

Mental disorders, comorbidities, and suicidality at 30 years of age in a Brazilian birth cohort

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ARTICLE INFO

Keywords:
Comorbidity
Suicide
Public mental health

ABSTRACT

Background: Studies on mental disorders prevalence and comorbidity, including suicidality, are scarce in low and middle-income settings. We aimed to describe the pattern of comorbidity between mental disorders and their association with suicidality.

Methods: In 1982, all hospital deliveries in Pelotas (Southern Brazil) were identified ($n = 5914$) and have been prospectively followed. Participants were evaluated for the presence of common mental disorders (CMD) at the ages of 18–19, 23 and 30 years. In 2012–13 (30 years of age), trained psychologists evaluated 3657 individuals for disorders using the Mini International Neuropsychiatric Interview.

Results: Prevalence of suicidal wishing, suicidal planning and lifetime suicidal attempt was 4.9%, 3.8% and 6.6%, respectively. Suicidal wishing was most strongly associated with having joint major depressive episode (MD) and lifetime suicidal attempt ($OR = 26.4$, 95%CI:13.9–50.4) with comorbid MD with mania/hypomania ($OR = 21.2$, 95%CI:6.93–65.1). Suicidal planning was most strongly associated with having joint MD and lifetime suicidal attempt ($OR = 44.7$, 95%CI:22.6–88.4), with comorbid MD and social anxiety disorder ($OR = 30.6$, 95%CI:13.0–72.0), and joint social anxiety disorder with lifetime suicidal attempt ($OR = 26.3$, 95%CI:8.33–82.7). Independently of other disorders, prospective and cross-sectional measures of CMD were associated with higher rates of suicidality.

Limitations: We do not have data on suicide deaths in follow-up and the diagnostic instrument used at 30 years of age was not used in all previous follow-up.

Conclusion: MD and social anxiety have independent and combined associations with suicidality, and also with they occur with lifetime suicidal attempt and other mental disorders.

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1. Introduction

Mental health problems, especially depressive disorders, are major contributors to the global burden of disease. It was estimated that there were over 253 million cases of major depressive disorder worldwide in 2013 [14]. According to the 2010 global burden of disease report, suicide was responsible for 36.2 million disability-adjusted life years (DALYs), of which 22.5 million were attributable to mental health problems, with 46.1% of the latter being due to depression [12]. According to the World Health Organization (WHO) [46], “over 800,000 people

die due to suicide every year and many others attempt suicide”. In 2015, suicide accounted for 1.4% of all deaths worldwide, 75% of which occurred in low- and middle-income countries. It should be noted that in the same year, according to Pew Research Center, 84% of population lived in low- and middle-income countries, what indicate that the relative rate of suicide is lower than in high-income countries.

It is important to note that, recent studies have been showing that externalizing disorders can be strong predictors of suicidal behavior. A study verify that only post-traumatic stress disorder and disorders characterized by irritability and impulsive/aggressive behavior (i.e., bipolar disorder, conduct disorder, oppositional defiant disorder, and attention-deficit/hyperactivity disorder) predicted unplanned attempts among ideators [35]. In the same sense, it was verified that

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externalizing disorders such as intermittent explosive disorder and conduct disorder are most common among suicidal behavior [36].

In Brazil, the mortality rate due to suicide is lower than USA, but increased among young adults, particularly among men [30]. A cross-sectional population-based study identified suicide risk in young adults between 18 and 35 years of age in south Brazil and found a prevalence of 13% [45].

Thoughts like being worthless and that it should be better to be dead, may or may not lead to self-harming behaviors, including suicide. According to [32] theories of suicidality are now incorporating the fact that in most suicide ideators do not attempt suicide and thus there must be separate risk factors for suicidal thinking and suicidal action. In their meta-analysis, the authors found that anxiety disorders, especially post-traumatic stress disorders, as well as drug use disorders and sexual abuse, were moderately more common among people who attempted suicide compared to those who were limited to suicidal ideations.

A key predictor of suicidal ideation versus suicide attempts is whether the thoughts involve intent and active planning of the suicide method [28]. Recent studies have assessed whether suicidal ideation involves intent or not (suicidal wishing vs suicidal planning), which has been associated with factors such as unemployment, acute stressors, and history of mental disorders, specially depressive-like symptoms and comorbidity between mood and anxiety disorders [17,24,47]. According to the National Comorbidity Survey, in the USA 67% of people diagnosed with lifetime generalized anxiety disorder (GAD) was diagnosed with major depression (MD) at some point in their lives, and 20% of people with MD was diagnosed with GAD [26]. Comorbidity of mood and anxiety disorders is associated with several markers of clinical severity, including earlier age of onset, higher number of depressive episodes and greater risk of suicide [15]. Similarly, among people with major depression, social anxiety disorder (SAD) is associated with more severe depression [29]; however, studies on the association between SAD and suicidality in general populations, especially in low- and middle-income countries, are scarce.

Comorbidity between depression, anxiety and other mental disorders is also associated with an increased risk of suicide [17,40] and has important implications for both diagnosis and treatment, which can lead to direct and indirect patient costs [29]. The high rate of comorbidity between mental disorders makes it difficult to isolate the effects of each one on suicidality. Studies should simultaneously evaluate mental disorders and different aspects of suicidal behavior. However, population-based studies with such data are rare. In the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a prospective national study in the USA, the risk of attempting suicide was positively associated with a general psychopathology factor representing the shared effect across all mental disorders [19]. A nationwide study of Korean adults, suggested that comorbid mental disorders such as bipolar disorder and alcohol use disorder may contribute to impulsive suicidal behaviors in unplanned attempters such as falling and the ingestion of chemical agents [25].

In addition, previous studies have also highlighted the importance of non-specific, but clinically relevant, symptoms of anxiety and depression, that do not meet diagnostic criteria for particular Axis I disorders [18]. These symptoms of common mental disorders have a negative effect on quality of life, causing considerable functional disability and subsequently important personal, social and economic losses [38]. Common mental disorders are related to symptoms such as mental suffering, insomnia, headache, fatigue, irritability, forgetfulness, difficulty concentrating, sadness, anxiety and somatic concern [16].

