised coefficient β=0.179, SE=0.08, p=0.025) and on SI (β=0.415, SE=0.07, p<.001).

Indirect effects. For any sexual orientation, the indirect effects of childhood maltreatment (standardised coefficient β=0.104, SE=0.04, p=0.004) and bullying (β=0.099, SE=0.04, p=0.008) on the relationship between sexual orientation and any mental disorder were significant. The indirect effects of childhood maltreatment (β=0.128, SE=0.04, p=0.001) and bullying (β=0.097, SE=0.04, p=0.004) on the relationship between sexual orientation and SI were also statistically significant, with a ratio over the total effect of 0.54. The indirect effect mediated by any mental disorder was β=0.05 (SE=0.03). The ratio to the total effect of all mediation effects considered in the relationship between sexual and SI was 0.66. Path analysis for each of the sexual orientation categories are presented as supplementary material **(Figures S1, S2 and S3)**.

Direct effects. Any sexual orientation was positively associated with childhood maltreatment (standardised coefficient β=0.352, SE=0.08, p<.001), bullying (β=0.403, SE=0.07, p<.001) and SI (β=0.139, SE=0.10, p=0.165). However, the latter was not found to be statistically significant at the significance level α=0.05.

The direct effect of sexual orientation on any mental disorder (β=-0.024, SE =0.11) did not show statistical significance either. **Table 3** summarises the total and direct effects of sexual orientation on any mental disorders and SI, and the indirect effects of childhood/adolescence adversities and any mental disorders; as well as the ratio of all the indirect and direct effects over the total effect.

-- Insert Table 3 --

A second path analysis was conducted to assess the relationship between perceived sexual orientation discrimination and SI among homosexual and bisexual respondents and the extent to which this relationship is mediated by any mental disorder **(Figure 2)**. The results showed **a standardised total effect** of β=0.451 (SE=0.15, p-value=0.003). The **direct effect** of perceived discrimination due to sexual orientation on any mental disorder was β=0.346 (SE=0.15, p=0.023). In turn, any mental disorder was significant associated with SI (β=0.660, SE=0.15, p<.001). Therefore, the **mediation effect** of any mental disorder on the relationship between perceived sexual orientation discrimination and SI was β=0.228, SE=0.12, p=0.059, representing a ratio over the total effect of 0.51. The **direct effect** between perceived sexual orientation discrimination and SI was similar in magnitude (β=0.223, SE=0.19; p=0.240), although it was not found to be statistically significant. Model goodness of fit was adequate (CFI=0.968; TLI=0.928; RMSEA=0.06, σ=.007).

DISCUSSION

Our results show that LGB university students and those who are unsure about their sexual orientation have an increased risk for suicidal thoughts and behaviours (STB). For those unsure and for bisexual students, the risk for any mental disorder is also higher. A novel finding is that the effect of sexual orientation on suicidal ideation (SI) is mediated by both childhood/adolescence adversities and mental disorders. Specifically, perceived sexual orientation discrimination increases the risk for mental disorders among homosexual and bisexual Spanish university students. Mental disorders partially mediate the relationship between perceived sexual orientation discrimination and SI. The direct effect of perceived sexual orientation discrimination appears to be not statistically significant. This is more likely due to the small size of the subsample studied than an actual no mediating effect. This study fills a knowledge gap about the risk for mental disorders and STB among LGB Spanish university students. It also describes the role of childhood adversities (maltreatment, bullying), perceived sexual orientation discrimination and mental disorders in the risk for SI among this population.

Comparison with other studies

Consistent with previous research [3,5,54], the risk for STB among LGB Spanish university students is much higher than for heterosexuals. A higher risk for mental disorders was also found, specifically for bisexual students and those unsure about their sexual orientation. The increased risk for STB and mental

disorders among LGB university student could be related to the hostile environment caused by the adverse experiences (e.g. discrimination, bullying) suffered by them.

Childhood maltreatment and bullying mediate the association between sexual orientation, mental disorders and SI. For LGBs, the risk for SI seems to be higher when both childhood/adolescence adversities and mental disorders appear. The burden of childhood maltreatment is significantly greater among sexual minority youths compared to heterosexuals [55,56]. A previous study reported that childhood maltreatment ranged from 7.9% (physical neglect) to 12.7% (emotional abuse) among LGB youths, higher than rates found in comparable samples of heterosexuals [6]. In comparison, our data show considerably higher proportions of childhood maltreatment among LGB university students. Exposure to childhood maltreatment causes emotional dysregulation [57], which in fact predisposes mental disorders [58].

Perceived sexual orientation discrimination increases the risk of suffering a mental disorder. This finding is coherent with the minority stress model which shows that stressful social environment causes mental health problems [20]. It is in part through the development of mental disorders that sexual orientation discrimination is associated with SI. The effect size of sexual orientation discrimination on SI is similar to that of mental disorders, even though results are not statistically significant. Our results tend to concur with those of Burton et al., showing that sexual minority-specific discrimination was responsible for the higher prevalence of depressive symptoms and suicidality in LGB adolescents.

Showing a smaller effect size on suicidality than on depressive symptoms [59]. In addition, our findings are consistent with previous findings showing that discriminatory experiences work as stressors for LGB people and, in turn, are significantly associated with mental disorders [60], psychological distress [60–62] and depressive symptoms [59,60].

Perceived sexual orientation discrimination may contribute to additional stress for LGBs beyond the general life stressors that all people experience [20]. Previous studies showed that internalised homophobia mediates in the association between discrimination and symptoms of depression [63]. This suggests that internalised homophobia may have an important role in the association between discrimination and STB and, more specifically, SI. However, we could not include internalised homophobia in our analyses due to a small sample. Larger studies are needed to determine the mediating factors between discrimination and STB.

Our study suggests that experiencing any kind of abuse during childhood or adolescence, including sexual orientation discrimination, can adversely affect the mental health of LGB young adults and increase the risk for mental disorders and suicidality. Previous literature suggests that psychological distress and internalised homophobia may be implicated [6]. The specific mechanisms could not be examined in this study. Further research is needed to clarify whether internalised homophobia or psychological distress mediate the association between perceived sexual orientation discrimination and STB. In addition, studies including bigger samples of LGB youths are needed.

Strengths and limitations

For the best of our knowledge this is the first study testing mediation models of childhood/adolescence adversities on the risk for mental disorders and SI among LGB university students. The study provides evidence about mental health disparities among LGB Spanish university students for the first time. In addition, it is also pioneer in assessing the role of mental disorders in the relationship between perceived sexual orientation discrimination and SI among Spanish LGB university students. Finally, data comes from a study which is part of an international initiative (World Mental Health International College Survey (WMH-ICS)), using a highly standardised method in several countries, which facilitates future comparisons.

Some study limitations should be considered when interpreting our results. First, the sample of interest (LGB students) was relatively small, due to the cumulative effects of a low response rate at baseline survey and, at a lower extent to some follow-up losses. Therefore, even though some differences in the risk for mental disorders and STB among LGBs by gender have been previously reported [25,54,68,69] this could not be assessed. However, the proportion of LGB subsample was similar to the observed in university studies [5,64,65]. Second, lack of statistical power due to low response rate and missing data should be considered, but they have been amended applying population-based adjustments and inverse-probability weights, which have proven to be an effective method for reducing non-response bias [66,67]. Third, the assessment of mental disorders and STB was based on self-reports and not on direct clinical assessment.

Nonetheless, we performed a clinical reappraisal study showing a good diagnostic agreement has been reported with clinical judgement [41].

Conclusions

Spanish LGB university students are or have been more frequently exposed to any form of maltreatment or discrimination (childhood maltreatment, bullying and perceived sexual orientation discrimination). This exposure is associated with a higher risk for mental disorders. Childhood/adolescence adversities and mental disorders both mediate the association between sexual orientation and SI. The association between perceived sexual orientation discrimination and SI is partially mediated by mental disorders. Further research should clarify whether there are other factors involved in the association between discrimination due to sexual orientation and SI.

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Table 1. Characteristics of the students included in the analysis according to sexual orientation (absolute numbers and weighted proportions). The UNIVERSAL (*University and Mental Health*) study.

		Heterosexual n = 1,029		**Homosexual (Gay/Lesbian) n = 43**		**Bisexual n = 70**		**Unsure n = 73**		**Asexual/ other n = 9**		**Total n = 1224**	
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Age													
	18	764	67.9	31	58.4	48	65	61	86.3	5	41.5	909	68.2
	>18	265	32.1	12	41.6	22	35	12	13.7	4	58.5	315	31.8
Gender													
	Female	788	57.2	15	21.3	58	62.7	51	54	9	100	921	55.8
	Male	235	42.4	28	78.7	12	37.3	20	44.4	--	--	295	43.8
	Transgender	6	0.4	--	--	--	--	2	1.6	--	--	8	0.4
Centre													
	Basque Country University (UPV-EHU)	329	40.5	12	49.1	27	63.1	39	69.9	3	44.8	410	43.8
	Pompeu Fabra University (UPF)	301	13.4	16	18.2	22	12.3	22	13.5	2	7.7	363	13.6
	Balearic Islands University (UIB)	151	13.8	8	12.3	5	4.7	2	2.7	--	--	166	12.5
	Cádiz University (UCA)	132	21.6	5	13.7	5	4.1	2	5.6	3	40.6	147	19.5
	Miguel Hernandez University (UMH)	116	10.7	2	6.8	11	15.8	8	8.3	1	6.9	138	10.6

Table 1 *(continued)*

Academic Field													
	Arts and Humanities	112	8.2	7	13.6	13	13.4	10	21.4	3	16.4	145	9.5
	Science	96	8.1	6	17.6	5	4.6	10	9.2	--	--	117	8.4
	Health Sciences	286	16	7	7.7	16	13.1	20	18.6	2	10.8	331	15.5
	Social and Legal Sciences	399	47.9	21	54.8	27	49.4	26	38.8	3	54.6	476	47.9
	Engineering and Architecture	136	19.8	2	6.3	9	19.5	7	12	1	18.2	155	18.6
Country of birth													
	Spain	957	95.5	39	93.6	61	86.9	69	97.5	9	100	1135	95.2
	Non Spain	72	4.5	4	6.4	9	13.1	4	2.5	--	--	89	4.8
Parents' university studies													
	At least one	502	45.5	13	22.9	33	48.2	30	29.1	5	41	583	43.5
	Neither	527	54.5	30	77.1	37	51.8	43	70.9	4	59	641	56.5
Living at first term													
	Parents' home	590	57.7	25	67.4	44	61.1	45	62.2	7	62.3	711	58.7
	Other	439	42.3	18	32.6	26	38.9	28	37.8	2	37.7	513	41.3
Childhood maltreatment	Emotional	205	18	12	31	23	29.3	19	22.2	3	56.3	262	19.7
	Physical	93	8.1	6	11.2	14	25.1	11	18.6	3	56.3	127	10.1
	Sexual	11	1	1	0.6	3	6.7	2	2.2	--	--	17	1.3
	Neglect	59	6	6	10.7	8	14.9	13	20	1	3.4	87	7.4
	Any	206	24.4	15	35.1	28	45.2	30	43.5	4	59.7	337	27.3

Table 1 *(continued)*

Bully victimisation	Physical	54	5.4	6	18.4	9	13.5	3	5	--	--	72	6.4
	Verbal	304	27.7	24	69.9	33	51.1	27	34.6	5	27.2	393	31.4
	Cyber	25	2.2	2	8	8	11	2	4.3	--	--	37	3
	Any	310	28.6	24	69.9	33	51.1	27	34.6	5	27.2	400	32.1
Mental disorders[(a)]													
Mood	Lifetime	358	31.5	19	28.7	44	66.3	38	48.5	3	40.2	462	34.2
	12-month	173	16.6	12	18.6	28	33	21	28.9	3	40.2	273	18.4
Anxiety	Lifetime	304	26.2	14	18.5	25	37	24	32.5	4	49.1	372	26.9
	12-month	166	15	9	12.3	17	23	13	16	3	30.4	208	15.4
Substance	Lifetime	246	27.4	15	28.9	30	53.5	28	37	4	45.4	324	29.5
	12-month	220	24.8	13	21.9	18	32.2	26	33.7	4	45.4	291	26.6
Any mental disorder	Lifetime	575	55.1	26	44.6	57	83.8	49	71.4	6	72.7	713	57.1
	12-month	393	39.8	21	36.2	46	67.4	38	49.5	6	72.7	504	41.8
Suicidal thoughts and behaviours													
Ideation	Lifetime	239	20.6	21	39.2	41	48.8	38	49.1	5	63.6	344	24.9
	12-month	66	5.7	7	7	16	18.1	15	13.4	4	59.7	108	7.2
Plan	Lifetime	135	12.9	15	34.4	31	32.6	21	25.1	5	63.6	207	16
	12-month	39	3.4	4	4.7	7	7.4	8	7.5	4	59.7	62	4.3
Attempt	Lifetime	16	1.1	3	3.6	3	3.7	4	4.2	--	--	26	1.5
	12-month	2	0.3	1	1	--	--	2	1.2	--	--	5	0.3

[(a)] **Mood** includes major depression or bipolar disorder; **Anxiety** includes panic disorder or generalised anxiety disorder; **Alcohol or substance** includes abuse or dependence.

Table 2. Bivariate associations between sexual orientation, mental disorders and suicidal thoughts and behaviours among Spanish university students. The UNIVERSAL (*University and Mental Health*) study (n = 186).

		Homosexual (Gay/Lesbian)*		**Bisexual***		**Unsure***	
		aOR**	**95%IC**	**aOR****	**95%IC**	**aOR****	**95%IC**
Mental disorders[(a)]							
Mood	Lifetime	0.9	0.5-1.7	**4.7**	**2.6-8.3**	**2.1**	**1.3-3.6**
	12-month	1.2	0.6-2.3	**2.8**	**1.5-5.2**	**2.2**	**1.3-4.0**
Anxiety	Lifetime	0.8	0.4-1.6	1.5	0.8-2.7	1.4	0.8-2.5
	12-month	0.9	0.4-2.1	1.5	0.8-2.8	1	0.5-2.1
Substance	Lifetime	0.9	0.5-1.6	**2.7**	**1.6-4.7**	1.5	0.9-2.6
	12-month	0.6	0.3-1.3	**2.8**	**1.6-4.8**	1.4	0.8-2.5
Any mental disorder	Lifetime	0.7	0.4-1.2	**4.1**	**2.0-8.4**	**2.1**	**1.2-3.6**
	12-month	0.8	0.4-1.4	**3.0**	**1.7-5.4**	1.4	0.9-2.4
Suicidal thoughts and behaviours							
Suicidal ideation	Lifetime	**2.4**	**1.3-4.4**	**3.4**	**2-5.9**	**3.6**	**2.1-5.9**
	12-month	1.2	0.4-3.6	**3.9**	**1.9-8.3**	**2.8**	**1.3-6.0**
Suicidal attempt	Lifetime	**6.1**	**1.1-32.2**	2.1	0.4-10.5	**5.1**	**1.2-20.7**

*** Category of reference:** heterosexuals.

***Adjusted by:** age, sex, country of origin, university and academic field.

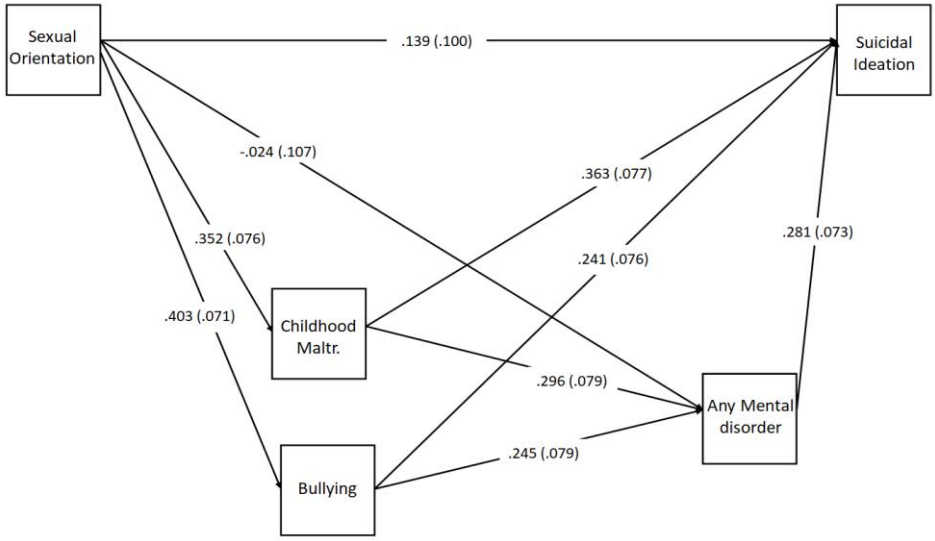
[(a)] Mood includes major depression or bipolar disorder; **Anxiety** includes panic disorder or generalised anxiety disorder; **Alcohol or substance** includes abuse or dependence.

