

Loneliness as a symptom of major depression in youth: a cohort study

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Abstract

This study evaluated loneliness as an associate symptom and severity indicator of major depressive disorder (MDD) in adolescents and young adults. We used data from the Brazilian High-Risk Cohort Study when participants were aged 14–23 ($n = 1,905$) and 18–28 years ($n = 2,052$). We examined loneliness centrality in a depressive symptom network and evaluated its role as a severity indicator by comparing clinical groups defined by clinician-diagnosed MDD and the presence of loneliness. Four groups were established: MDD with loneliness, MDD without loneliness, loneliness without MDD, and neither MDD nor loneliness. Cross-sectional and longitudinal associations with life-threatening outcomes (suicide attempt, psychiatric admission, death), poor life chances (criminal convictions, substance use, NEET), and well-being were assessed using regression models adjusted for sociodemographic factors and social isolation. Loneliness was part of the depressive construct and the network's most central symptom. Individuals with MDD and loneliness showed higher concurrent odds of life-threatening outcomes (OR: 3.963, 95% CI: 2.571, 6.177) and lower well-being (B: -2.100, 95% CI: -3.096, -1.104), than those depressed without loneliness. Prospectively, this group showed poorer well-being (B: -1.477, 95% CI: -2.420, -0.534). These findings support loneliness as an associate symptom and severity indicator of MDD. Assessing loneliness may improve clinical characterization and help identify young people at greater risk of persistent impairment.

1. Introduction

Major depressive disorder (MDD) is a clinical syndrome marked by dysfunctions across distinct psychobiological dimensions, causing functional impairment (Zachar and Kendler, 2017). Growing evidence shows that loneliness is closely linked to MDD, particularly during adolescence and young adulthood (Achterbergh et al., 2020; Mann et al., 2022; Wang et al., 2018). Quantitative and qualitative studies consistently identify loneliness as a core feature of the depressive experience (Fusar-Poli et al., 2023; Manfro et al., 2021; Viduani et al., 2024, 2021). However, loneliness is not currently considered a clinical indicator of depression.

Loneliness is itself a major public health concern (Holt-Lunstad, 2022; Solmi et al., 2020). Defined as the subjective feeling of being alone and without social support, it should be distinguished from social isolation, a quantitative phenomenon characterized by living alone and having few social relationships (Perlman and Peplau, 1981). A recent meta-analysis found a prevalence of loneliness ranging from 6.8% to 17.1% among adolescents (Surkalim et al., 2022). Beyond its high prevalence, loneliness affects physical and mental health (Hodgson et al., 2020; Holt-Lunstad and Perissinotto, 2023; Leigh-Hunt et al., 2017; Wang et al., 2023) and the socioeconomic future of young adults (Bryan et al., 2024), and is a risk factor for early mortality (Holt-Lunstad et al., 2015). Despite this burden, loneliness receives little attention in the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD-11) (American Psychiatric Association, 2022; World Health Organization, 2024).

At the molecular level, evidence suggests depression and loneliness are closely intertwined, which may explain their longitudinal bidirectional association (Abdellaoui et al., 2018; Abdellaoui and Verweij, 2021; Sbarra et al., 2023). Clinically, loneliness is likewise associated with depression (Mann et al., 2022; Wang et al., 2018), and network analyses of depressive symptoms show that loneliness is a central symptom in

adolescents, even relative to other MDD diagnostic criteria (Manfro et al., 2021; Mullarkey et al., 2019). In fact, interventions targeting social support have a protective effect on depression (Gariépy et al., 2016).

Beyond its structural role within depression, loneliness may also identify individuals at greater clinical severity. Depression is associated with a range of adverse social, psychological, and behavioral outcomes that affect functioning and long-term life trajectories (Fusar-Poli et al., 2023; Kieling et al., 2024). These adverse consequences can be broadly categorized into life-threatening situations, poor life chances, and well-being, reflecting different dimensions of vulnerability and resilience and aligning with the United Nations' Sustainable Development Goals (Hoffmann et al., 2024; Patel et al., 2018). If loneliness distinguishes depressed individuals with worse outcomes than depression alone, it may represent a clinically meaningful severity indicator. However, this hypothesis remains largely untested.

The present study therefore aims to replicate whether loneliness is part of the latent construct of depression using confirmatory factor analysis (CFA), replicate its centrality within the depressive syndrome using network analysis, and advance the field by testing whether loneliness serves as a severity indicator of adverse life outcomes when operationalized alongside other depressive symptoms, including those in the DSM. We hypothesize that (1) loneliness will be part of the latent depression construct, with a high factor loading, and central in a network of depressive symptoms, with high expected influence; and (2) loneliness will be a severity indicator in depression, such that individuals with MDD and loneliness will present worse current and future clinical and functional outcomes than those with MDD without loneliness.