1.1. Aims of the study

In the present study, we aimed to describe the pattern of comorbidity between mental disorders and their association with suicidality, in a population that has been prospectively followed since birth.

2. Materials and methods

2.1. Data sources, data collection, and study sample

In 1982, all maternity hospitals in Pelotas, a southern Brazilian city, were visited daily. We identified 99.2% of all births in the city, and the 5914 live births whose families lived in the urban area of the city were selected and their mothers interviewed. These individuals have been followed on several occasions and further details on study methodology have been published elsewhere. [5].

In 2000, male cohort adolescents (mean age 18.2 years) were identified and 2250 were interviewed. In 2001, a systematic subsample of 27% of female participants, with a mean age of 18.9 years, was visited at home. In 2004, when individuals had a mean age of 22.8 years, we attempted to follow the whole cohort. Participants were interviewed and examined at home. [44].

From June 2012 to February 2013, at a mean age of 30.2 years, we tried to locate the entire cohort using multiple strategies. Cohort members were invited, by telephone contact, to visit our research clinic, where they were interviewed and examined by trained personal (four psychologists trained and supervised by a specialist in psychodiagnostic assessment) [21].

2.2. Measures

The visit included a psychological interview, using the Mini International Psychiatric Interview (MINI) V5.0 validated for Brazil [1] to evaluate the presence of (i) major depressive episode (MDE) during the last 2 weeks; (ii) lifetime episode of mania/hypomania; (iii) GAD during the last 6 months; and (iv) SAD during the last month. In addition, the presence of suicidal risk was assessed using five questions from the MINI. We considered an individual as a case of major depression (MD) if they currently had a MDE and did not report a lifetime episode of mania/hypomania. We also used the Beck depression inventory (BDI-II), but to assess suicidal thoughts and wishing [6]. Because the clinical diagnosis of major depression requires the presence of functional impairment, at the end of the MDE and GAD module, we applied the following question: "Do these problems negatively affect your life with respect to school, work, home, family, and friends: 'not at all', 'a bit', 'more or less', or 'a lot'?" Individuals that were positive for MD and responded "more or less" or "a lot" to this question, were considered as having MD or GAD with impairment. Specific details on how all mental health variables were measured can be found in the supplementary material (Supplementary Methods).

To assess suicidality, we used the following questions from the MINI:

1. During the last month, did you think that you would be better off dead or wish you were dead?
2. During the last month, did you want to harm yourself, or to hurt or injure yourself?
3. During the last month, did you think about killing yourself?
If YES, during the last month, did you plan a way of killing yourself?
4. At any time during your life, did you try to kill yourself?

In addition, we used one of the statements in the BDI-II, which refers to "suicidal thoughts and wishing". Possible responses were: i) I do not have any thoughts of killing myself; ii) I have thoughts of killing myself, but I would not carry them out; iii) I would like to kill myself; iv) I would kill myself if I had the chance.

Using the data from MINI and BDI, we created a variable called "current suicidal ideation" with three categories:

- (i) No suicidal ideation: includes those who responded "no" to questions 1 to 3 and reported in the BDI-II that they did not have any thoughts of killing themselves.
- (ii) Suicidal wishing without intent: includes those who reported in the BDI-II that he or she had suicidal thoughts, but would not carry them out, or answered "yes" only to question 1.

- (iii) Suicidal planning with intent: includes those who: responded “yes” to questions 2 or 3, or both; or answered options “iii)” or “iv)” in the BDI-II item referring to thoughts and suicidal wishing. If any individual met criteria for suicidal wishing and suicidal planning at the same time, they were categorized as suicidal planning.

Question 4 was treated as a separate item, and those who responded “yes” were considered as having a lifetime suicidal attempt (LS).

The self-reported questionnaire (SRQ-20), validated for Brazil, was used to assess Common Mental Disorder symptoms at 18/19, 23 and 30 years of age. Males and females with a score of six and eight or more, respectively, were considered positive for Common Mental Disorder [31]. In total, 1447 men and 703 women had Common Mental Disorder information for all three visits. For these individuals, we created a variable indicating the number of Common Mental Disorder episodes during adulthood (18–30 years), ranging from 0 to 3.

2.3. Statistical analyses

In previous publications, we have shown that follow-up rates at 30 years were higher in females [22]; given this and the fact that the prevalence of mental disorders is higher in women, prevalence of each disease for the whole population could be overestimated. Therefore, we estimated the weighted prevalence considering the original (baseline) proportion of females/males in the cohort as follows: Weighted Prevalence = (Prevalence of each mental disorder in men × %men at baseline) + (Prevalence of each mental disorder in women × %females at baseline). We used chi-square tests to compare proportions between males and females.

To describe comorbidities between mental disorders, we used the BioVenn tool, which is a web application used to produce area-proportional Venn diagrams. [23]. In addition, a graphical representation of the studied mental disorders was performed separately for each sex. The size of the circles is directly proportional to the prevalence, and line transparency is inversely proportional to the correlation between a given pair of disorders, darker lines correspond to stronger positive correlations, while lighter lines correspond to weaker positive correlations. Since all disorders are binary variables, tetrachoric correlation coefficients were used.

We used multinomial regression models for the outcome current suicidal ideation, because it was a nominal variable with three categories. These models calculate the odds ratio (OR) for each category of the outcome, in relation to the same reference category –in this case “no suicidal ideation”.

For mental health and lifetime suicidal attempt, the prevalence ratio was estimated using Poisson regression with robust adjustment of the variance. [4].

For suicide-related variables, MDE (with and without impairment), mania/hypomania, GAD (with and without impairment) and SAD were adjusted for each other in multivariable models. We used MDE instead of MD for the prediction of suicidality because it would be inappropriate to include in the same regression model MD and mania/hypomania, given that they are mutually exclusive. In models where the outcome was current suicidal ideation, LS was also included as an independent variable.

Analyses of the associations between both Common Mental Disorder and SRQ-20 scores at 30 years with suicidality were adjusted for mental health disorders, evaluated with the MINI (without impairment) and LS. Analyses of the association between the number of Common Mental Disorder episodes in adulthood and suicidality were adjusted for the same mental health disorders, but not LS. All multivariable models were adjusted for sex and we tested if this variable modified the associations. We used STATA v.12.1 for statistical analysis.