Table 3. Total, direct and indirect standardised effects of sexual orientation, any mental disorder, childhood maltreatment and bullying on suicidal ideation. Path analysis results. The UNIVERSAL (*University and Mental Health*) study (n = 1,224).

	Standardised Effect (SE)	**p-value**	**Ratio over the total effect**
Sexual orientation to any mental disorder			
Total effect	0.179 (0.08)	0.025	
Total indirect	0.203 (0.06)	0.06	1.13
Indirect through childhood maltreatment	0.104 (0.04)	0.004	0.58
Indirect through bullying	0.099 (0.04)	0.008	0.55
Direct effect	-0.024 (0.11)	0.82	-0.13
Sexual orientation to suicidal ideation			
Total effect	0.415 (0.07)	<0.001	
Total indirect	0.275 (0.06)	<0.001	0.66
Indirect through any mental disorder*****	0.050 (0.03)	0.05	0.12
Indirect through childhood maltreatment	0.128 (0.04)	0.001	0.31
Indirect through bullying	0.097 (0.03)	0.004	0.23
Direct effect	0.139 (0.10)	0.165	0.34

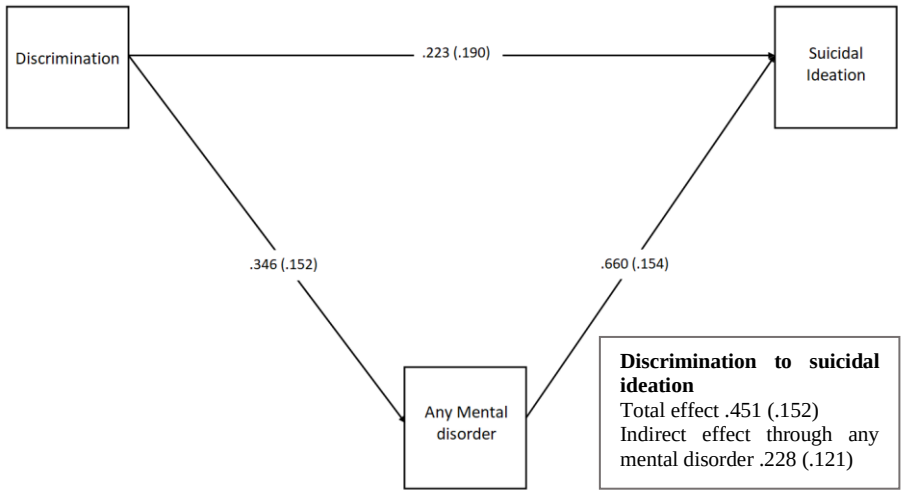
***Sum of the following indirect effects:** a) Indirect effect through maltreatment and any mental disorder; b) indirect effect through bullying and any mental disorder; c) Indirect through any mental disorders (not through maltreatment nor bullying).

Figure 1. Path analysis model depicting the direct and indirect effects of childhood/adolescence adversities, mental disorders on suicidal ideation among LGB Spanish university students. The UNIVERSAL (*University and Mental Health*) study (n = 1,224).



Values represent standardised path coefficients and corresponding multiple imputations adjusted standard errors within parenthesis. **Sexual orientation:** sexual orientation: homosexual, bisexual or unsure (lifetime); **Childhood maltr.:** any childhood maltreatment prior to 17 years of age; **Bullying:** any form of bullying prior to 17 years of age; **Any mental disorder:** any mental disorder (lifetime); **Suicidal ideation:** suicidal ideation (lifetime).

Figure 2. Path analysis model depicting the direct and indirect effects of perceived sexual orientation discrimination and mental disorders on suicidal ideation among homosexual and bisexual Spanish university students. The UNIVERSAL (*University and Mental Health*) project (n = 113).



Values represent standardised path coefficients and corresponding MI-adjusted standard errors within parenthesis. **Discrimination:** perceived sexual orientation discrimination among homosexual and bisexual students (12-month); **Any mental disorder:** any mental disorder (12-month); **Suicidal ideation:** suicidal ideation (12-month).

6. SUMMARY OF FINDINGS AND DISCUSSION

In this doctoral thesis, the risk for suicidal thoughts and behaviour (STB) according to gender and sexual orientation was examined together with other risk and protective factors, carrying out a systematic review of the literature with meta-analysis. It was also examined with empirical data from a cohort study (UNIVERSAL) of Spanish university students. Results responding to the five specific objectives formulated in this thesis are summarised and discussed in this section, addressing first the role of gender, and then the role of sexual orientation.

1. **Gender commonalities and differences in the risk for suicidal thoughts and behaviours (STB) among adolescents/young adults**

a) **Objectives:** ***to assess the risk for suicidal thoughts and behaviours (STB) and to identify risk and protective factors for STB according to gender among adolescents/young adults.***

Summary of findings

Female adolescents/young adults are at higher risk for suicide attempt compared to males of the same age. In contrast, males have higher risk for suicide. Our systematic review was based on observational analytical studies analysing gender as a risk factor for

STB, among other factors. Regarding the risk for suicide, we can only provide the evidence from one of the included studies and from what is known by mortality statistics showing that suicide more often occurs among males. Due to lack of additional studies, a meta-analysis could not be performed.

We identified risk factors for suicide attempt and suicide death among adolescents/young adults which are not related to gender. These include having any previous mental or substance abuse disorder, and having been exposed to interpersonal violence (i.e., bullying, childhood maltreatment, community violence). Additionally, for suicide death, having relatives with a previous history of suicidal behaviour is also a risk factor among both males and females. For attempted suicide, risk factors which were only identified among women include mental disorders (eating disorder, post-traumatic stress disorder (PTSD), bipolar disorder and symptoms of depressive disorder), having been a victim of dating violence, having interpersonal problems and previous abortion. Male-specific risk factors for suicide attempt are disruptive behaviour/conduct problems, hopelessness, parental separation/divorce, friends' suicidal behaviour and having access to suicide means. The latter also increases the risk for suicide death, as well as for drug abuse and conduct disorders. We did not identify specific risk factors for suicide among females in this thesis. This result is related to the scarcity of studies analysing the risk for suicide and its associated risk and protective factors among women.

This finding, in turn, is likely due to the fact that suicide is a rare outcome in this group.

To further accomplish this thesis' objectives, data of an empirical study of Spanish university students (UNIVERSAL study) were analysed. Specifically, we investigated how risk and protective factors for suicidal ideation (SI) interacted with gender. We found that lifetime mood disorder is a common risk factor for SI in both genders. Female-specific risk factors include exposure to violence between parents, anxiety disorder and alcohol/substance disorder. Male-specific risk factors include physical childhood maltreatment, death of any of the parents and hopelessness. Family and peer support exert a protective effect for SI among females only.

Discussion

Female adolescents/young adults have higher risk for suicide attempt, while there is scarcity of data about the risk for suicide

Our finding of a high risk for suicide attempts among female adolescents/young adults is consistent with previous findings [57,136], while males being at higher risk for suicide is congruent with information obtained from vital statistics registries. However, there is still scarcity of data assessing the risk for suicide among adolescents/young adults as well as the related risk factors and protective factors. Further longitudinal studies assessing both the risk for suicide and the implicated factors are needed.

Regardless of gender, mental disorders and previous adversities increase the risk for STB among adolescents/young adults

Meta-analyses of published literature and the results from the UNIVERSAL study tend to agree in regard of the role of gender and the risk factors for STB among adolescents/young adults. Specifically, a history of any mental disorder, including mood disorder, increases the risk for suicide attempts and suicide among adolescents/young adults, while suffering from a mood disorder increases the risk for suicidal ideation more than five times among Spanish university students of both genders.

Our findings show that having been exposed to childhood and adolescence adversities (childhood maltreatment, bullying and community violence) also significantly increases the risk for STB among female and male youths. Previous results showed that youth who die by suicide had experienced childhood maltreatment more often and at an earlier age than their peers: 60% *vs* 18% by age 9 and 77% *vs* 34% by age 14 [137]. The impact of childhood maltreatment seems to depend on the age when it occurred, affecting the individual's ability to flourish cognitively, emotionally and behaviourally in their environment [138]. Sexual abuse has been strongly related to suicide attempt among youths. The magnitude of this association is stronger in boys than in girls [35] and it is independent of the presence of physical or emotional maltreatment. But the difference in the magnitude of association has not been evident in young adults [139]. Similarly, the results obtained in this

thesis do not show a gender difference in the magnitude of the association between different types of childhood maltreatment and STB. The gender difference in the magnitude of this association suggests that the nature, timing and reporting of the abuse may also differ across genders. On the one hand, childhood sexual abuse among boys typically occurs prior to puberty, is more forceful and usually perpetrated by another male [139]. On the other hand, episodes of childhood sexual abuse are more often reported by females [139,140]. Lower rates of reported abuse among males could be due to their relative reluctance to disclose the abuse [141].

Many risk factors for STB among adolescents/young adults differ by gender

Among females, the risk for STB is mostly related to internalising disorders and to conflicts in interpersonal relationships. For males, externalising disorders, parental separation or death, hopelessness and access to means seem to have an important role in the risk for STB. Access to means has been consistently mentioned as a relevant risk factor for STB, predominantly among males [142]. In contexts where a high percentage of households own firearms, it is likely that access to means becomes even more relevant. In the United States there are 120 civilian firearms per 100 persons, while in Spain this estimate is substantially lower: 7.5 civilian firearms per 100 persons [143]. Ecological studies have consistently linked state, regional and national levels of firearm availability with firearm-related suicide rates among various demographic groups [144–

[146] as well as overall suicide rates [147], particularly among people under the age of 25 [148–150]. Access to means was only analysed through the systematic review and meta-analysis. Among female adolescents/young adults, no studies assessing the role of access to means were found to fulfil inclusion criteria. Therefore, before conclusions can be reached, further studies assessing the role of access to means in adolescents/young adults are needed.

Gender differences in the associations of STB with internalising and externalising disorders, interpersonal problems and stressful events (such as parental separation or death of any of them), may be due to different coping strategies used by females and males to regulate their emotions and face stressful life events. In general, females have a larger repertoire of emotion regulation strategies, but their effectiveness, specifically of the adaptive ones (e.g. reappraisal), depends on the context in which they are used [151]. In fact, coping strategies can be determined by macro-level social contexts which may model and reinforce conformity to expected 'masculine' or 'feminine' perceptions, emotions and behaviours. However, maladaptive strategies (e.g. rumination) may have detrimental effects in a wider range of circumstances, increasing the possibility of psychopathology [151]. Males usually drink alcohol to cope, which may partially account for their higher frequency of alcohol misuse, compared to females. Another frequent emotion regulation strategy among males is anger rumination, linked to greater aggressive behaviour in youth and adult males [152,153], which, in turn, is associated with externalising disorders and STB[60]. Most of the

results in this thesis would be consistent with the above explanations. However, we found that for Spanish university students, alcohol or substance abuse increases the risk for STB among females only. Further longitudinal research is needed to confirm whether there are differences by gender in the mechanisms through which alcohol and substance abuse increase the risk for STB.

b) Objective: ***to determine if there are any differences between genders in the associations of the identified risk factors and protective factors for STB among Spanish university students.***

Summary of findings

Among Spanish university students, significant gender interactions were observed for the association between suicidal ideation (SI) and violence between parents, lifetime anxiety disorder, hopelessness, chronic health conditions or physical impairment and family support.

Discussion

Significant interactions between gender and some of the risk factors for SI suggest gender-specific variations in the causal mechanisms underlying the associations between risk factors and SI. Some of the mechanisms underlying those differences have been already

discussed above. Below, gender differences in the association between hopelessness and family support with SI will be discussed.

Hopelessness is quite predictive of suicidal ideation[154] and it is believed to play an important intermediate role between a stressful event and subsequent suicidal behaviours [155]. Very few studies have evaluated gender differences in hopelessness among individuals with STB, and results have been largely inconclusive. A previous review on gender differences in depression concluded that there is insufficient evidence to support the widely held notion that cognitive parameters, such as hopelessness, predispose females to mood disorders (19).

Differences in coping strategies and differences in female's and male's environment could be the key to better understand the mechanism through which hopelessness increases the risk for mental disorders and STB. Among university students, it has been reported that the perception of social support mediates the relationship between depressive symptoms and SI[156]. In particular, among those students with higher levels of social support, the association between depressive symptoms and hopelessness was diminished. A university student who feels depressed, but has a strong supportive social network, may be protected against developing hopelessness about his or her situation and, in turn, be less likely to experience suicidal ideation[156].

In general, females are mostly embedded in a social network, whereas the males' environment is characterised by isolation and competition. In this competitive world of men, men have many difficulties to talk about their suffering, hopelessness and suicidal thoughts with close persons or professional caregivers [157–159]. However, as a coping strategy, males may engage in activities with friends more than women, but they do not label these activities as peer support or coping strategies [151]. Also, the tendency among males to solve their problems on their own, and to consider seeking for help as the recognition of incompetence, results in fewer contacts with mental health services [157,160]. Women, in contrast, might not consider the need for help as negative and have a greater capacity to ask for it [157–159,161].

Males' desire for self-management may explain the gender differences suggested by the observed interaction between gender and family support; it might also explain the protective effects of such support observed only among female university students. It is also likely that male adolescents/young adults with a favourable family environment feel a need to cope with stressful situations on their own [162]. They also might perceive serious problems as minor or transient (e.g. heavy alcohol consumption) [163], leading them to not seek help in their families. This issue points to the need for further research to clarify whether the perception of level of family support is lower among males. In addition to gender differences in the seeking of help, such a lower level could be based on a cultural

belief that males are stronger and should be able to face adversities on their own [140].

2. Sexual orientation and the risk for suicidal thoughts and behaviours (STB) among adolescents/young adults

a) Objective: ***to assess the risk for suicidal thoughts and behaviours (STB) among lesbian, gay and bisexual (LGB) adolescents/young adults and to identify risk and protective factors for STB in this group.***

Summary of findings

Based on the results of this thesis, LGB adolescents/young adults have higher risk for STB compared to heterosexuals. Specifically, homosexual (gay/lesbian) and bisexual Spanish university students, and those who are not sure about their sexual orientation, show a two to more than three times higher risk for suicidal ideation (SI) than their heterosexual peers. An increased risk for lifetime suicide attempt was also observed for homosexual students and students reporting not being sure about their sexual orientation, but not among bisexual students.

Based on the results of the systematic review of the literature and the meta-analyses, the risk for suicide attempt is higher among gay or bisexual male adolescents/young adults, compared with heterosexuals. This association holds when gay and bisexual males

are analysed separately. Apparently, no risk for suicide attempt exists for lesbian or bisexual female adolescents/young adults. This association is statistically significant only when lesbians are compared to heterosexual women. However, these results should be interpreted with caution because they are based on a limited amount of data due to shortage of literature assessing the risk for STB stratified by gender among LGB adolescents/young adults.

A non-significant positive association between depression and suicide attempt among LGB adolescents/young adults was found. However, this result comes from a meta-analysis of solely two studies because only a few studies fulfilled the systematic review inclusion criteria. Further research is needed to assess a wider range of risk and protective factors for STB among LGB adolescents/young adults.

Discussion

Results show that there is higher risk for STB among LGB adolescents/young adults compared with heterosexuals. The risk would probably differ among sexual minority individuals if gender would be taken into account. Bisexual individuals may be at greater risk for stigmatisation by heterosexuals and by the gay and lesbian communities for not having exclusively same-sex attractions and relationships [164]. Studies comparing bisexuals to gay and lesbian adults [165,166] and youths [167–169] have provided inconsistent evidence for increased risk for depression and suicide among bisexual youth.

Some studies have reported an interaction effect between gender and sexual orientation, with bisexual girls showing highest risk more frequently [167,168]. The above-mentioned conclusion is contrary to what was found in this thesis, in which only lesbian adolescents/young adults showed an increased risk for suicide attempt and suicide. However, it is probable that the absence of results is related to the small number of cases.

Previous literature has assessed the intersections of sexual identity, race/ethnicity and sex in relation to mental health, substance use, violence and sexual risk among high school students. In general, sexual minority youth demonstrated poorer health outcomes compared to heterosexuals. For instance, one study reported differences between non-heterosexual male and female adolescents in violence and substance use, although only biological sex was considered [170]. Another study examined the interaction between gender and sexual orientation regarding attempted suicide, reporting more than twice as much risk for suicide attempt for females; no interaction between sexual orientation and gender was observed [171]. However, this study included a sample of psychiatric youth inpatients with different characteristics than the general population or than university students [171]. There is an urgent need to study the intersections between gender and sexual orientation, using longitudinal studies, especially in this age group in which the overlapping characteristics (age, sexual orientation, gender, among others) make adolescents/young adults a vulnerable population for STB.

The Minority Stress Theory (MST) explains the increased risk for STB among LGB adolescents/young adults. This theory proposes how external stressors (e.g. discrimination, stigma and prejudice) create a hostile environment that promotes the perception of being different from the majority among LGB individuals, internalising the homophobic attitudes (internalised homophobia) [48,129]. MST states that the increased risk for STB in this population is given by the psychological stress that adverse situations may cause, augmenting not only the vulnerability for STB, but also for factors which predispose for suicidality such as risky health behaviours and mental disorders. The MST points to both distal and proximal causes of distress and encourages to direct relevant interventions at both the individual and structural levels [92].

b) Objective: ***to assess the role of perceived sexual orientation discrimination and internalised homophobia in the risk for suicidal thoughts and behaviours (STB) among LGB Spanish university students.***

Summary of findings

The risk for SI among LGB Spanish university students is mediated by both childhood/adolescence adversities (maltreatment and bullying) and mental disorders (mood, anxiety and alcohol and substance disorder). Sexual orientation discrimination increases the risk for mental disorders, but not for SI. Moreover, mental disorders

do not seem to have a mediatory effect in the relationship between sexual orientation discrimination and SI.

Discussion

Risk for childhood maltreatment can vary according to a number of social and cultural factors. For instance, sexual orientation has been linked to an increased risk for childhood maltreatment: In fact, LGB youths are 2.9 times more likely to experience childhood sexual abuse and 1.3 times more likely to experience childhood physical abuse than their heterosexual counterparts [172]. Moreover, adult lesbians report a childhood sexual abuse rate almost two times higher than heterosexual women[80]. These results have been consistently found across research studies with a wide range of sampling methodologies [173–175]. In addition, bullying is also more prevalent among LGB youth [78]. Based on the results from a survey conducted during 2001–2009 among a large population-based sample of high school students (grades 9th to 12th), LGB students reported more frequently being involved in physical fights as well as having missed school because they felt unsafe [79]. Mental disorders such as depression, anxiety, substance abuse and disruptive behaviour have all been associated to childhood maltreatment [176,177]. Childhood emotional abuse is a strong predictor of mental disorders among LGB and, at the same time, can probably moderate the effects of physical and sexual maltreatment on the development of mental disorders. In fact, Balsam et al. reported that, although physical and sexual abuse are associated to mental

disorders, this relationship was no longer significant when adjusted for emotional abuse [175]. Similarly, bullying exerts negative effects on the mental health of LGB individuals [178,179]. Negative effects of being involved in bullying have been found in cross-sectional studies, including STB [180,181], depression [182], violent behaviour [183] and delinquency [184], physical health problems [185,186] and school and psychosocial maladjustment [185,186]. Longitudinal studies have also found higher probability of mental disorders in early adulthood associated to bullying [187]. Furthermore, the frequency, duration and severity of the discrimination may increase the risk for negative health outcomes [80].

The results of this thesis are consistent with previous research showing that both childhood maltreatment and bullying increase the risk for mental disorders and STB. Novel findings from the mediation analyses in this thesis found that the association of sexual orientation with SI is mediated by childhood and adolescence adversities, maltreatment and bullying, as well as by mental disorders. Furthermore, this mediatory effect is still observed when analysing each sexual orientation category separately, meaning homosexuals, bisexuals or those who are not sure about their sexual orientation.

Our results substantially address the previous knowledge gap about STB among LGB young adults. However, further longitudinal research, including larger samples, is needed to better assess the role of factors such as internalised homophobia, which may have an

important contribution on the relationship between sexual orientation discrimination and mental disorders, and STB, in particular.

Scarcity of data about protective factors for STB among adolescents/young adults

There is agreement that suicide is a public health challenge, which requires a response involving a community-wide risk reduction approach coupled with a focus on the enhancement of protective factors [188]. However, relatively little research so far has focused on identifying individual, family and community factors which may protect against the development of suicidal behaviour in young people [189]. This field is an almost unexploited area by researchers.

Protective factors are characteristics or resources that reduce the impact of risk, making it less likely for an individual to consider or attempt suicide in the context of risk [190]. A useful conceptualisation of protective factors and their relative importance in the face of unmodifiable risk factors is needed. For those inevitable risk factors for STB (e.g. death of any of the parents), modifiable protective factors provide a more efficient focus for prevention [191]. Identifying modifiable protective factors at multiple levels is also critical in the reduction in STB risk among LGB youths.

In fact, in the systematic review performed in this thesis, among the studies meeting the inclusion criteria, only 10 analysed protective

factors of suicide attempt and suicide death in adolescents/young adults. Our analyses of the UNIVERSAL study data were performed to identify potential protective factors among university students thus expanding previous knowledge. Results show protective associations between family and peers/others support with SI, but only among females. Gender differences among coping strategies and seeking of help, previously discussed, may explain these results. Even when these results are consistent with previous literature [47,192], a knowledge gap remains in terms of the protective factors for STB for adolescents/young adults, including university students. Further research in this regard is definitively needed to fill the knowledge gap about protective factors for STB for LGB adolescents/young adults, a high-risk population.

7. CONCLUSIONS

1. **While it is well-established that males have a greater rate of death by suicide than females, our results show that female adolescents/young adults have higher risk for suicide attempt than males of the same age range. Common risk factors of suicide attempt and suicide death for both genders are exposure to any form of interpersonal violence** (childhood maltreatment, bullying, and community violence) **and any previous mental or substance abuse disorder**. Mood disorders carry specific risk for suicidal ideation.

2. **There are gender differences regarding risk factors for suicidal thoughts and behaviours (STB) among adolescents/young adults. For females, risk for STB is mostly associated to internalising disorders and to interpersonal difficulties. For males, risk for STB is related to externalising disorders, hopelessness, and to specific stressful life-events** such as death of any of the parents and history of parental psychopathology.

3. **There is a need to better understand the mechanisms underlying gender differences in the association between STB and anxiety, alcohol or substance disorder, violence between parents, hopelessness and family support among youths. A profound knowledge of mechanisms and**

pathways of gender differences in the risk for STB would allow a more precise preventive approach.

4. **A hostile or adverse environment with different kinds of maltreatment, discrimination and victimisation predisposes to risk factors for STB such as mental disorders or psychological distress, or act as a trigger for the occurrence of STB among adolescents/young adults.** Further research evaluating context factors should be conducted. This would strengthen the recommendations on preventive strategies combining the individual level with the community level.

5. **Lesbian, gay, bisexual (LGB) adolescents/young adults and those who are not sure about their sexual orientation are at higher risk for STB compared to heterosexuals, with some specific factors acting among them**. **The risk for suicidal ideation among LGBs is mediated by previous exposure to childhood maltreatment, bullying and a history of any mental disorder. Perceived sexual orientation discrimination increases the risk for any mental disorder among LGB adolescents/young adults. The association between perceived sexual orientation discrimination and SI is partially mediated by mental disorders.**

6. **Family support and peers/others support are protective factors for suicidal ideation among female adolescents/young adults. A knowledge gap remains about the protective factors for STB among adolescents/young adults. Protective factors at multiple levels are crucial for the reduction in STB risk among youths. Further research to fill this knowledge gap is needed.**

8. RECOMMENDATIONS

8.1 Prevention

From a public health perspective, there is an urgent need for developing and implementing effective preventive strategies for suicidal thoughts and behaviours (STB) in adolescents/young adults. In general, preventing the most prevalent risk factors for STB (as it is the case of mental disorders), and reducing the negative health effects associated to the exposure to different forms of interpersonal violence (e.g. childhood maltreatment, bullying, discrimination) should certainly diminish the risk for STB. In addition, strategies focused on promoting hope and optimism could help to buffer suicidal ideation and attempts [193,194]. Importantly, since the risk for STB differs according to gender and sexual orientation, it is crucial to consider high-risk subpopulations (e.g. females for suicide attempt, LGB) to adequately prevent STB. Moreover, it is desirable to request the adolescents/young adults about their preferences regarding mental health preventive strategies. As well as to study the context, considering that successful experiences would not always have the same effectiveness depending on the context. The results of this thesis suggest some specific recommendations for a more effective prevention for STB.

Timely identification of mental disorders is crucial, since they have been widely demonstrated as risk factors for STB in

adolescents/young adults. Interventions for an early identification of probable cases of mental disorders, as well as of those who already suffer from them, at the school/university environments would be helpful reducing subsequent onset of STB. Community factors such as bullying or interpersonal violence increase the risk for STB, but family support is a strong protective factor. Early detection and integral care for individuals suffering mental disorders, as well as the joint reduction of risk factors and strengthening of protective ones may be one of the keys for prevention.

However, STB are complex outcomes, as indicated by the ecological model of factors analysed in this thesis. It is therefore necessary to consider that factors interact with each other and those with considerable magnitudes of association but showing non-statistically significant results may still play an important role on the risk for STB [191]. On the other hand, the presence of predisposing factors, such as mental disorders and others, does not necessarily imply any suicidal behaviour. As a result, suicidal behaviour is particularly difficult to predict, which points to the fact that evidence-based interventions should be implemented, which are currently lacking.

Gender: Gender differences in STB among adolescents/young adults reported in this thesis should be considered for the development and implementation of preventive strategies. The risk for STB is more strongly associated with internalising disorders in females and with externalising disorders in males. Generic

prevention strategies focusing on the most prevalent mental disorders, particularly internalising and externalising disorders, are required. Help-seeking behaviours differ across genders. In general, females are more willing to use prevention centres and to communicate about their inner feelings or personal circumstances [195], identifying friends and professionals as likely sources for help [60]. Therefore, school-based programs, including simulations at class and open classes [196], and screening at primary care settings [197] could be beneficial for females. Since males are more reluctant to express their feelings or personal situations, and are also not prone to get actively involved in suicide awareness programs [198], school-wide screening [199] and public campaigns [200] may facilitate prevention among them. These strategies target individuals at risk, guaranteeing anonymity, and encourage them to enter into treatment or seek for help [199,200]. An effective option among males could be online interventions for preventing mental disorders and STB, which appears to be accepted among young people [201,202]. Screening and feedback online interventions seem to increase service use, by directing at-risk individuals who would not otherwise seek help to access appropriate evidence-based online programs or to access traditional mental health services [203].

Sexual orientation: LGB adolescents/young adults should be considered a high-risk population in the preventive strategies for STB, in particular when other factors, such as mental disorders and psychological distress, are also present. The increased STB risk faced by LGB adolescents/young adults is mostly driven by an

adverse context, not due to their self-definition [48]. Preventive strategies and public policies should focus on creating a safer context for the LGB, effectively preventing the discrimination and victimisation suffered by this subpopulation. Therefore, interventions at the community level, including schools and universities, educating the population in tolerance to diversity and promoting a culture against any kind of discrimination would create a safer environment for sexual minority youth, preventing the negative effects on their mental health and consequently decreasing the risk for STB.

University setting: A large proportion of young adults access university studies. It has been suggested that without adequate intervention, university students suffering the effects for STB would be at risk for academic failure and long-term negative consequences [105]. Universities must ensure a healthy environment for students. Specifically, the identification and attention of high-risk cases of mental disorders and STB should be a priority, without neglecting the early detection of predisposing factors. Gatekeeper preventive intervention is an example of an intervention at university setting. Gatekeepers intervention improves knowledge, skills and self-efficacy regarding suicide intervention in university settings [204]. It has been recommended that a combination of individual strategies building personal skills with a setting-based approach could improve the overall university setting [205]. However, in general, universities do not have the necessary infrastructure to face the challenges of the suggested interventions. In this scenario, internet-

based interventions can be a sustainable alternative. In this respect, the World Mental Health consortium aims to develop a sustainable, user-friendly, electronic infrastructure for automatically assessing and monitoring mental health problems (and associated risk factors) at the college level and to offer innovative internet-based interventions for mental health promotion, prevention and early intervention [206]. The implementation of these interventions can reach many more students, help to timely detect possible cases of mental disorders, and, in turn, may prevent the occurrence of STB. In addition, ensuring self-regulation and coping strategies prior to the onset of college stressful life events might be helpful [207]. Especially in the improvement of skills training and education about how to deal with interpersonal conflicts and stressful life events should be a primary focus in school-based life skills education.

Finally, suicide is a condition which deserves integrated understanding that takes into account biological, clinical, subjective and social factors [208]. Up to now, most prevention strategies have narrowly focused on identifying proximal, individual-level risk factors, rather than considering population mental health in terms of complex social and ecological relations [209]. There is an urgent need to combine strategies focusing on individual risk factors (e.g. early treatment of mental disorders) with those with a public health population-level risk approach (e.g. reinforcing community protective factors). An example of a successful comprehensive strategy was carried out in the Air Force in the United States [210]. Its key components included: consistent and regular communication

around the topic of suicide prevention, destigmatisation of seeking help for a mental health problems, improved collaboration among community prevention agencies, and the identification and training of 'everyday' gatekeepers [211]. In this sense, data are essential to better understand the potential impact of protective factors that act in the presence of apparent risk factors to mitigate adverse outcomes, considering that protective factors modify according to the context. Strengthening protective factors rather than just avoiding risk is essential for suicide prevention.