3. Results

In 2012–13, 3701 individuals were interviewed. Of these, 3657 had data on at least one mental health variable. Prevalence of Common Mental Disorder was 24.3%. Generalized anxiety disorder and major depression were the most prevalent mental health disorders: 16.4% of the subjects had at least one of these diagnoses and 4.2% had both. Impairment was observed among 63.8% of the subjects with GAD and 63.3% of those with MD. Among those diagnosed with MD and MD with impairment, 33.8% and 18.6% reported that this was their first episode, respectively. In total, 19.0% of individuals had at least one mental disorder according to the MINI, 14.8% and 28.5%, among men and women, respectively. Unweighted and weighted prevalence estimates were almost identical.

Regarding suicidality, 8.7% were positive for current suicidal ideation (Suicidal wishing = 4.9% and Suicidal planning = 3.8%), and 6.6% reported lifetime suicidal attempt. Women had a higher prevalence of Common Mental Disorder, suicidality, and all mental health diagnoses, except mania or mania/hypomania (Table 1).

Fig. 1 shows that the patterns of comorbidities were similar among males and females. The strongest correlation was between MDE and GAD. Even though the magnitude of some correlation coefficients may seem different between the sexes, statistical tests of interaction with sex yielded *p*-values greater than 0.05. Therefore, the main analyses for comorbidities were not stratified by sex. Stratified analyses are shown in Supplementary Table 1.

Fig. 2 and Table 2 show that the two most common comorbidities at 30 years were MD with GAD, and mania/hypomania with GAD. Among those with MD, and among those with a lifetime episode of mania/hypomania, the prevalence of GAD was 52.8% and 52.7%, respectively. However, among those with GAD, the prevalence of MD was 33.0%, and of mania/hypomania 8.6%. For SAD, 27.3% had MD and 42.2% GAD. In addition, 39.2% who reported a lifetime episode of mania/hypomania and 52.9% of those who were positive for mania had a major depressive episode during the last two weeks.

Fig. 3 and Table 2 show that the most prevalent mental disorders among those with current suicidal ideation and lifetime suicidal attempt were MD (32.3%) and GAD (34.0%). In addition, 78.7% of those with current suicidal ideation and 63.2% of those with a lifetime suicidal attempt were positive for Common Mental Disorder. The prevalence estimates of current suicidal ideation and lifetime suicidal attempt among those with no mental disorders were 3.7% and 3.8%, respectively. Mania had a slightly higher prevalence of suicidal wishing, and a lower prevalence of lifetime suicidal attempt when compared to mania/hypomania. Current suicidal ideation and lifetime suicidal attempt were reported by 39.2% and 18.9% of those with SAD, respectively.

Table 3 shows that, independently of other mental disorders, all mental health variables were associated with current suicidal ideation. Also, all mental health variables were associated with lifetime suicidal attempt, except for mania/hypomania, mania and SAD. In adjusted models of current suicidal ideation, major depressive episode and lifetime suicidal attempt had the strongest associations with suicidal wishing (OR = 6.19 (95%CI: 4.13–9.26) and OR = 6.10 (95%CI: 4.03–9.22), respectively), and Suicidal planning (OR = 7.08 (95%CI: 4.46–11.2) and OR = 8.63 (95%CI: 5.46–13.6), respectively). In addition, independently of any other mental disorder and sex, those with SAD had a odds of Suicidal planning 5.18 (95%CI: 2.89; 9.31) times higher, and those positive for MDE had an odds 3.93 (95%CI: 2.83; 5.46) times higher of reporting a lifetime suicidal attempt.

Table 3 also shows the associations between suicidality and having combinations of two mental disorders. For the outcome lifetime suicidal attempt, measures of association were generally stronger for some combinations of disorders when compared to their individual effects. However, confidence intervals for the effects of having comorbid mental disorders, in most cases, included the mean OR of the individual effect of at least one of the disorders; therefore, we cannot rule out that

Table 1
Mental disorders prevalence and differences between males and females at 30 years of age in a Brazilian.

	Total N (%)	Male N (%)	Female N (%)	p-value ^a	Weighted Total ^b %
Common mental disorder (SRQ)	885 (24.3)	374 (21.3)	511 (27.1)	<0.001	24.1
MINI diagnoses					
MD	282 (7.9)	72 (4.2)	210 (11.3)	<0.001	7.7
MDi	177 (5.0)	51 (3.0)	126 (6.9)	<0.001	4.9
Mania/Hypomania	74 (2.1)	33 (1.9)	41 (2.2)	0.55	2.0
Mania	34 (1.0)	15 (0.9)	19 (0.9)	0.65	0.9
GAD	452 (12.7)	122 (7.1)	330 (17.8)	<0.001	12.3
GADi	283 (8.1)	74 (4.3)	209 (11.6)	<0.001	7.9
SAD	128 (3.6)	34 (2.0)	94 (5.1)	<0.001	3.5
Suicidality					
Suicidal wishing	173 (4.9)	56 (3.3)	117 (6.4)	<0.001	4.8
Suicidal planning	135 (3.8)	39 (2.3)	96 (5.2)	<0.001	3.7
Lifetime suicidal attempt	235 (6.6)	81 (4.7)	154 (8.3)	<0.001	6.5

^a Chi-squared test comparing the prevalence of disease between males and females. ^b Weighted Prevalence = (Prevalence of each mental disorder in men * %men at baseline) + (Prevalence of each mental disorder in women * %females at baseline). BDI=Beck depression inventor. GAD = Generalized anxiety disorder. GADi Generalized anxiety disorder with impairment. MD = Major depression. MDi = Major Depression with impairment. SAD = Social anxiety disorder. SRQ = Self-reported questionnaire.

these higher rates were found by chance. The only exception was MDE + GAD in adjusted models: having both disorders increased the odds of a lifetime suicidal attempt 5.84 times (95% CI: 4.17–8.19), compared to those without either MDE or GAD.