8.2 Research

The results of this thesis show that there are gender differences and differences according to sexual orientation in the risk for suicidal thoughts and behaviours (STB) among adolescents/young adults, including the Spanish university students. However, there are new knowledge gaps to fill in this area. In general, confirmation with larger, longitudinal data is needed. More important, there is the need to identify the mechanisms underlying gender differences in STB and the possible mediators and pathways for STB among females and males. As well as to analyse the role of relevant factors such as psychological distress and internalised homophobia in the risk for STB among sexual minority youth.

Consistent with the prevention recommendations above, the analysis of potential protective factors and their effects on the prevention for STB in adolescents/young adults is necessary.

Including the identification their mechanisms of action by gender and sexual orientation.

The study of intersectionality in the risk for STB is almost inexistent. Intersectionality is *"the complex, cumulative manner in which the effects of different forms of discrimination combine, overlap, or intersect"* [212], it is use to illustrate the interplay between any kinds of discrimination [213,214]. Research to better understand the intersections between gender and sexual orientation, but also including some other health determinants (e.g. race or ethnicity), which can modify the way in which risk and protective factors for STB exert their effect on adolescents/young adults, ought to be conducted.

Assessing the burden and impact of STB on Spanish university students is crucial. In view of the previous results from other contexts suggesting that suicide rates have increased on university campuses [100,101], related to the rise of the number of students enrolled in the university and a higher proportion of them presenting mental disorders [96,100–102]. Previous research has also shown that severe lifetime STB has a strong negative association with early academic performance or university dropout among university population [105]. Moreover, university settings represent an opportunity for intervention [205]. Research to fill these knowledge gaps is required.

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OTHER PUBLICATIONS

Miranda-Mendizábal A, Vargas I, Mogollón-Pérez AS, Eguiguren P, Samico I, López J, et al. Knowledge and use of clinical coordination mechanisms in healthcare networks in Latin America. Gac Sanit. 2018. [Epub ahead of print].

ANNEX 1. MOOSE checklist for meta-analyses of observational studies

MOOSE checklist for meta-analyses of observational studies

Item No	Recommendation
Reporting of background should include	
1	Problem definition
2	Hypothesis statement
3	Description of study outcome(s)
4	Type of exposure or intervention used
5	Type of study designs used
6	Study population
Reporting of search strategy should include	
7	Qualifications of searchers (e.g. librarians and investigators)
8	Search strategy, including time period included in the synthesis and key words
9	Effort to include all available studies, including contact with authors
10	Databases and registries searched
11	Search software used, name and version, including special features used (e.g. explosion)
12	Use of hand searching (e.g. reference lists of obtained articles)
13	List of citations located and those excluded, including justification
14	Method of addressing articles published in languages other than English
15	Method of handling abstracts and unpublished studies
16	Description of any contact with authors
Reporting of methods should include	
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested
18	Rationale for the selection and coding of data (e.g. sound clinical principles or convenience)
19	Documentation of how data were classified and coded (e.g. multiple ratters, blinding and interrater reliability)
20	Assessment of confounding (e.g. comparability of cases and controls in studies where appropriate)

Item No	Recommendation
Reporting of methods should include	
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results
22	Assessment of heterogeneity
23	Description of statistical methods (e.g. complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated
24	Provision of appropriate tables and graphics
Reporting of results should include	
25	Graphic summarizing individual study estimates and overall estimate
26	Table giving descriptive information for each study included
27	Results of sensitivity testing (e.g. subgroup analysis)
28	Indication of statistical uncertainty of findings
Reporting of discussion should include	
29	Quantitative assessment of bias (e.g. publication bias)
30	Justification for exclusion (e.g. exclusion of non-English language citations)
31	Assessment of quality of included studies
Reporting of conclusions should include	
32	Consideration of alternative explanations for observed results
33	Generalization of the conclusions (e.g. appropriate for the data presented and within the domain of the literature review)
34	Guidelines for future research
35	Disclosure of funding source

***Source*:** Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012.

ANNEX 2. Supplementary material for article 1

Supplementary material for this article:

Miranda-Mendizabal A, Castellví P, Parés-Badell O, Alayo I, Almenara J, Alonso I, et al. Gender differences in suicidal behavior in adolescents and young adults: systematic review and meta-analysis of longitudinal studies. Int J Public Health. 2019;64(2):265–83.

Table S1. MOOSE checklist of the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)

Reporting of background should include	
Problem definition	√
Hypothesis statement	
Description of study outcome(s)	√
Type of exposure or intervention used	√
Type of study designs used	√
Study population	√
Reporting of search strategy should include	
Qualifications of searchers (e.g. librarians and investigators)	√
Search strategy, including time period included in the synthesis and keywords	√
Effort to include all available studies, including contact with authors	√
Databases and registries searched	√
Search software used, name and version, including special features used (e.g. explosion)	√
Use of hand searching (e.g. reference lists of obtained articles)	√
List of citations located and those excluded, including justification	√
Method of addressing articles published in languages other than English	√
Method of handling abstracts and unpublished studies	√
Description of any contact with authors	√
Reporting of methods should include	
Description of relevance of appropriateness of studies assembled for assessing the hypothesis to be tested	√
Rationale for the selection and coding data (e.g. sound clinical principles or convenience)	√
Documentation of how data were classified and coded (e.g. multiple raters, blinding, and interrater reliability)	√
Assessment of confounding (e.g. comparability of cases and controls in studies where appropriate)	√
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	√
Assessment of heterogeneity	√

Reporting of methods should include	
Description of statistical methods (e.g. complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	√
Provision of appropriate tables and graphics	√
Reporting of results should include	
Graphic summarizing individual study estimates and overall estimate	√
Table giving descriptive information for each study included	√
Results of sensitivity testing (e.g. subgroup analysis)	√
Indication of statistical uncertainty of findings	√
Reporting of discussion should include	
Quantitative assessment of bias (e.g. publication bias)	√
Justification for non-exclusion (e.g. exclusion of non-English-language citations)	√
Assessment of quality of included studies	√
Reporting of conclusion should include	
Consideration of alternative explanations for observed results	√
Generalization of the conclusion (e.g. appropriate for the data presented and within the domain of the literature review)	√
Guidelines for future research	√
Disclosure of funding source	√

Table S2. Quality of assessment of included articles in the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)*

a. Cohort Studies

Study	Domains								
	Selection			Comparability		Outcome			
	Representativeness of Exposed Cohort¥	Selection of Non Exposed Cohort¥	Ascertainment of Exposure¥	Demonstration Outcome of Interest Not Present at Start of Study¥	Comparability of Cohorts on the basis of Design or Analysis‡	Ascertainment of Outcome¥	Adequate Length of Follow Up¥	Adequacy of Follow Up¥	Total stars
Cohort studies									
Kaplan H & Pokonny A, 1976	*	*	_	*	*	_	_	_	4
Reinherz HZ et al. 1995	*	*	*	*	**	_	*	*	8
Silverman AB et al. 1996	*	*	*	*	*	*	*	*	8
McKeown RE et al. 1998	*	*	*	_	*	_	_	_	4
Wichstrom L. 2000	*	*	_	_	*	_	_	*	4
Borowsky I et al. 2001	*	*	*	*	**	_	_	_	5
Lewinsohn P et al. 2001	*	*	*	*	**	*	*	_	8
Sourander A et al. 2001, 2009	*	*	*	_	*	_	*	_	5
Fergusson D et al. 2003	*	*	*	*	**	_	*	*	8
Bearman P et al. 2004	*	*	*	*	**	-	-	*	7
Ialongo NS et al. 2004	*	*	*	*	**	*	*	_	8
D´Augelli A et al. 2005	*	*	*	*	*	_	_	_	5
Feigelman W et al. 2006, Thompson M et al. 2007; Exner-Cortens D et al. 2013; Van Dulmen M et al. 2013; Abrutyn S et al. 2014; Turanovic JT & Pratt TC 2015	*	*	*	*	**	_	*	*	8

Table S2 *(continued)*

Study	Domains								
	Selection			Comparability		Outcome			
	Representativeness of Exposed Cohort¥	Selection of Non Exposed Cohort¥	Ascertainment of Exposure¥	Demonstration Outcome of Interest Not Present at Start of Study¥	Comparability of Cohorts on the basis of Design or Analysis‡	Ascertainment of Outcome¥	Adequate Length of Follow Up¥	Adequacy of Follow Up¥	Total stars
Kidd S et al. 2006	*	*	_	_	*	_	_	_	3
Rodríguez-CanoT et al. 2006	_	*	*	*	*	_	*	_	5
Ackard D et al. 2007	*	*	*	*	**	_	_	*	7
Brezo J et al. 2007, 2008	*	*	*	*	**	_	*	_	7
Crow S et al. 2008	*	*	_	*	**	_	*	*	7
Dupéré V et al. 2008	*	*	*	_	*	_	*	_	5
Lambert SF et al., 2008	_	*	_	*	**	_	*	*	6
Nrugham L et al. 2008, 2015	*	*	*	*	**	_	*	_	7
Wong J et al. 2008	*	*	*	*	*	_	_	_	5
Wilcox H et al. 2009	*	*	*	*	*	_	*	_	6
Batty G et al. 2010	*	*	*	*	**	*	*	*	9
Peter T et al. 2010	*	*	*	*	*	_	_	_	5
Roberts RE et al. 2010	*	*	*	*	**	_	_	*	7
Klomek A et al. 2011	*	*	*	*	**	*	*	*	9
Young R et al. 2011	*	*	*	*	**	_	*	*	8
Fried L et al. 2012	*	*	*	*	*	_	_	_	5
Guan K et al. 2012	*	*	*	*	*	_	_	_	5
Hurtig T et al. 2012	*	*	_	*	*	_	*	_	5
Nkansah-Amankra S et al. 2012	*	*	*	*	**	_	*	_	7
Wanner B et al. 2012	*	*	*	*	**	_	*	_	7

Table S2 *(continued)*

Study	Domains								
	Selection			Comparability		Outcome			
	Representativeness of Exposed Cohort¥	Selection of Non Exposed Cohort¥	Ascertainment of Exposure¥	Demonstration Outcome of Interest Not Present at Start of Study¥	Comparability of Cohorts on the basis of Design or Analysis‡	Ascertainment of Outcome¥	Adequate Length of Follow Up¥	Adequacy of Follow Up¥	Total stars
Winterrowd E & Canetto SS, 2013	*	*	*	*	**	_	_	*	7
Chang S-S et al. 2014	*	*	*	*	**	_	*	_	7
Chuan-Yu C et al. 2014	*	_	*	*	**	*	*	*	8
Conner K et al. 2014	*	*	*	*	*	_	_	*	6
Luntano T et al. 2014	*	*	*	*	**	*	*	*	9
Mars B et al. 2014	*	*	*	*	*	_	*	_	6
Miranda R et al. 2014	*	*	*	*	**	_	*	_	7
Soller B et al. 2014	*	*	*	*	**	_	*	_	7
Swanson E et al. 2014	*	*	_	*	**	_	*	*	7
Finkelstein Y et al. 2015	*	*	*	*	*	*	*	*	8
Scott L et al. 2015	*	*	*	*	**	_	*	*	8
You J et al. 2015	*	*	*	*	**	_	_	*	7
Conway PM et al. 2016	*	*	*	*	*	*	_	*	7
Feigelman W et al. 2016	*	*	*	*	*	*	*	_	7
Meza JI et al. 2016	*	*	*	_	**	_	*	*	7
Mok P et al. 2016	*	*	*	*	*	*	*	*	8
Weiser et al. 2016	*	*	*	*	**	_	*	*	8
Hishinuma ES et al. 2017	*	*	_	*	*	_	*	*	6

b. Case-control Studies

Study	Case Definition¥	Representativeness of Cases¥	Selection of Controls¥	Definition of Controls¥	Comparability of Cases and Controls‡	Ascertainment of Exposure¥	Same Method Ascertainment Both Groups¥	Non Response Rate¥	Total of stars
Case-control studies									
Salk L et al. 1985	*	*	*	_	*	_	*	_	5
King CA et al. 1990	_	*	*	*	*	_	*	_	5
Rotheram-Borus M & Shrout P, 1990	*	*	*	*	*	_	_	_	5
Garnefski N et al. 1992	_	*	*	*	**	_	*	*	7
Brent DA et al. 1993, 1999	_	*	*	*	**	_	*	_	6
Adams D et al. 1994	_	*	*	_	**	*	*	_	6
Shaffer D et al. 1996	*	*	_	*	**	_	*	*	7
Beautrais A et al. 1998	*	*	*	*	**	_	*	_	7
Lyon ME et al. 2000	_	_	_	*	**	_	*	_	4
Ikeda RM et al. 2001	*	*	*	*	**	_	*	_	7
Donald M et al. 2005	_	*	*	*	**	_	_	_	5
Ostry A et al. 2007	*	*	*	*	**	*	*	*	9
Bilgin M et al. 2007	_	_	*	*	_	_	*	_	3
Freitas G et al. 2008	_	*	*	*	*	_	*	*	6
Christiansen E et al.2011, 2012	*	*	*	*	**	*	*	*	9
Cheng C-CJ et al. 2014	*	*	*	*	*	*	*	*	8

*Highest quality studies are awarded up to nine stars. ¥A maximum of one star can be allotted in this category. ‡A maximum of two stars can be allotted in this category. _None star was allotted.

SUPPLEMENTARY TEXT S1 OF THE SYSTEMATIC REVIEW OF GENDER DIFFERENCES IN SUICIDAL BEHAVIOR IN ADOLESCENTS AND YOUNG ADULTS (covered up until January 2017)

Search strategy and selection criteria of the broader systematic review

A broad-scope and inclusive initial search strategy was carried out, with no restrictions of population or age, in order to identify predictors of suicidal-related behaviors. Text-word, titles and Mesh terms were used as search terms resulting initially in 26,882 references after removal of duplicates (Fig. 1). Based on this search strategy other analyses in different populations and risk factors, are currently being carried out.

All the keywords used for inclusion and exclusion, as well as search terms used to identify suicide attempt, suicidal behavior, population and study design are provided (see below). The following databases were searched: Cochrane Library, Medline, PsychINFO, EMBASE and Web of Science. A search in grey literature was conducted using the OpenGrey database, and reference lists from previous reviews and books were examined. Searching in all databases covered up until January 2017. No restrictions of language or year of publication were applied. Corresponding authors for articles written in languages other than English and Spanish were contacted.

A multidisciplinary team of psychiatrists, psychologists, statisticians, epidemiologists and public health professionals was established to perform the review. Five groups of independent peer reviewers assessed all references. During title review discrepancies between reviewers were included. During title and abstract review phases, reviewers were blinded from seeing the article's author, journal and year of publication to

minimize selection bias. A third independent reviewer resolved any discrepancies during abstract and full text review.