Regarding suicidal wishing and Suicidal planning (Table 3), we observed that the highest ORs for suicidal wishing were among those with LS + MDE [OR = 26.4 (95% CI: 13.9–50.4)] and MDE + Mania/Hypomania [OR = 21.2 (95% CI: 6.93–65.1)]. The ORs for those with MDE + GAD and SAD+Mania/Hypomania were 10.6 (95% CI: 6.54–17.3) and 9.85 (95% CI: 1.81–53.7), respectively. Similarly, for Suicidal planning, the highest ORs were observed among those with LS + MDE [OR = 44.7 (95% CI: 22.6–88.4)], MDE + SAD [OR = 30.6 (95% CI: 13.0–72.0)], and LS + SAD [OR = 26.3 (95% CI: 8.33–82.7)]. In absolute

terms, 40.7%, 47.8% and 51.0% of those with LS + MDE, MDE + SAD and LS + SAD, were positive for Suicidal planning, respectively.

Table 4 shows that, independently of the diagnosis of any other mental disorders and sex, those positive for Common Mental Disorder at 30 years had an odds 6.38 [95%CI (4.26–9.57)] and 7.27 [95%CI (4.22–12.5)] times higher of having suicidal wishing and suicidal planning, respectively, and a risk 3.49 (2.55–4.78) times higher of LS. In addition, every point increase in the SRQ-20 at 30 years was associated with an increased odds of suicidal wishing (30%), suicidal planning (37%) and reporting of a LS (19%). We found that for each Common Mental Disorder episode, in the three follow-ups from 18 to 30 years, the odds for suicidal wishing [OR = 2.27 95%CI (1.82–2.82)], suicidal planning [OR = 2.34 95%CI (1.78–3.06)] and risk of a LS [PR = 1.70

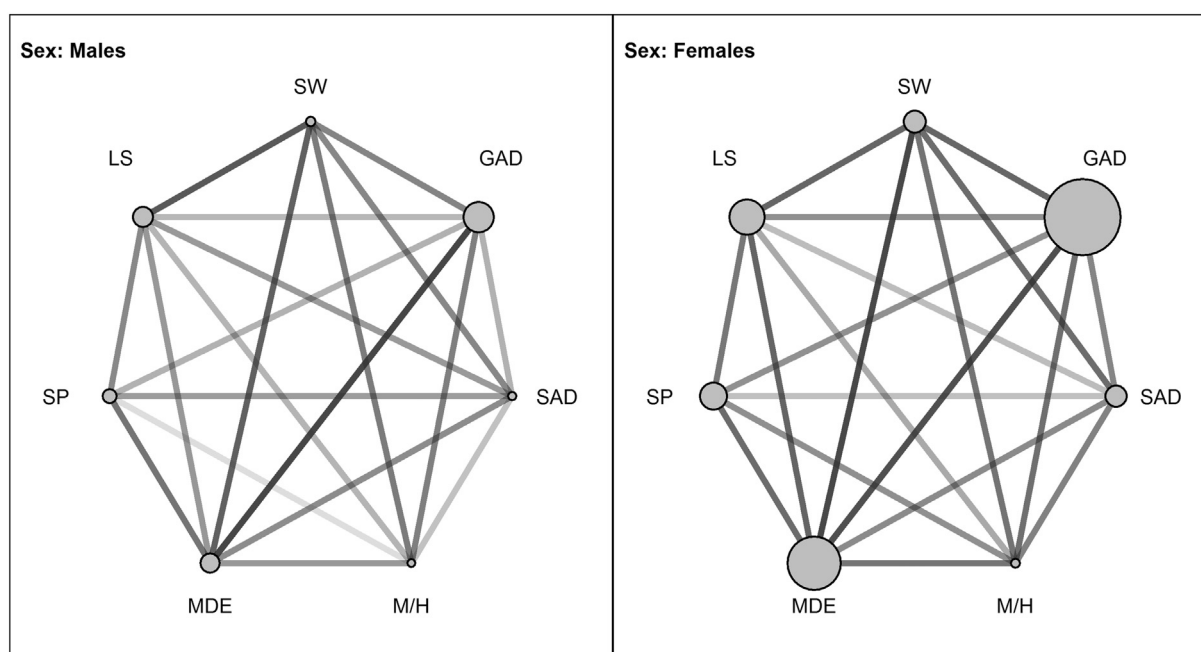


Fig. 1. Pattern of comorbidities between MINI diagnoses and suicidality, and the burden of mental disease in males and females at 30 years. The size of the circles is directly proportional to the prevalence, and line transparency is inversely proportional to the tetrachoric correlation between a given pair of disorders: darker lines correspond to stronger positive correlations, while lighter lines correspond to weaker positive correlations. MDE = Major depressive episode during the last 2 weeks. GAD = Generalized anxiety disorder. M/H = Mania/Hypomania. SAD = Social anxiety disorder. SW=Suicidal wishing. SP=Suicidal planning. LS = Lifetime suicidal attempt.

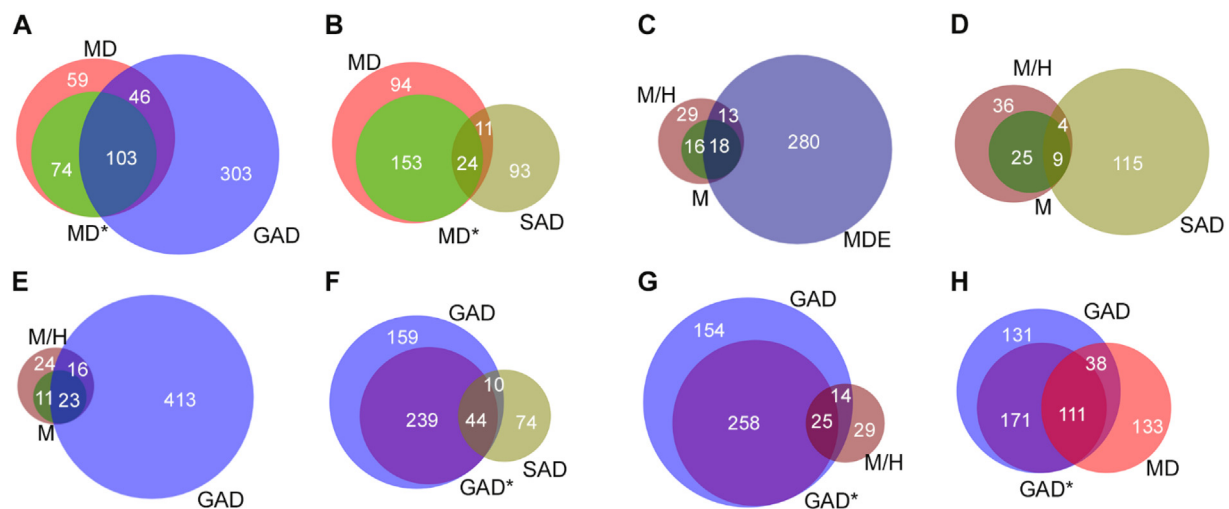


Fig. 2. Mental health comorbidities at 30 years. A = Major depression with and without impairment, and Generalized anxiety disorder ($N = 3576$). B = Major depression with and without impairment, and Social anxiety disorder ($N = 3572$). C = Mania/Hypomania, Mania without hypomania and major depression ($N = 3572$). D = Mania/Hypomania, Mania without hypomania and Social anxiety disorder ($N = 3572$). E = Mania/Hypomania, Mania without hypomania and Generalized anxiety disorder ($N = 3572$). F = Generalized anxiety disorder with and without impairment, and Social anxiety disorder ($N = 3573$). G = Generalized anxiety disorder with and without impairment, and Mania/Hypomania ($N = 3573$). H = Generalized anxiety disorder with and without impairment, and major depression ($N = 3573$). I = Major depression or generalized anxiety disorder with and without impairment and Social anxiety disorder. *Mental health disorder with impairment. MD = Major depression. MDE = Major depressive episode during the last 2 weeks. GAD = Generalized anxiety disorder. M/H = Mania/Hypomania. M = Mania without hypomania. SAD = Social anxiety disorder.

Table 2
Mental disorders prevalence and differences between males and females at 30 years of age in a Brazilian.

	MD N (%)	MDi N (%)	M/H N (%)	Mania N (%)	GAD N (%)	GADi N (%)	SAD N (%)	SW N (%)	SP N (%)	LS N (%)	NMD N (%)	NMDS N (%)
MD ^a	NA	NA	29 (39.2)	18 (52.9)	149 (33.0)	111 (39.2)	35 (27.3)	59 (34.1)	61 (45.2)	72 (32.3)	NA	NA
M/H	NA	NA	NA	NA	39 (8.6)	25 (8.8)	10 (7.8)	13 (7.5)	19 (14.1)	15 (6.4)	NA	NA
GAD	149 (52.8)	103 (58.2)	39 (52.7)	23 (67.7)	NA	NA	54 (42.2)	63 (36.4)	71 (52.6)	80 (34.0)	NA	NA
SAD	35 (12.6)	24 (13.7)	13 (18.3)	9 (27.3)	54 (12.1)	44 (15.7)	NA	18 (10.4)	30 (22.9)	24 (10.3)	NA	NA
SW	59 (21.3)	43 (24.6)	13 (18.1)	9 (26.5)	63 (14.2)	46 (16.6)	18 (14.8)	NA	NA	50 (22.1)	71 (2.5)	NA
SP	61 (22.0)	43 (24.6)	19 (26.4)	9 (26.5)	71 (16.0)	55 (19.9)	30 (24.6)	NA	NA	52 (23.0)	34 (1.2)	NA
LS	76 (27.1)	55 (31.3)	15 (20.8)	6 (17.7)	80 (17.8)	56 (19.9)	24 (18.9)	50 (28.9)	52 (39.4)	NA	109 (3.8)	82 (2.9)
Total	282 (7.9)	177 (5.0)	74 (2.1)	34 (1.0)	444 (12.6)	277 (7.9)	128 (3.6)	173 (4.9)	135 (3.8)	235 (6.6)	2897 (81.0)	2792 (78.1)

^a Major depression was defined as having a major depressive episode during the last 2 weeks and not having a lifetime episode of mania/hypomania, however for the mania/hypomania and mania rows MD is defined as having a major depressive episode during the last 2 weeks only. GAD = Generalized anxiety disorder. GADi = Generalized anxiety disorder with impairment. LS = Lifetime suicidal attempt. MD = Major depression. MDi = Major depression with impairment. NMD = No mental disorder. NMDS = No mental disorder or suicidal wishing or intent/planning. SAD = Social anxiety disorder. SP = Suicidal planning. SW = Suicidal wishing.

95%CI(1.43–2.03)] were higher. There was no evidence of effect modification by sex.

4. Discussion

In this study, we found that MD and GAD were the most prevalent mental disorders, and the burden of disease was higher among females. In addition, we recalculated the total prevalence of each disease using the baseline proportions of males and females and found no differences compared with the unweighted estimates, suggesting that differences in follow-up rates by sex did not influence the overall prevalence. It is important to mention that, although in general the burden of mental disease is higher in women, this is predominantly due to a higher prevalence of internalizing problems, like mood and anxiety disorder. However, externalizing problems, like substance abuse and antisocial disorders are higher among men. [7,41].

In this young adult cohort, we found a high comorbidity between mood disorders and GAD, with more than 50% of individuals with MD or mania also having GAD, and with about one third of those diagnosed with GAD having comorbid major depression. Other large population-based epidemiological studies have also consistently identified high comorbidity between MDE and GAD [2,27]. It is known that comorbid MD

and GAD are the most common form of comorbidity that involves depression and anxiety [13], and that the presence of such comorbidities complicates the course, making recovery more difficult [48].

Among those with social anxiety disorder, almost one out of three had major depressive, and more than 40% had GAD. Importantly, GAD and SAD have similar levels of comorbidity with MDE. Therefore, studies should not only focus on MDE/GAD comorbidity, but with other anxiety disorders, especially SAD. Brown et al [8] found that approximately 40–50% of individuals with a diagnosis of SAD also had major depressive disorder. Moreover, a multicenter study found that 19.5% of those with SAD had MD symptoms and co-occurrence of other anxiety disorders was high and increased when MD was present (65.2%). [37] It is important to note that patients with SAD who present comorbid psychiatric are more likely to have more severe symptoms, resistance to treatment and decreased functioning. As well, they have higher suicide rates when compared to those who do not have comorbidities. [33].