For the broad-scope review, studies were included if they met all of the following criteria: (a) reporting suicide death or attempt as dependent variable; (b) assessing at least one risk or protective factor of any of these outcomes; (c) study population age range between 12 and 26 years old, both inclusive; (d) population-based longitudinal studies (non-clinical and non-institutionalized sample cohorts; or case-control where control group was of the same age range and population-based). Ecological and cross-sectional studies were excluded. Using an expert consensus reported previously, suicide death (or simply, suicide) was defined as any fatal act done with the intention of taking one's own life, while suicide attempt was defined as any act of self-injury with intention to die [15]. Other suicide-related behaviors (e.g., suicide ideation) were excluded. Using the listed criteria, 197 studies were identified for qualitative synthesis.

Detailed search strategy

Search terms by database

Components	Keywords	
	Inclusion keywords	**Exclusion keywords**
Population	Humans	Animals
Outcome	Suicide Suicidal behavior Suicide ideation Suicide plan Suicide attempt Non-suicidal self-injury Parasuicide Self-injure Deliberate self-harm Suicidality Non-fatal suicidal behavior	
Exposure	Risk factor Causality Relationship Association Prediction Harm Adverse Antecedent History Etiology Protective factor Prevention Improvement Prevalence Incidence	
Study design	Experimental study Randomized controlled trial Controlled clinical trial Clinical trial Longitudinal study Observational study Cohort study Case control study Time series study Prospective study Retrospective study Follow-up Cross-sectional study	Case series Case report
Others		Type of publications: - Comments - Letter - Editorial

Search Strategy in each selected database:

1. **Medline (Pubmed): Search January 17th, 2017**

	Search Strategy
#24	(#20 AND #21 AND #22) NOT (#18 OR #19 OR #20)
#23	(#14 OR #15 OR #16 OR #17)
#22	(#10 OR #11 OR #12 OR #13)
#21	(#5 OR #6 OR #7 OR #8 OR #9)
#20	(#3 OR #4)
#19	(#1 NOT (#1 AND #2))
#18	case reports[Publication Type]
#17	(("prospective studies"[MeSH Terms] OR ("prospective"[All Fields] AND "studies"[All Fields]) OR "prospective studies"[All Fields] OR ("prospective"[All Fields] AND "study"[All Fields]) OR "prospective study"[All Fields]) OR ("retrospective studies"[MeSH Terms] OR ("retrospective"[All Fields] AND "studies"[All Fields]) OR "retrospective studies"[All Fields] OR ("retrospective"[All Fields] AND "study"[All Fields]) OR "retrospective study"[All Fields]) OR Follow-up[All Fields] OR ("cross-sectional studies"[MeSH Terms] OR ("cross-sectional"[All Fields] AND "studies"[All Fields]) OR "cross-sectional studies"[All Fields] OR ("cross"[All Fields] AND "sectional"[All Fields] AND "study"[All Fields]) OR "cross sectional study"[All Fields]))
#16	(("cohort studies"[MeSH Terms] OR ("cohort"[All Fields] AND "studies"[All Fields]) OR "cohort studies"[All Fields] OR ("cohort"[All Fields] AND "study"[All Fields]) OR "cohort study"[All Fields]) OR ("case-control studies"[MeSH Terms] OR ("case-control"[All Fields] AND "studies"[All Fields]) OR "case-control studies"[All Fields] OR ("case"[All Fields] AND "control"[All Fields] AND "study"[All Fields]) OR "case control study"[All Fields]) OR (("time"[MeSH Terms] OR "time"[All Fields]) AND series[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "study"[All Fields] OR "biomedical research"[MeSH Terms] OR ("biomedical"[All Fields] AND "research"[All Fields]) OR "biomedical research"[All Fields])))

	Search Strategy
#15	(("controlled clinical trial"[Publication Type] OR "controlled clinical trials as topic"[MeSH Terms] OR "controlled clinical trial"[All Fields]) OR ("clinical trial"[Publication Type] OR "clinical trials as topic"[MeSH Terms] OR "clinical trial"[All Fields]) OR ("longitudinal studies"[MeSH Terms] OR ("longitudinal"[All Fields] AND "studies"[All Fields]) OR "longitudinal studies"[All Fields] OR ("longitudinal"[All Fields] AND "study"[All Fields]) OR "longitudinal study"[All Fields]) OR (Observational[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "study"[All Fields] OR "biomedical research"[MeSH Terms] OR ("biomedical"[All Fields] AND "research"[All Fields]) OR "biomedical research"[All Fields]))
#14	((Experimental[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "study"[All Fields] OR "biomedical research"[MeSH Terms] OR ("biomedical"[All Fields] AND "research"[All Fields]) OR "biomedical research"[All Fields])) OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trial"[All Fields] OR "randomised controlled trial"[All Fields]))
#13	(("risk factors"[MeSH Terms] OR ("risk"[Tiab] AND "factors"[Tiab]) OR "risk factors"[Tiab] OR ("risk"[Tiab] AND "factor"[Tiab]) OR "risk factor"[Tiab]))
#12	(("etiology"[Subheading] OR "etiology"[Tiab] OR "causality"[Tiab] OR "causality"[MeSH Terms]) OR Relationship[Tiab] OR ("association"[MeSH Terms] OR "association"[Tiab]) OR Prediction[Tiab] OR Harm[Tiab] OR Adverse[Tiab] OR Antecedent[Tiab] OR ("history"[Subheading] OR "history"[Tiab] OR "history"[MeSH Terms]))
#11	((“protective factors”[Tiab] OR (“protective”[Tiab] AND “factor”[Tiab]) OR (“protective”[Tiab] AND “factors”[Tiab]) OR "prevention"[Tiab]) OR Improvement[Tiab])
#10	(prevalence[MeSH Terms] OR incidence[MeSH Terms] OR prevalence[Tiab] OR incidence[Tiab])
#9	(("deliberate"[All Fields] AND "self"[All Fields] AND "harm"[All Fields]) OR "deliberate self-harm"[All Fields])
#8	((Non-suicidal[All Fields] AND self-injury[All Fields]) OR ("self-injurious behavior"[MeSH Terms] OR ("self-injurious"[All Fields] AND "behavior"[All Fields]) OR "self-injurious behavior"[All Fields] OR "parasuicide"[All Fields]) OR Self-injure[All Fields] OR ("self-injurious behavior"[MeSH Terms] OR ("self-injurious"[All Fields] AND "behavior"[All Fields]) OR "self-injurious behavior"[All Fields]))

	Search Strategy
#7	("suicide, attempted"[MeSH Terms] OR ("suicide"[All Fields] AND "attempted"[All Fields]) OR "attempted suicide"[All Fields] OR ("suicide"[All Fields] AND "attempt"[All Fields]) OR "suicide attempt"[All Fields])
#6	((suicidal[All Fields] AND ("behaviour"[All Fields] OR "behavior"[MeSH Terms] OR "behavior"[All Fields])) OR (("suicide"[MeSH Terms] OR "suicide"[All Fields]) AND (ideation[All Fields] OR plan[All Fields])))
#5	(suicid*) OR "suicide"[MeSH Terms] OR "suicide"[All Fields])
#4	editorial [Publication Type]
#3	letter[Publication Type]
#2	human[MeSH Terms]
#1	animal[MeSH Terms]

2. Embase: Search January 17th, 2017

	Search Strategy
#6	(#3 AND #4 AND #5) NOT (#1 OR #2)
#5	'experimental study'/exp OR 'experimental study' OR 'randomized controlled trial'/exp OR 'randomized controlled trial' OR 'controlled clinical trial'/exp OR 'controlled clinical trial' OR 'clinical trial'/exp OR 'clinical trial' OR 'longitudinal study'/exp OR 'longitudinal study' OR 'observational study'/exp OR 'observational study' OR 'cohort analysis'/exp OR 'cohort analysis' OR 'case control study'/exp OR 'case control study' OR 'prospective study'/exp OR 'prospective study' OR 'retrospective study'/exp OR 'retrospective study' OR 'follow-up'/exp OR 'follow-up' OR 'cross-sectional study'/exp OR 'cross-sectional study' OR 'cohort study'/exp OR 'cohort study' OR 'time series study'
#4	'risk factor'/exp OR 'risk factor':ti,ab OR 'prediction'/exp OR 'prediction':ti,ab OR 'association'/exp OR 'association':ti,ab OR 'prevention'/exp OR 'prevention':ti,ab OR 'causality'/exp OR 'causality':ti,ab OR 'relationship':ti,ab OR 'adverse':ti,ab OR 'antecedent':ti,ab OR 'etiology'/exp OR 'etiology':ti,ab OR 'protective factor':ti,ab OR prevalence/exp OR incident/exp
#3	suicid* OR 'suicidal behavior'/exp OR 'suicidal behavior' OR 'automutilation'/exp OR 'automutilation' OR 'suicide'/exp OR 'suicide' OR 'suicide ideation'/exp OR 'suicide ideation' OR 'suicide plan' OR 'suicide attempt'/exp OR 'suicide attempt' OR 'non-suicidal self-injury' OR 'parasuicide'/exp OR 'parasuicide' OR 'self-injure' OR 'deliberate self-harm' OR suicidality
#2	letter/exp OR editorial/exp OR “case report”/exp
#1	animal/exp NOT (animal/exp AND human/exp)

3. Web of Science: Search October 21, 2013

	Search Strategy
#6	(#3 AND #4 AND #5) NOT (#1 OR #2)
#5	TS=(Experimental study OR Randomized controlled trial OR Controlled clinical trial OR Clinical trial OR Longitudinal study OR Observational study ORCohort study OR Case control study OR Time series study OR Prospective study OR Retrospective study OR Follow-up OR Cross-sectional study)
#4	TS=(Risk factor OR Causality OR Relationship OR Association OR Prediction OR Harm OR Adverse OR Antecedent OR History OR $Etiology OR Protective factor OR Prevention OR Improvement OR prevalence OR incidence)
#3	TS=(Suicid* OR suicide OR Suicidal behavior OR Suicide ideation OR Suicide plan OR Suicide attempt OR Non-suicidal self-injury OR Parasuicide OR Self-injure OR Deliberate self-harm OR Suicidality OR Non-fatal suicidal behaviour)
#2	DT=(letter) OR TI=(editorial) OR TI=(case report)
#1	TS=(animal NOT (animal AND human))

4. The Cochrane Library: Search January 20th, 2017

	Search Strategy
#39	(#14 and #29 and #37) not (#3 or #38)
#38	MeSH descriptor: [Case Reports] explode all trees
#37	#30 or #31 or #32 or #33 or #34 or #35 or #36
#36	MeSH descriptor: [Cross-Sectional Studies] explode all trees
#35	MeSH descriptor: [Case-Control Studies] explode all trees
#34	MeSH descriptor: [Cohort Studies] explode all trees
#33	MeSH descriptor: [Longitudinal Studies] explode all trees
#32	MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees
#31	MeSH descriptor: [Randomized Controlled Trial] explode all trees
#30	MeSH descriptor: [Research Design] explode all trees
#29	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28
#28	improvement:ti,ab,kw
#27	prevention:ti,ab,kw
#26	protective factor*:ti,ab,kw
#25	etiology:ti,ab,kw
#24	history:ti,ab,kw
#23	antecedent:ti,ab,kw

	Search Strategy
#22	adverse:ti,ab,kw
#21	harm:ti,ab,kw
#20	prediction:ti,ab,kw
#19	association:ti,ab,kw
#18	relationship:ti,ab,kw
#17	MeSH descriptor: [Causality] explode all trees
#16	risk factor*:ti,ab,kw
#15	MeSH descriptor: [Risk] explode all trees
#14	#2 or #3 or #4 or #5 or #6 or #7 #8 or #9 or #10 or #11
#13	Deliberat* self-harm
#12	self-injur*
#11	Parasuicide
#10	Non-suicid* self-injury
#9	suicid* attempt*
#8	suicid* plan
#7	suicid* ideation
#6	suicid* behavi*
#5	suicid*
#4	MeSH descriptor: [Suicide] explode all trees
#3	#2 not (#2 and #1)
#2	MeSH descriptor: [Animals] explode all trees
#1	MeSH descriptor: [Humans] explode all trees

5. PsycInfo (EBSCOHost): Search January 21th, 2017

	Search Strategy
#1	((DE “suicidal ideation” OR Suicidal Ideation OR DE "Suicide+" OR DE "Assisted Suicide" OR (DE “suicidology”) OR suicid***** *OR* (suicidal AND behav*) OR “suicidal ideation” OR “suicide plan” *OR* “suicide attempt” OR “attempted suicide” *OR* suicidality *OR* **“**suicide prevention” *OR* parasuicide *OR* **“**self-injurious behavior” *OR* "non-suicidal self-injury” *OR* self-injur* *OR* "non-fatal suicidal behavior" *OR* "non-fatal suicidal behaviour" OR (DE "Suicide Prevention")) AND (DE "risk factors" OR “risk factors” OR DE “causality” OR (TI causalit* OR AB causalit*) OR (TI relationship OR AB relationship) OR (TI Association* OR AB Association*) OR DE "Prediction" OR DE "Harm Reduction" OR (TI adverse OR AB adverse) OR (TI History OR AB History) OR DE "Etiology" OR (DE "Protective Factors") OR (TI “Protective factors” OR AB “Protective factors”) OR (DE "Prevention") OR (DE "Accident Prevention") OR prevalence OR incidence OR (DE "Primary Mental

	Health Prevention") OR (DE "Relapse Prevention") OR (TI improve* OR AB improve*)) AND (DE "Clinical Trials+" OR DE "Experimental Design" OR DE "Between Groups Design" OR DE "Clinical Trials" OR DE "Cohort Analysis" OR DE "Followup Studies" OR DE "Hypothesis Testing" OR DE "Longitudinal Studies" OR DE "Repeated Measures" OR DE "Prospective Studies" OR DE "Case-control" OR DE "Cross-sectional" OR DE "Time Series" OR DE "Retrospective Studies")) NOT ((DE "Animals+" OR DE "Female Animals" OR DE "Infants (Animal)" OR DE "Invertebrates" OR DE "Male Animals" OR DE "Vertebrates") OR (DE "Case report"))

6. OpenGrey: Search January 20th, 2017

	Search Strategy
#1	((suicide* OR (suicide* (behaviour OR behaviour)) OR (suicide* attempt*) OR (deliberate self-harm) OR (suicidality) OR self-injur*) AND (risk factor* OR causalit* OR relationship* OR association* OR prediction* OR harm* OR adverse OR antecedent* OR history OR etiology OR protective factor* OR prevention* OR improvement* OR incidence) AND (longitudinal study OR observational study OR cohort study OR ((case AND control) study) OR prospective study OR retrospective study OR "follow-up") AND (young* OR youth OR child* OR adolescent* OR (college student*) OR (university student*) OR (young worker*))

SUPPLEMENTARY TEXT S2 THE SYSTEMATIC REVIEW OF GENDER DIFFERENCES IN SUICIDAL BEHAVIOR IN ADOLESCENTS AND YOUNG ADULTS (covered up until January 2017)

References of included articles (n=77) (Studies n=67)

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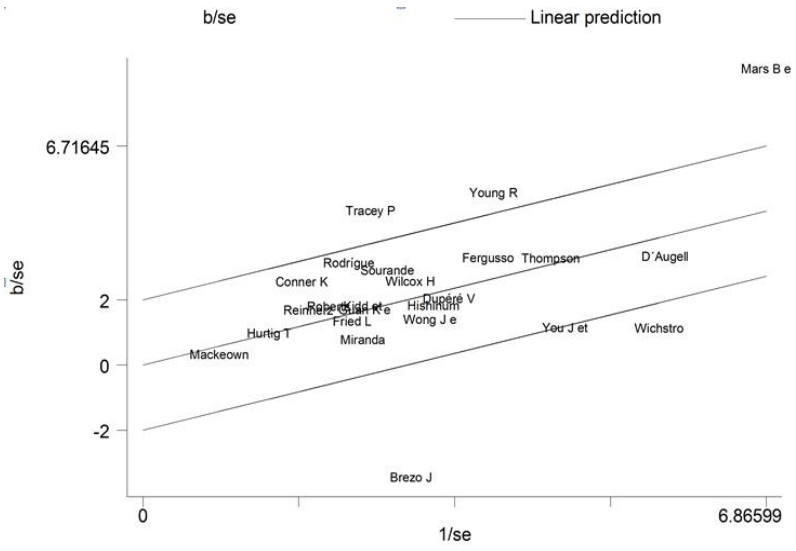
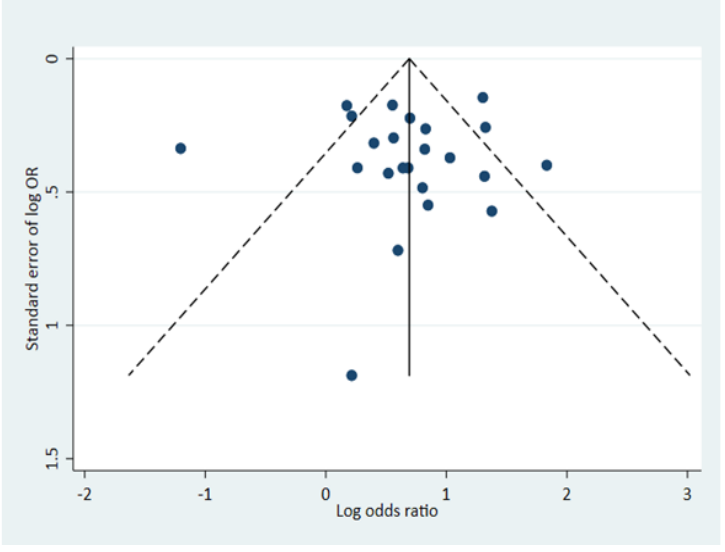
Figure S1. Galbraith plot (a) and Funnel plot (b) of being female as risk factor of suicide attempt – results of the systematic review of gender differences in suicidal behavior in adolescents and young adults (covered up until January 2017)



(a) Galbraith plot



(b) Funnel plot (Egger test = 0.847)

ANNEX 3. Supplementary material for article 3

Supplementary material for this article:

Miranda-Mendizábal A, Castellví P, Parés-Badell O, Almenara J, Alonso I, Blasco MJ, et al. Sexual orientation and suicidal behaviour in adolescents and young adults: systematic review and meta-analysis. Br J Psychiatry. 2017;211:77–87.

Data supplement DS1
Detail search strategy: Search terms by database

Components	Keywords	
	Inclusion keywords	**Exclusion keywords**
Population	Humans	Animals
Outcome	Suicide Suicidal behavior Suicide ideation Suicide plan Suicide attempt Non-suicidal self-injury Parasuicide Self-injure Deliberate self-harm Suicidality Non-fatal suicidal behavior	
Exposure	Risk factor Causality Relationship Association Prediction Harm Adverse Antecedent History Etiology Protective factor Prevention Improvement Prevalence Incidence	
Study design	Experimental study Randomized controlled trial Controlled clinical trial Clinical trial Longitudinal study Observational study Cohort study Case control study Time series study Prospective study Retrospective study Follow-up Cross-sectional study	Case series Case report
Others		Type of publications: - Comments - Letter. - Editorial

Search Strategy in each selected database:

1. **Medline (Pubmed): Search October 27, 2013**

	Search Strategy
#24	(#20 AND #21 AND #22) NOT (#18 OR #19 OR #20)
#23	(#14 OR #15 OR #16 OR #17)
#22	(#10 OR #11 OR #12 OR #13)
#21	(#5 OR #6 OR #7 OR #8 OR #9)
#20	(#3 OR #4)
#19	(#1 NOT (#1 AND #2))
#18	case reports[Publication Type]
#17	(("prospective studies"[MeSH Terms] OR ("prospective"[All Fields] AND "studies"[All Fields]) OR "prospective studies"[All Fields] OR ("prospective"[All Fields] AND "study"[All Fields]) OR "prospective study"[All Fields]) OR ("retrospective studies"[MeSH Terms] OR ("retrospective"[All Fields] AND "studies"[All Fields]) OR "retrospective studies"[All Fields] OR ("retrospective"[All Fields] AND "study"[All Fields]) OR "retrospective study"[All Fields]) OR Follow-up[All Fields] OR ("cross-sectional studies"[MeSH Terms] OR ("cross-sectional"[All Fields] AND "studies"[All Fields]) OR "cross-sectional studies"[All Fields] OR ("cross"[All Fields] AND "sectional"[All Fields] AND "study"[All Fields]) OR "cross sectional study"[All Fields]))
#16	(("cohort studies"[MeSH Terms] OR ("cohort"[All Fields] AND "studies"[All Fields]) OR "cohort studies"[All Fields] OR ("cohort"[All Fields] AND "study"[All Fields]) OR "cohort study"[All Fields]) OR ("case-control studies"[MeSH Terms] OR ("case- control"[All Fields] AND "studies"[All Fields]) OR "case-control studies"[All Fields] OR ("case"[All Fields] AND "control"[All Fields] AND "study"[All Fields]) OR "case control study"[All Fields]) OR (("time"[MeSH Terms] OR "time"[All Fields]) AND series[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "study"[All Fields] OR "biomedical research"[MeSH Terms] OR ("biomedical"[All Fields] AND "research"[All Fields]) OR "biomedical research"[All Fields])))

	Search Strategy
#15	(("controlled clinical trial"[Publication Type] OR "controlled clinical trials as topic"[MeSH Terms] OR "controlled clinical trial"[All Fields]) OR ("clinical trial"[Publication Type] OR "clinical trials as topic"[MeSH Terms] OR "clinical trial"[All Fields]) OR ("longitudinal studies"[MeSH Terms] OR ("longitudinal"[All Fields] AND "studies"[All Fields]) OR "longitudinal studies"[All Fields] OR ("longitudinal"[All Fields] AND "study"[All Fields]) OR "longitudinal study"[All Fields]) OR (Observational[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "study"[All Fields] OR "biomedical research"[MeSH Terms] OR ("biomedical"[All Fields] AND "research"[All Fields]) OR "biomedical research"[All Fields]))))
#14	((Experimental[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "study"[All Fields] OR "biomedical research"[MeSH Terms] OR ("biomedical"[All Fields] AND "research"[All Fields]) OR "biomedical research"[All Fields])) OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trial"[All Fields] OR "randomised controlled trial"[All Fields]))
#13	(("risk factors"[MeSH Terms] OR ("risk"[Tiab] AND "factors"[Tiab]) OR "risk factors"[Tiab] OR ("risk"[Tiab] AND "factor"[Tiab]) OR "risk factor"[Tiab]))
#12	(("etiology"[Subheading] OR "etiology"[Tiab] OR "causality"[Tiab] OR "causality"[MeSH Terms]) OR Relationship[Tiab] OR ("association"[MeSH Terms] OR "association"[Tiab]) OR Prediction[Tiab] OR Harm[Tiab] OR Adverse[Tiab] OR Antecedent[Tiab] OR ("history"[Subheading] OR "history"[Tiab] OR "history"[MeSH Terms]))
#11	((“protective factors”[Tiab] OR (“protective”[Tiab] AND “factor”[Tiab]) OR (“protective”[Tiab] AND “factors”[Tiab]) OR "prevention"[Tiab]) OR Improvement[Tiab])
#10	(prevalence[MeSH Terms] OR incidence[MeSH Terms] OR prevalence[Tiab] OR incidence[Tiab])
#9	(("deliberate"[All Fields] AND "self"[All Fields] AND "harm"[All Fields]) OR "deliberate self-harm"[All Fields])

	Search Strategy
#8	((Non-suicidal[All Fields] AND self-injury[All Fields]) OR ("self-injurious behavior"[MeSH Terms] OR ("self-injurious"[All Fields] AND "behavior"[All Fields]) OR "self-injurious behavior"[All Fields] OR "parasuicide"[All Fields]) OR Self-injure[All Fields] OR ("self-injurious behavior"[MeSH Terms] OR ("self- injurious"[All Fields] AND "behavior"[All Fields]) OR "self-injurious behavior"[All Fields]))
#7	("suicide, attempted"[MeSH Terms] OR ("suicide"[All Fields] AND "attempted"[All Fields]) OR "attempted suicide"[All Fields] OR ("suicide"[All Fields] AND "attempt"[All Fields]) OR "suicide attempt"[All Fields])
#6	((suicidal[All Fields] AND ("behaviour"[All Fields] OR "behavior"[MeSH Terms] OR "behavior"[All Fields])) OR (("suicide"[MeSH Terms] OR "suicide"[All Fields]) AND (ideation[All Fields] OR plan[All Fields])))
#5	(suicid*) OR "suicide"[MeSH Terms] OR "suicide"[All Fields])
#4	editorial [Publication Type]
#3	letter[Publication Type]
#2	human[MeSH Terms]
#1	animal[MeSH Terms]

2. Embase: Search October 21, 2013

	Search Strategy
#6	(#3 AND #4 AND #5) NOT (#1 OR #2)
#5	'experimental study'/exp OR 'experimental study' OR 'randomized controlled trial'/exp OR 'randomized controlled trial' OR 'controlled clinical trial'/exp OR 'controlled clinical trial' OR 'clinical trial'/exp OR 'clinical trial' OR 'longitudinal study'/exp OR 'longitudinal study' OR 'observational study'/exp OR 'observational study' OR 'cohort analysis'/exp OR 'cohort analysis' OR 'case control study'/exp OR 'case control study' OR 'prospective study'/exp OR 'prospective study' OR 'retrospective study'/exp OR 'retrospective study' OR 'follow-up'/exp OR 'follow-up' OR 'cross-sectional study'/exp OR 'cross-sectional study' OR 'cohort study'/exp OR 'cohort study' OR 'time series study'
#4	'risk factor'/exp OR 'risk factor':ti,ab OR 'prediction'/exp OR 'prediction':ti,ab OR 'association'/exp OR 'association':ti,ab OR 'prevention'/exp OR 'prevention':ti,ab OR 'causality'/exp OR 'causality':ti,ab OR 'relationship':ti,ab OR 'adverse':ti,ab OR 'antecedent':ti,ab OR 'etiology'/exp OR 'etiology':ti,ab OR 'protective factor':ti,ab OR prevalence/exp OR incidente/exp
#3	suicid* OR 'suicidal behavior'/exp OR 'suicidal behavior' OR 'automutilation'/exp OR 'automutilation' OR 'suicide'/exp OR 'suicide' OR 'suicide ideation'/exp OR 'suicide ideation' OR 'suicide plan' OR 'suicide attempt'/exp OR 'suicide attempt' OR 'non- suicidal self-injury' OR 'parasuicide'/exp OR 'parasuicide' OR 'self-injure' OR 'deliberate self-harm' OR suicidality
#2	letter/exp OR editorial/exp OR “case report”/exp
#1	animal/exp NOT (animal/exp AND human/exp)

3. Web of Science: Search October 21, 2013

	Search Strategy
#6	(#3 AND #4 AND #5) NOT (#1 OR #2)
#5	TS=(Experimental study OR Randomized controlled trial OR Controlled clinical trial OR Clinical trial OR Longitudinal study OR Observational study ORCohort study OR Case control study OR Time series study OR Prospective study OR Retrospective study OR Follow-up OR Cross-sectional study)
#4	TS=(Risk factor OR Causality OR Relationship OR Association OR Prediction OR Harm OR Adverse OR Antecedent OR History OR $Etiology OR Protective factor OR Prevention OR Improvement OR prevalence OR incidence)

	Search Strategy
#3	TS=(Suicid* OR suicide OR Suicidal behavior OR Suicide ideation OR Suicide plan OR Suicide attempt OR Non-suicidal self-injury OR Parasuicide OR Self-injure OR Deliberate self-harm OR Suicidality OR Non-fatal suicidal behaviour)
#2	DT=(letter) OR TI=(editorial) OR TI=(case report)
#1	TS=(animal NOT (animal AND human))

4. The Cochrane Library: Search October 17, 2013

	Search Strategy
#39	(#14 and #29 and #37) not (#3 or #38)
#38	MeSH descriptor: [Case Reports] explode all trees
#37	#30 or #31 or #32 or #33 or #34 or #35 or #36
#36	MeSH descriptor: [Cross-Sectional Studies] explode all trees
#35	MeSH descriptor: [Case-Control Studies] explode all trees
#34	MeSH descriptor: [Cohort Studies] explode all trees
#33	MeSH descriptor: [Longitudinal Studies] explode all trees
#32	MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees
#31	MeSH descriptor: [Randomized Controlled Trial] explode all trees
#30	MeSH descriptor: [Research Design] explode all trees
#29	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28
#28	improvement:ti,ab,kw
#27	prevention:ti,ab,kw
#26	protective factor*:ti,ab,kw
#25	etiology:ti,ab,kw
#24	history:ti,ab,kw
#23	antecedent:ti,ab,kw
#22	adverse:ti,ab,kw
#21	harm:ti,ab,kw
#20	prediction:ti,ab,kw
#19	association:ti,ab,kw
#18	relationship:ti,ab,kw
#17	MeSH descriptor: [Causality] explode all trees
#16	risk factor*:ti,ab,kw

	Search Strategy
#15	MeSH descriptor: [Risk] explode all trees
#14	#2 or #3 or #4 or #5 or #6 or #7 #8 or #9 or #10 or #11
#13	Deliberat* self-harm
#12	self-injur*
#11	Parasuicide
#10	Non-suicid* self-injury
#9	suicid* attempt*
#8	suicid* plan
#7	suicid* ideation
#6	suicid* behavi*
#5	suicid*
#4	MeSH descriptor: [Suicide] explode all trees
#3	#2 not (#2 and #1)
#2	MeSH descriptor: [Animals] explode all trees
#1	MeSH descriptor: [Humans] explode all trees

5. PsycInfo (EBSCOHost): Search October 22, 2013

	Search Strategy
#1	((DE “suicidal ideation” OR Suicidal Ideation OR DE "Suicide+" OR DE "Assisted Suicide" OR (DE “suicidology”) OR suicid***** *OR* (suicidal AND behav*) OR “suicidal ideation” OR “suicide plan” *OR* “suicide attempt” OR “attempted suicide” *OR* suicidality *OR* **“**suicide prevention” *OR* parasuicide *OR* **“**self-injurious behavior” *OR* "non-suicidal self-injury” *OR* self-injur* *OR* "non-fatal suicidal behavior" *OR* "non- fatal suicidal behaviour" OR (DE "Suicide Prevention")) AND (DE "risk factors" OR “risk factors” OR DE “causality” OR (TI causalit* OR AB causalit*) OR (TI relationship OR AB relationship) OR (TI Association* OR AB Association*) OR DE "Prediction" OR DE "Harm Reduction" OR (TI adverse OR AB adverse) OR (TI History OR AB History) OR DE "Etiology" OR (DE "Protective Factors") OR (TI “Protective factors” OR AB “Protective factors”) OR (DE "Prevention") OR (DE "Accident Prevention") OR prevalence OR incidence OR (DE "Primary Mental Health Prevention") OR (DE "Relapse Prevention") OR (TI improve* OR AB improve*)) AND (DE "Clinical Trials+" OR DE "Experimental Design" OR DE "Between Groups Design" OR DE "Clinical Trials" OR DE "Cohort Analysis" OR DE "Followup Studies" OR DE "Hypothesis Testing" OR DE "Longitudinal Studies" OR DE "Repeated Measures" OR DE "Prospective Studies" OR DE “Case-control” OR DE “Cross-sectional” OR DE "Time Series" OR DE "Retrospective Studies")) NOT ((DE “Animals+” OR DE "Female Animals" OR DE "Infants (Animal)" OR DE “Invertebrates” OR DE "Male Animals" OR DE "Vertebrates") OR (DE “Case report”))

6. OpenGrey: Search July 1, 2014 (Limit publication date: October 27, 2013)

	Search Strategy
#1	((suicide* OR (suicide* (behaviour OR behaviour)) OR (suicide* attempt*) OR (deliberate self-harm) OR (suicidality) OR self-injur*) AND (risk factor* OR causalit* OR relationship* OR association* OR prediction* OR harm* OR adverse OR antecedent* OR history OR etiology OR protective factor* OR prevention* OR improvement* OR incidence) AND (longitudinal study OR observational study OR cohort study OR ((case AND control) study) OR prospective study OR retrospective study OR “follow-up”) AND (young* OR youth OR child* OR adolescent* OR (college student*) OR (university student*) OR (young worker*))

Table DS1 Population attributable risk

Prevalence of LBG (%)	P_0 (%)	RR	PAR (%)
4	4	2.15	4.4
8	4	2.15	8.4
13	4	2.15	13

Prevalence of being LGB was calculated based on data from studies reporting this.[18-23,31] P_0: prevalence of suicide attempts in heterosexuals.