Thus, when evaluating suicidality, we found that the measures of association of mental disorders with and without impairment were almost identical. In addition, the only disorders associated with a previous lifetime suicide attempt were MDE, GAD and SAD. All MINI diagnoses were associated with current suicidal ideation (wishing and planning), but MDE and lifetime suicidal attempt were the strongest

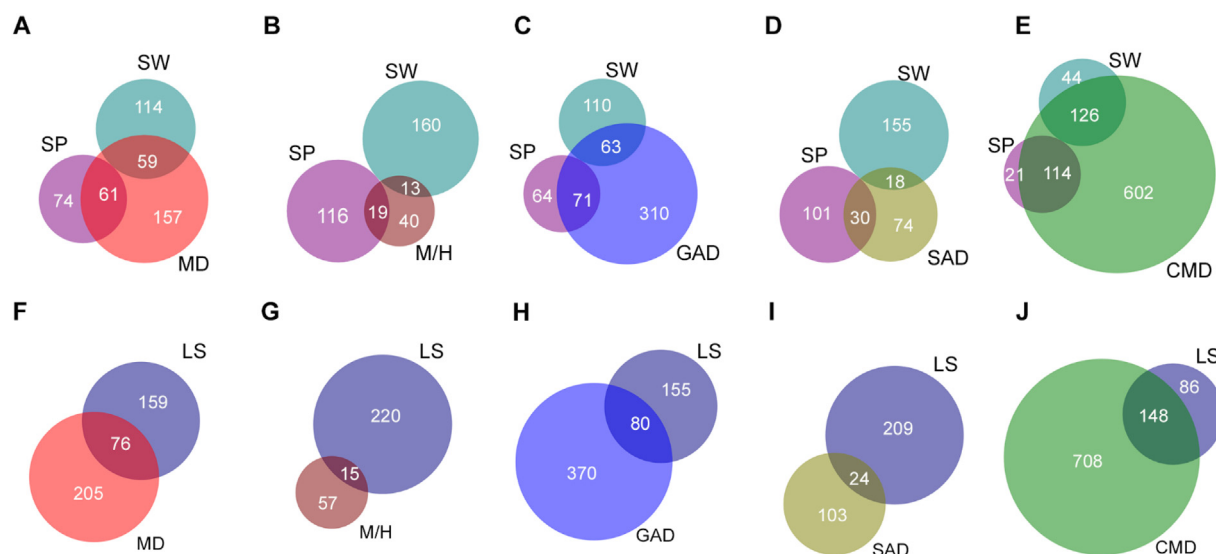


Fig. 3. Suicidal wishing, planning and lifetime attempt, and mental health comorbidities at 30 years. A = Suicidal wishing, suicidal planning and major depression ($N = 3533$). B = Suicidal wishing, suicidal planning and Mania/Hypomania ($N = 3533$). C = Suicidal wishing, suicidal planning and Generalized anxiety disorder ($N = 3533$). D = Suicidal wishing, suicidal planning and Social anxiety disorder ($N = 3533$). E = Suicidal wishing, suicidal planning and common mental disorders ($N = 3533$). F = Lifetime suicidal attempt and major depression ($N = 3567$). G = Lifetime suicidal attempt and Mania/Hypomania ($N = 3567$). H = Lifetime suicidal attempt and Generalized anxiety disorder ($N = 3567$). I = Lifetime suicidal attempt and Social anxiety disorder ($N = 3567$). J = Lifetime suicidal attempt and common mental disorders ($N = 3567$). MD = Major depression. GAD = Generalized anxiety disorder. M/H = Mania/Hypomania. SAD = Social anxiety disorder. SW = Suicidal wishing. SP = Suicidal planning. LS = Lifetime suicidal attempt. CMD = Common mental disorders.

Table 3

Univariable and multivariable models evaluating the association between mental health disorders, comorbidities (having two mental disease) and suicidality at 30 years.

	Crude			Adjusted ^a		
	Suicidal wishing ^b	Suicidal planning ^b	Lifetime suicidal attempt	Suicidal wishing ^b	Suicidal planning ^b	Lifetime suicidal attempt
	PR (95%CI)	PR (95%CI)	PR (95%CI)	PR (95%CI)	PR (95%CI)	PR (95%CI)
Individual mental disorders						
MDE	12.5 (8.85–17.6)	22.1 (15.2–32.1)	5.87 (4.61–7.46)	6.19 (4.13–9.26)	7.08 (4.46–11.2)	3.93 (2.83–5.46)
MDEi	14.6 (9.89–21.6)	20.2 (13.3–30.6)	6.02 (4.63–7.84)	6.75 (4.29–10.6)	5.67 (3.39–9.49)	3.65 (2.52–5.29)
Mania/Hypomania	6.46 (3.39–12.3)	13.0 (7.32–23.2)	3.31 (2.07–5.28)	2.89 (1.36–6.14)	3.65 (1.69–7.89)	1.41 (0.82–2.42)
Mania	11.0 (4.79–25.3)	44.3 (6.20–33.0)	2.72 (1.30–5.68)	3.67 (1.42–9.49)	3.40 (1.23–9.38)	0.88 (0.37–2.11)
GAD	5.38 (3.86–7.49)	10.4 (7.29–14.9)	3.57 (2.78–4.59)	2.01 (1.34–3.01)	3.18 (2.02–5.01)	1.63 (1.16–2.30)
GADi	6.55 (4.51–9.50)	13.2 (9.02–19.4)	3.75 (2.84–4.94)	2.22 (1.41–3.50)	3.70 (2.25–6.07)	1.49 (1.02–2.15)
SAD	4.93 (2.88–8.46)	12.6 (7.90–20.1)	3.10 (2.11–4.55)	2.35 (1.27–4.35)	5.18 (2.89–9.31)	1.38 (0.89–2.12)
LS	10.2 (6.99–14.8)	16.3 (11.0–24.1)	NA	6.10 (4.03–9.22)	8.63 (5.46–13.6)	NA
Comorbidities^c						
MDE + SAD	23.6 (9.73–57.5)	104 (48.7–220)	7.61 (4.90–11.8)	9.74 (3.74–25.4)	30.6 (13.0–72.0)	4.65 (2.64–8.19)
MDE + Mania/hypomania	49.9 (17.8–140)	110 (39.8–304)	6.37 (3.47–11.7)	21.2 (6.93–65.1)	22.9 (7.05–74.6)	3.91 (1.93–7.93)
MDE + GAD	17.9 (11.5–27.8)	44.2 (27.6–70.7)	7.23 (3.41–9.67)	10.6 (6.54–17.3)	20.2 (11.7–34.7)	5.84 (4.17–8.19)
GAD+Mania/Hypomania	12.9 (5.46–30.6)	38.1 (17.7–82.0)	3.86 (1.94–7.67)	4.85 (1.80–13.1)	10.1 (3.83–26.6)	1.42 (0.66–3.07)
GAD+SAD	11.6 (5.20–25.8)	51.4 (26.7–99.2)	4.44 (2.56–7.69)	3.6 (1.45–8.96)	14.6 (6.50–32.9)	1.51 (0.81–2.84)
SAD+Mania/Hypomania	28.3 (6.29–128)	69.0 (17.0–280)	2.64 (0.73–9.53)	9.85 (1.81–53.7)	19.8 (3.82–103)	0.73 (0.20–2.66)
LS + MDE	43.7 (23.8–80.4)	106 (56.9–196)	NA	26.4 (13.9–50.4)	44.7 (22.6–88.4)	NA
LS + Mania/Hypomania	33.3 (8.82–126)	56.3 (14.8–214)	NA	16.7 (3.76–74.2)	23.5 (4.95–111)	NA
LS + GAD	19.7 (10.6–36.6)	63 (34.7–114)	NA	6.36 (3.16–12.8)	16.6 (8.11–33.8)	NA
LS + SAD	19.6 (6.14–62.9)	79.3 (29.7–211)	NA	7.59 (2.11–27.3)	26.3 (8.33–82.7)	NA