RR: relative risk.

PAR: population attributable risk.

Table DS2 Risk factors for suicide attempts in LGB adolescents and young adults

Author	Percentage of suicide attempts	Risk factor	Suicide attempts %/M(SD)	
			Yes (n=61)	**No (n=300)**
D´Augelli A et al. 2005	16.9	Ever called sissy/tomboy	72	60
		Parents called youth sissy/tomboy	**59**	**27**
		Parents discouraged gender-atypical behaviour	69	30
		Parents called youth LGB	55	35
		History of family suicidality	**38**	**23**
		History of family depression	**10**	**6**
		Family socioeconomic status	3.16 (1.36)	2.99 (1.37)
		Age of first awareness of same-sex attractions	8.66 (2.53)	10.07 (3.44)
		Age of self-identification as LGB	12.59 (2.43)	13.92 (2.39)
		Age of first disclosure of sexual orientation	13.41 (2.18)	14.34 (2.02)
		Openness with family members about sexual orientation	**3.97 (0.98)**	**3.01 (1.53)**
		Age of disclosure of sexual orientation to a parent	13.57 (2.79)	14.89 (2.24)
		Years of awareness of sexual orientation	8.45 (2.32)	6.92 (3.63)
		Years between self-identification and first disclosure	1.00 (1.63)	.90 (1.67)
		Openness about sexual orientation with friends	4.28 (1.28)	4.15 (1.16)
		Openness about sexual orientation in junior high school	0.55 (1.12)	0.72 (1.24)
		Childhood gender atypicality	**3.68 (1.39)**	**2.94 (1.43)**
		Parental psychological abuse	**1.78 (0.85)**	**1.09 (0.69)**
		Gay-related verbal abuse	8.03 (6.67)	4.51 (4.80)

Table DS2 *(continued)*

Author	Percentage of suicide attempts	Risk factor	Suicide attempts
			OR (95%CI)
Silenzio V et al. 2007	4.5[a]	Problem drinking	1.97 (0.42-9.12)
		Problem drug use	1.78 (0.46-6.91)
		Depression	1.11 (0.99-1.25)
Mustanski B et al. 2013	5.5	Past suicide attempt	**10.52 (2.00-55.27)**
		Depression	0.98 (0.84-1.14)
		Hopelessness	1.82 (0.79-4.19)
Burns M et al. 2015	14	Black	1.29 (0.58-2.87)
		Latino	1.44 (0.57-3.59)
		Other	3.02 (1.10-8.25)

[a] Percentage from the total LGBs in the sample (Table 1).

Bold letters show higher prevalence or media values, and significant odd ratios.

Figure DS1 Forest plot (a), Galbraith plot (b) and Funnel plot (c) of sexual orientation as risk factor for suicide attempts, comparing gay and bisexual against heterosexual men

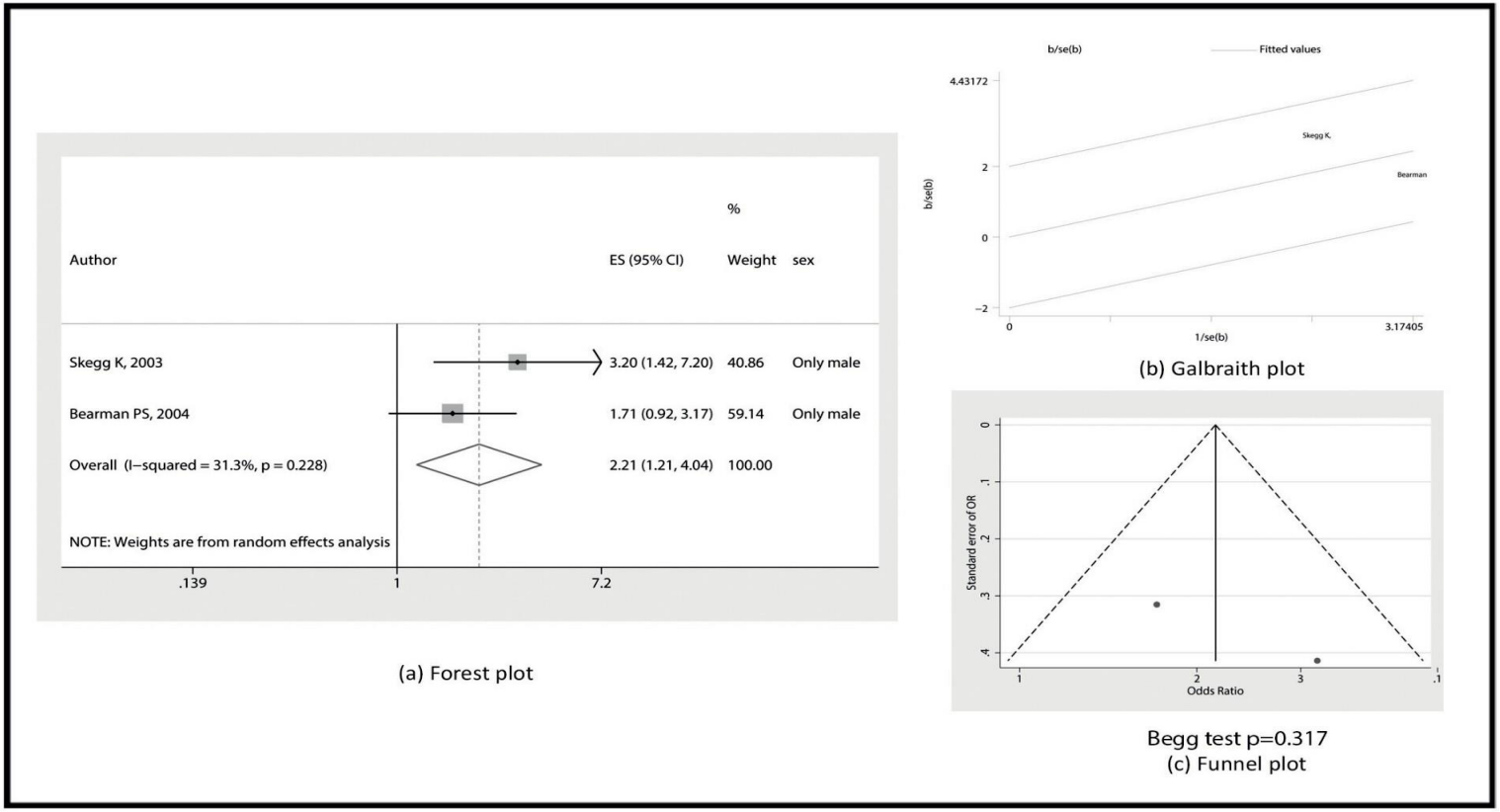


Figure DS2 Forest plot (a), Galbraith plot (b) and Funnel plot (c) of sexual orientation as risk factor for suicide attempts, comparing lesbian and bisexual against heterosexual women

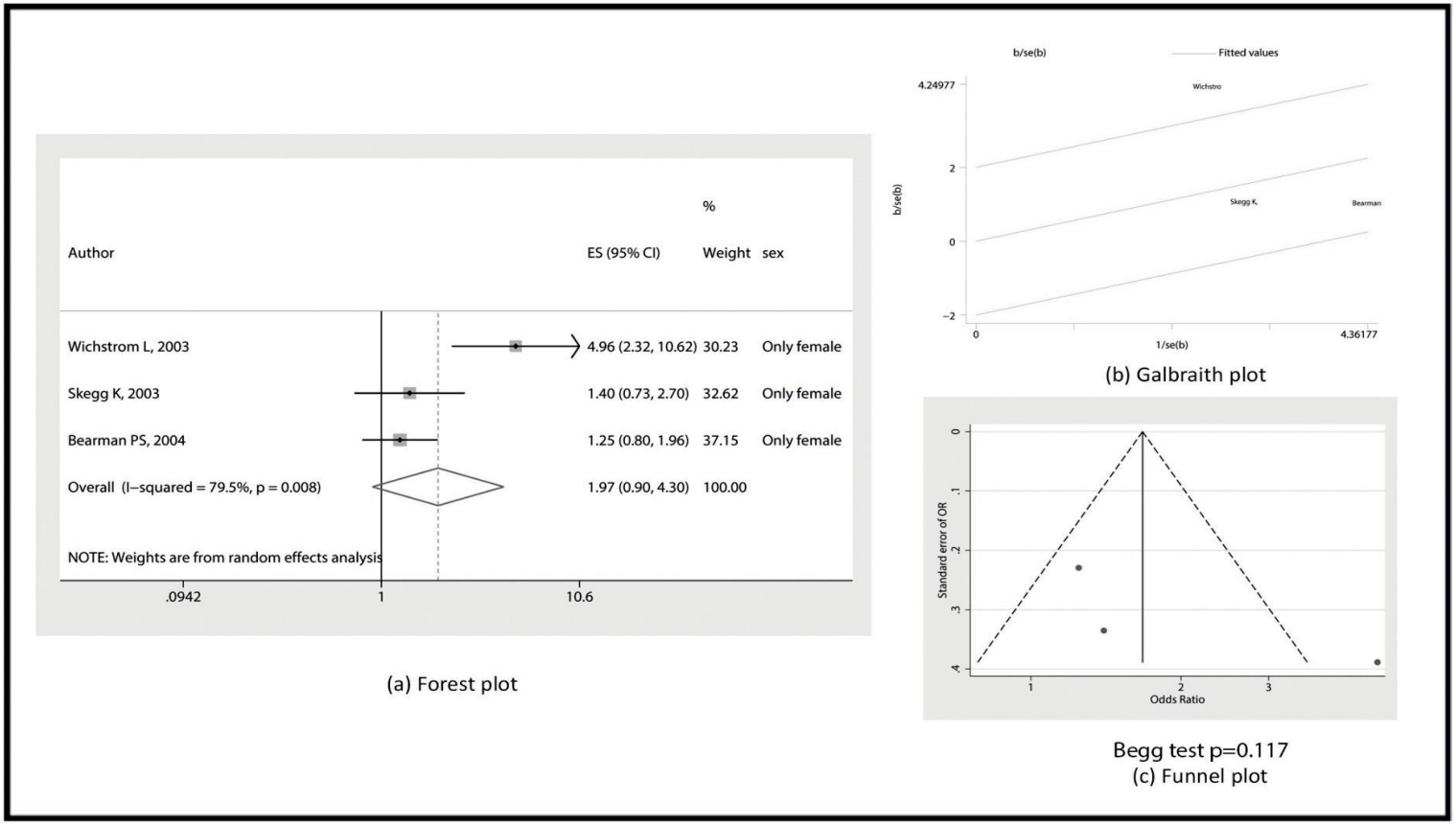


Figure DS3 Forest plots of sexual orientation as risk factor for suicide attempts, comparing a) gay versus heterosexual men, b) bisexual versus heterosexual men, c) lesbian versus heterosexual women, and d) bisexual versus heterosexual women