^a Models were adjusted for sex and all other mental disorders without impairment. ^b Suicidal wishing and suicidal planning are the outcome of a single multinomial regression, in which the reference was not having any current suicidal ideation. ^c All measures of association represent the comparison between the groups with both mental disorders vs group with none of the two evaluated mental disorders. GAD = Generalized anxiety disorder. GADi = Generalized anxiety disorder with impairment. LS = Lifetime suicidal attempt. MD = Major depression. MDE = Major depressive episode. MDEi = Major depressive episode with impairment. NA = Not applicable. PR = Prevalence ratio. SAD = Social anxiety disorder.

predictors. On the other hand, when evaluating suicidal planning, SAD had almost the same effect size compared to MDE with impairment. Therefore, although suicidal ideation and/or attempt is commonly postulated as a consequence of depressive symptomatology [3,42], in our study some anxiety problems like SAD were associated with higher rates of suicidal planning independently of their comorbidity with mood disorders. Previous population-based studies have suggested that anxiety disorders could be associated with suicidality

independently of depressive symptomatology. For example, data from the National Comorbidity Survey Replication (NCS-R) and the NESARC, both from the USA, reported that anxiety disorders were associated with suicidal ideation and/or attempt. Of note, these studies reported that SAD was a better predictor of suicidality than GAD [9,34,43], similar to our study.

When evaluating suicidal wishing and especially suicidal planning, the magnitude of the effect estimates were stronger among individuals

Table 4

Univariable and multivariable models evaluating the association between common mental disorder (CMD) at 30 years, SRQ-20 score at 30 years and number of CMD episodes from 18 to 30 years, and suicidality at 30 years.

	Crude			Adjusted		
	Suicidal wishing ^a	Suicidal planning ^a	Lifetime suicidal attempt	Suicidal wishing ^a	Suicidal planning ^a	Lifetime suicidal attempt
	OR (95%CI)	OR (95%CI)	PR (95%CI)	OR (95%CI)	OR (95%CI)	PR (95%CI)
CMD at 30 years ^b	12.4 (8.70–17.7)	23.5 (14.6–37.8)	5.41 (4.20–6.98)	6.38 (4.26–9.57)	7.27 (4.22–12.5)	3.49 (2.55–4.78)
SRQ-20 score ^b	1.38 (1.33–1.43)	1.51 (1.44–1.58)	1.21 (1.19–1.24)	1.30 (1.24–1.36)	1.37 (1.29–1.45)	1.19 (1.15–1.22)
CMD episodes ^c	2.69 (2.20–3.28)	3.47 (2.76–4.36)	2.02 (1.76–2.32)	2.27 (1.82–2.82)	2.34 (1.78–3.06)	1.70 (1.43–2.03)

^a Suicidal wishing and suicidal intent/planning are the outcome of a single multinomial regression, in which the reference was not having any current suicidal ideation. ^b Adjusted for sex, major depressive episode, mania/hypomania, general anxiety disorder, social anxiety disorder and lifetime suicidal attempt. The PR for the exposure SRQ-20 score refers to 1-point increase in total SRQ at 30 years. ^c Adjusted for sex, major depressive episode, mania/hypomania, general anxiety disorder and social anxiety disorder. The PR for CMD episodes refers to an increase on the risk for each episode during adulthood (18–30 years), and this variable was available for 1447 men and 703 females. PR = Prevalence ratio. SRQ = Self-reported questionnaire.

with comorbid mental diseases. We observed that MDE, in association with any other mental disorder, generally presented the strongest effect estimates. However, having any mental disorder and SAD, or previous lifetime suicidal attempt, was associated with considerably stronger effect estimates (which were, in some cases, three or even four times larger). Moreover, the highest OR for suicidal planning were seen among those with MDE + LS, MDE + SAD and LS + SAD. Clinicians should therefore be particularly concerned when assessing suicidality in patients who have comorbid disorders, especially those involving MDE and SAD. It is also always important to note that LS is a major risk factor for suicide [39]. According to a recent study, among people who attempt suicide, 1.6% die by suicide in the next 12 months and 3.9% die by suicide in the next 5 years [39].

Common Mental Disorder was positively associated with all suicide-related outcomes, even in adjusted models. Suggesting that independently of having any of MINI diagnoses, individuals with Common Mental Disorder at 30 years, or with a higher number of Common Mental Disorder symptoms, or Common Mental Disorder episodes during adulthood, had a higher risk of suicidality. This suggests that even when individuals do not have a diagnosis for a mental disorder, sub-clinical symptoms could still indicate increased risk of suicidal behavior. Suicide involves multidetermined causes, such as genetic factors, family history, early-life adversity, lack of social support, among others [11]. It should be noted that we did not assess whether these were present in individuals with CMD.