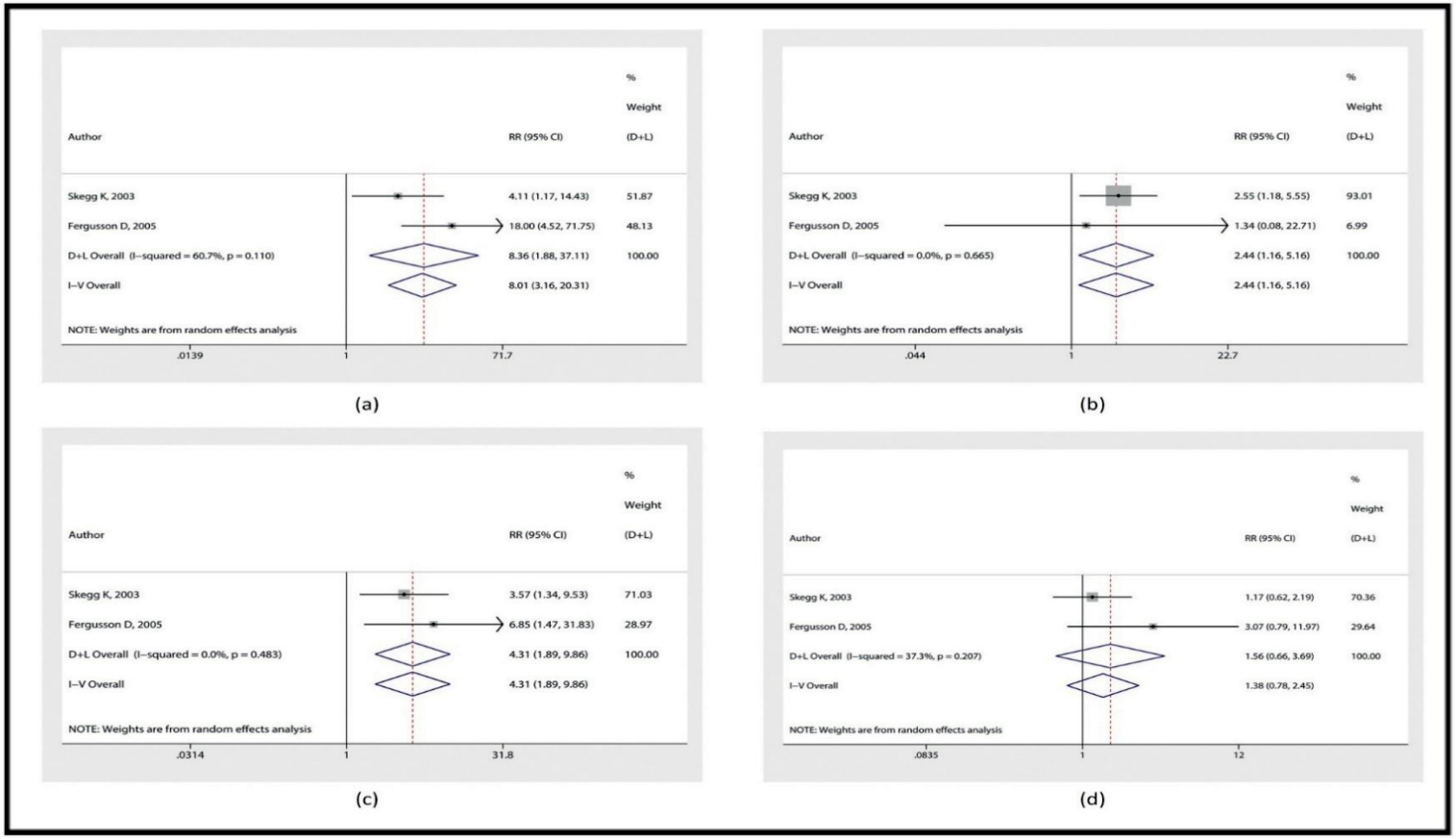
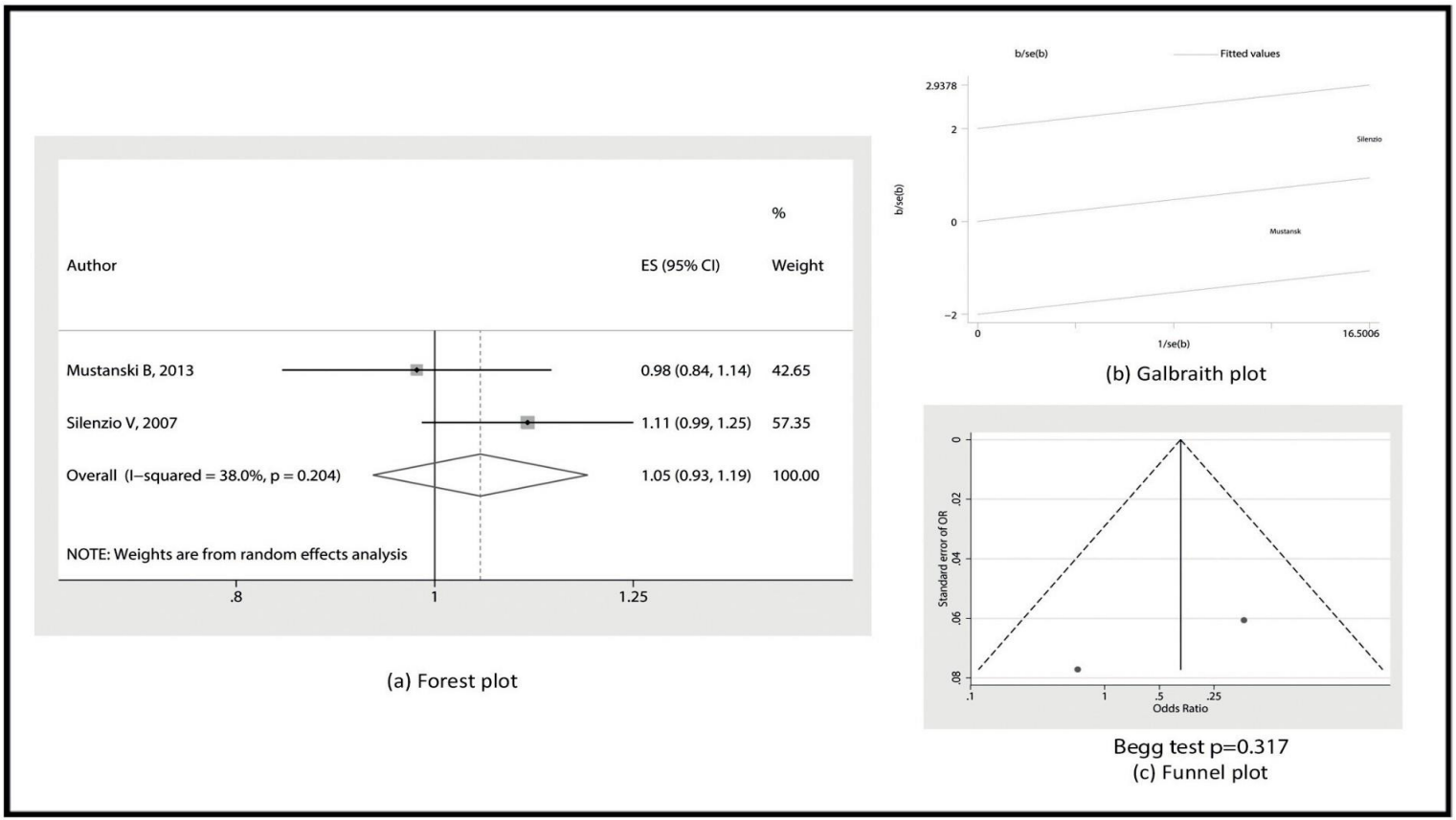


Figure DS4 Forest plot (a), Galbraith plot (b) and Funnel plot (c) of depression as risk factor for suicide attempts in lesbian, gay and bisexual adolescents and youths



ANNEX 4. Supplementary material for article 4

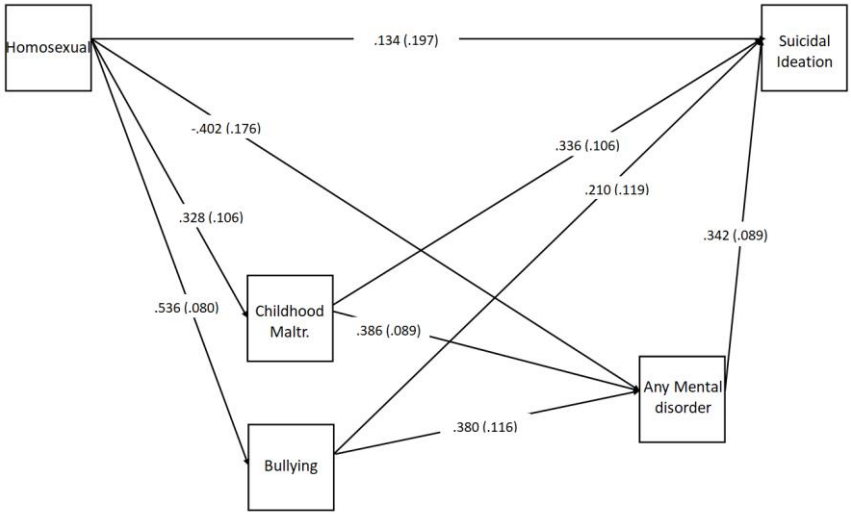
Supplementary material for this article:

Miranda-Mendizabal A, Castellví P, Vilagut G, Alayo I, Almenara J, Ballester L. Suicidal ideation risk among LGB Spanish university students: the role of childhood and adolescence adversities and mental disorders. Article to be submitted to the *"Journal of Adolescence Health"*.

Table S1. Perceived sexual orientation discrimination items (12-month) among homosexual and bisexual Spanish university students. The UNIVERSAL (University and Mental Health) study

	Homosexual (Gay/Lesbian) n=43		**Bisexual n=70**	
	n	**%**	**n**	**%**
Were you ignored, excluded or avoided by people close to you?	4	9.3	4	5.7
Were you rejected by a potential sexual or romantic partner?	0		3	4.3
Were you treated with hostility or coldness by strangers?	5	11.6	10	14.3
Did someone act as if you could not be trusted?	0		6	8.6
Did someone insult or make fun of you?	7	16.3	5	7.1
Were you denied a place to live or did you lose a place to live?	0		2	2.9
Was your personal property damaged or stolen?	0		1	1.4
Were you physically assaulted or beaten up?	1	2.3	0	
Were you treated poorly or made to feel inferior when receiving health care?	0		0	
Frequency				
None	33	76.7	54	77.1
1-2	9	20.9	13	18.6
3 or more	1	2.3	4	5.7

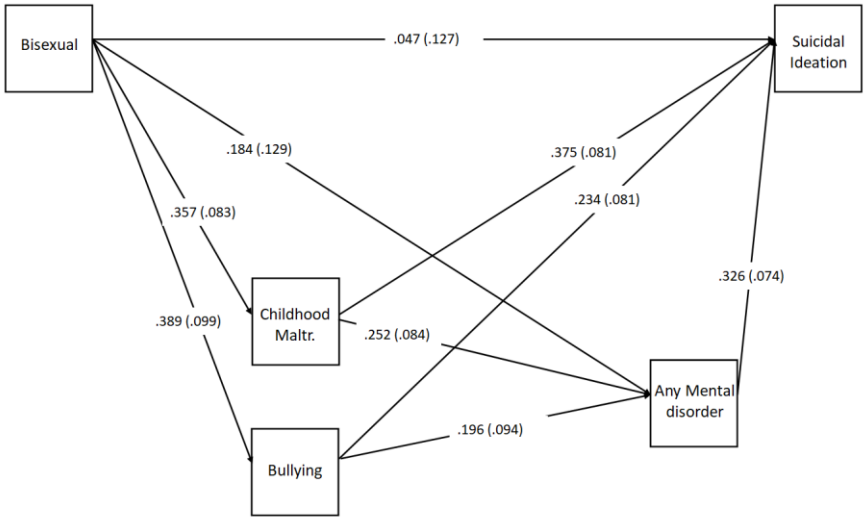
Figure S1. Path analysis model depicting the direct and indirect effects of childhood/adolescence adversities, mental disorders on suicidal ideation for homosexual (gay/lesbian) compared to heterosexual Spanish university students. Based on data from the UNIVERSAL (University and Mental Health) study (n=1,072)



Values represent standardized path coefficients.
Homosexual: homosexual (gay/lesbian) (lifetime); **Childhood Maltr.:** any childhood maltreatment prior to 17- year-olds; **Bullying:** any form of bullying prior to 17- year-olds; **Any mental disorder:** any mental disorder (12-month); **Suicidal ideation:** suicidal ideation (12-month).

Description: **total effect** of being homosexual (gay/lesbian) compared to being heterosexual on suicidal ideation (SI) (standardized coefficient β =0.331, SE =0.11, p =0.003) was statistically significant. Total effect on any mental disorders was non-statistically significant (β =-0.071, SE =0.12, p =0.552) **Indirect effects** for being homosexual, of childhood maltreatment (β =0.127, SE =0.06, p =0.023) and bullying (β =0.203, SE =0.08, p =0.009) on the relationship between sexual orientation and any mental disorder were significant. The indirect effect of childhood maltreatment (β =0.110, SE =0.05, p =0.039) on the relationship between sexual orientation and SI was significant, with a ratio over the total effect of 0.33. The indirect effect of bullying non-statistically significant (β =0.112, SE =0.06, p =0.073). The indirect effect mediated by any mental disorder was β =-0.02 (SE =0.04). The ratio to the total effect of all mediation effects considered in the relationship between sexual and SI was 0.61. Model goodness of fit was adequate (CFI =0.964; TLI =0.919; RMSEA =0.025, σ =0.002).

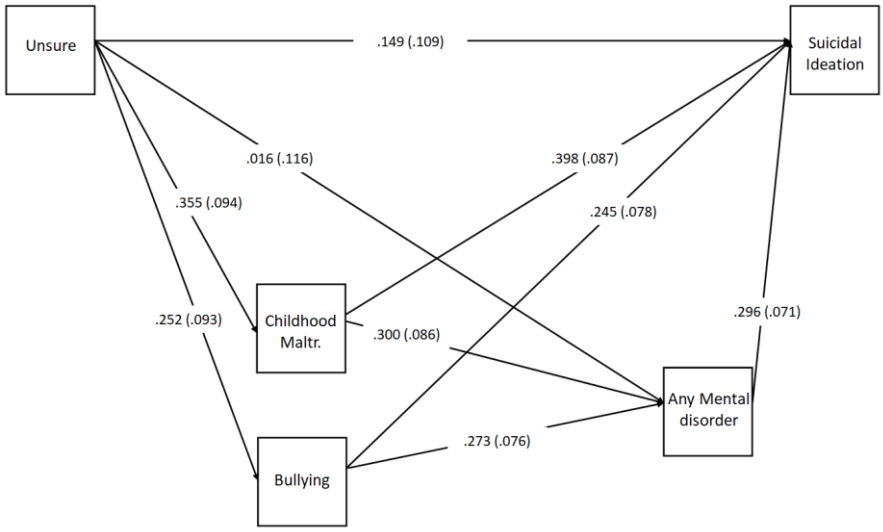
Figure S2. Path analysis model depicting the direct and indirect effects of childhood/adolescence adversities, mental disorders on suicidal ideation for bisexual compared to heterosexual Spanish university students. Based on data from the UNIVERSAL (University and Mental Health) study (n=1,099)



Values represent standardized path coefficients.
Bisexual: sexual orientation bisexual (lifetime); **Childhood Maltr.:** any childhood maltreatment prior to 17- year-olds; **Bullying:** any form of bullying prior to 17- year-olds; **Any mental disorder:** any mental disorder (12-month); **Suicidal ideation:** suicidal ideation (12-month).

Description: **total effects** of being bisexual compared to being heterosexual on suicidal ideation (SI) (standardized coefficient β =0.385, SE =0.09, p <.001) and on any mental disorders (β =0.350, SE =0.10, p <.001) were statistically significant. **Indirect effects** for being bisexual, of childhood maltreatment (β =0.090, SE =0.04, p =0.010) and bullying (β =0.076, SE =0.04, p =0.046) on the relationship between sexual orientation and any mental disorder were significant. The indirect effects of childhood maltreatment (β =0.134, SE =0.05, p =0.003) and bullying (β =0.090, SE =0.04, p =0.018) on the relationship between sexual orientation and SI were significant, with a ratio over the total effect of 0.58. The indirect effect mediated by any mental disorder was β =0.114 (SE =0.04). The ratio to the total effect of all mediation effects considered in the relationship between sexual and SI was 0.87. Model goodness of fit was adequate (CFI =0.989; TLI =0.976; RMSEA =0.016, σ =0.003).

Figure S3. Path analysis model depicting the direct and indirect effects of childhood/adolescence adversities, mental disorders on suicidal ideation for unsure compared to heterosexual Spanish university students. Based on data from the UNIVERSAL (University and Mental Health) study (n=1,102)



Values represent standardized path coefficients.
Unsure: not sure about sexual orientation (lifetime); **Childhood Maltr.:** any childhood maltreatment prior to 17- year-olds; **Bullying:** any form of bullying prior to 17- year-olds; **Any mental disorder:** any mental disorder (12-month); **Suicidal ideation:** suicidal ideation (12-month).

Description: **total effects** of being unsure about their sexual orientation compared to being heterosexual on suicidal ideation (SI) (standardized coefficient β =0.406, SE =0.096, p <.001) and on any mental disorders (β =0.182, SE =0.08, p 0.027) were statistically significant. **Indirect effects** for being bisexual, of childhood maltreatment (β =0.107, SE =0.04, p =0.017) and bullying (β =0.060, SE =0.03, p =0.049) on the relationship between sexual orientation and any mental disorder were significant. The indirect effects of childhood maltreatment (β =0.141, SE =0.04, p =0.001) and bullying (β =0.062, SE =0.03, p =0.024) on the relationship between sexual orientation and SI were significant, with a ratio over the total effect of 0.50. The indirect effect mediated by any mental disorder was β =0.005 (SE =0.03). The ratio to the total effect of all mediation effects considered in the relationship between sexual and SI was 0.51. Model goodness of fit was adequate (CFI =0.940; TLI =0.864; RMSEA =0.036, σ =0.002).