In general, our results support the notion that most mental disorders, including symptoms of Common Mental Disorder, had a similar association with suicidal wishing and suicidal planning. However, SAD was associated with a substantially elevated risk of suicidal planning rather than just suicidal wishing. Furthermore, when combining other mental disorders with SAD (comorbidity), suicidal planning risk was considerably larger among those with MDE, but also with GAD and Mania/Hypomania. This suggests that SAD may be particularly associated with suicidal planning and may have an interaction effect when combined with other mental disorders. According to the interpersonal theory of suicide, there are two interpersonal states related with the development of suicidal desire: thwarted belongingness and perceived burdensomeness, which are characterized by the perception that one has too few social connections, and feelings of loneliness. Thwarted belongingness, which is more common among those with social anxiety, and perceived burdensomeness, could be potential pathways by which SAD is associated with suicidality. [10].

It is important to mention that our study was not intended to test a causality model for suicidality. Since some of the associations were cross-sectional, and we are not able to establish the temporality of comorbidities, what we aimed to do was to explore the main mental health predictors of different aspects of suicidality using multivariable models in this population of young adults.

Limitations for this study include the fact that we did not analyze externalizing problems, which has been shown to be higher in men [7,41]

and could have given us a better understanding of the entire burden of mental disease. In addition, given that this study used data from a population-based cohort in young adults, the prevalence of some mental disorders was small. This limited our capacity to evaluate more complex patterns of comorbidities (eg. triple or quadruple burden of disease).

Absence of information on deaths due to suicide is another limitation. However, we have already reported that among the 325 cohort members known to be deceased up to age, 244 of them died during the first 4 years of life, 44 between the ages of 5 to 24 years, and only 19 of them died by external causes, mainly violence or accidents [20]. Therefore, we expect that the number of deaths due to suicide in this cohort is likely low.

Importantly, attrition rates could be lower in individuals with mental disorders and suicidality. Since the last follow-up was in the research clinic, individuals with severe depression, SAD, or even GAD, could have been more reluctant to participate. Any selection bias resulting from this was likely reduced by the fact that cohort members who did not go to the research clinic were invited to participate in a home interview. Moreover, individuals with missing data at the 30 years of age follow up, but who were followed at 23 years of age, did not show substantial differences in the prevalence of Common Mental Disorder when compared to those with mental health data at 30 years, suggesting that those followed did not substantially differ to those lost in terms of general mental health.

Supplementary Table 2, shows that at 30 years we followed more women, and individuals with less income and schooling. This might suggest that selection bias was an issue in this specific cohort, however, as we have seen when we calculated weighted prevalence for sex, trying to account for this possible bias, we see that they remained the same, suggesting at least that sex did not bias our results. Regarding income we see that even when we found significant *p* values for the differences in follow-up, rates disparities between income and schooling levels are not big, and therefore if there was any biased measure this might not have been very influential, especially in this study where measures of association are considerably strong. Upon adjustment, effect estimates for all mental health exposures decreased, and in some cases, confidence intervals included the reference. This shows the importance of having data for different mental comorbidities in order to identify the independent association of each specific mental disease with suicidality.

It is important to note that this study was based on a small area, so be careful to generalize the results to investigate the association between mental disorders and suicide attempt. Even so, our study is one of the first population-based studies among young adults from a middle-income setting with diagnostic information on the most prevalent mental disorders. We have been able to calculate the independent and comorbid association of each disorder with suicidality, as well as the cross-sectional and prospective association of Common Mental Disorder with suicidality.

In summary, in this cohort of Southern Brazilian young adults prospectively followed since birth, we have examined the burden and comorbidity of the most prevalent mental health disorders, showing the high comorbidity between MD and GAD, in both sexes, as well as the importance of looking for depressive symptoms and suicidality in those with SAD. In addition, we demystify the idea that suicidality is associated only with mood disorders, and show the independent association of anxiety disorders, especially SAD with suicidality. Our findings also support the notion that Common Mental Disorder symptomatology in adulthood, even without a specific mental health diagnosis, is also associated with an increased risk of suicidality.

Financial support

This article is based on data from the study “1982 Pelotas Birth Cohort” conducted by the Postgraduate Program in Epidemiology at Federal University of Pelotas (Brazil), with the collaboration of the Brazilian Public Health Association (ABRASCO). From 2004 to 2013, the Wellcome Trust supported the 1982 birth cohort study. The International Development Research Center, World Health Organization, Overseas Development Administration, European Union, National Support Program for Centers of Excellence (PRONEX), the Brazilian National Research Council (CNPq), Rio Grande do Sul State Research Support Foundation (FAPERGS) and the Brazilian Ministry of Health supported previous phases of the study.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Contributors

Luciana de Avila Quevedo coordinated the psychological evaluation of the cohort in the 2012–13 visit and preparation of the manuscript. Christian Loret de Mola supervised the psychological evaluation and collaborated in the data analysis and preparation of the manuscript. Rebecca Pearson and Joseph Murray collaborated in the preparation of the manuscript. Fernando Pires Hartwig collaborated in the data analysis and revised the manuscript. Helen Gonçalves coordinated the 2012–13 follow-up of the cohort and revised the manuscript. Ricardo Tavares Pinheiro coordinated the psychological evaluation of the cohort in the 2012–13 visit and revised the manuscript. Denise Petrucci Gigante coordinated the 2012–13 follow-up of the cohort and revised the manuscript. Janaína Vieira dos Santos Motta participated in the preparation of the manuscript. Lenice de Castro Muniz de Quadros supervised the psychological evaluation and revised the manuscript. Fernando C. Barros designed the study, coordinated the 2012–13 follow-up of the cohort and revised the manuscript. Bernardo Lessa Horta designed the study, coordinated the 2012–13 follow-up of the cohort and revised the manuscript.

Declaration of Competing Interest

None declared.

Acknowledgments

We would like to thank all members of the 1982 Pelotas birth cohort for their collaboration and all the people involved in data collection and processing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.comppsy.2020.152194>.

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