2. Methods

2.1 Study design and participants

We analyzed data from the Brazilian High-Risk Cohort Study (BHRCS), a school-based cohort oversampled for high family risk for psychopathology (Salum et al., 2025), when participants were aged 14–23 and 18–28 years. The cohort initially enrolled 2,511 children from 22 schools in Porto Alegre and 35 schools in São Paulo between January and March 2010, selected from either a random or a high-risk subsample based on early psychiatric symptoms and family risk for psychopathology. At 14–23 years, 1,905 participants took part (76.3% retention, 46.9% female); at 18–28 years, 2,052 participants took part (81% retention, 47.9% female). Parent-reports were collected by lay interviewers and self-reported outcomes by trained psychologists (see below for specific measures).

The study was approved by the National Research Ethics Commission (approval 2.448.062, CAAE 74563817.7.1001.5327) and by the ethics committees of the University of São Paulo and the Federal University of Rio Grande do Sul. Written informed consent was obtained from parents and participants at 14–23 years, and directly from participants at 18–28 years; none was excluded due to parental illiteracy (Salum et al., 2025).

The analysis followed three steps. First, using CFA, we tested whether loneliness aggregates within depression and established its clinical threshold. Second, using network analysis, we examined loneliness's centrality among other MDD symptoms. Third, we regressed clinical validators, including life-threatening events, poor life chances, and well-being, both when participants had 14–23 and 18–28 years across four

groups (neither MDD nor loneliness, MDD without loneliness, loneliness without MDD, and MDD with loneliness) to test whether loneliness indicates greater severity. Models accounted for age, sex, skin color, socioeconomic status, and social isolation (to account for the objective aspect of being alone) as confounders, and used sampling and inverse probability weights to address the oversampling procedure and attrition (supplementary material, page 3; Tables S1-S4).

2.2 Psychiatric assessment

2.2.1 Depressive symptoms and Major depressive disorder

Depressive symptoms at 14-23 years were assessed using the Brazilian Portuguese self-report Short Mood and Feelings Questionnaire (sMFQ) (Rosa et al., 2018) and the Development and Well-being Assessment (DAWBA) (Fleitlich-Bilyk and Goodman, 2004; Goodman et al., 2000). The sMFQ is a brief self-report measure asking about 13 symptoms, including loneliness, over the past two weeks, on a 3-point Likert-type scale (0 = Not true; 1 = Sometimes; 2 = True) (Angold et al., 1995). sMFQ was used in the CFA and network analysis.

MDD diagnosis was established with DAWBA, a semi-structured interview generating diagnostic probabilities aligned with DSM-5 and ICD-10 criteria, using skip rules (e.g., full symptom assessment only if participants screened positive for depressed/irritable mood or loss of interest) and open-ended questions. Trained psychologists conducted interviews directly with participants. Participants with 18 years or younger were also supplemented by information from DAWBA administered with the caregivers. DAWBA generated computerized diagnostic probability bands, which trained psychiatrists then reviewed alongside open-ended responses to confirm, refute, or adjust the final diagnosis.

2.2.2 Loneliness

Loneliness at 14-23 years was derived from sMFQ item 10 ("I felt lonely"). To make it comparable to the dichotomous DAWBA-based items, we binarized it using a CFA-derived threshold of 0.5 standard deviation (SD) above the mean, classifying only the highest response category ("True") as positive (supplementary material, page 3).

2.2.3 Clinical Groups

To evaluate the impact of including loneliness as a MDD symptom, we used the DAWBA-based clinician diagnosis and the presence of loneliness to establish four clinical groups: (1) neither MDD nor loneliness, (2) MDD without loneliness, (3) loneliness without MDD, and (4) MDD with loneliness.

2.3 Clinical Validators

Three clinical validators were used: life-threatening events, poor life chances, and well-being. Life-threatening events comprised any of: (1) lifetime self-reported suicide attempt, assessed at 18-28 years with the Columbia-Suicide Severity Rating Scale (C-SSRS), with a comparable measure available at 14-23 years based on the DAWBA item "Have you ever tried to hurt or kill yourself?" (Section H); (2) (2) psychiatric inpatient admission for emotional or behavioral problems in the previous three years, assessed at both 14-23 and 18-28 years using cohort-specific questions from the BHRCS protocol; or (3) death by any cause (14-23 and 18-28 years). Poor life chances comprised factors related to quality of life (e.g., health, employability, education) (Tucker, 2016), naming: (1) any criminal conviction (14-23 and 18-28 years); (2) moderate or high risk for substance use (tobacco, alcohol, cannabis, cocaine), assessed with the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) at 18-28 years, and via a cohort-specific confidential protocol at 14-23 years; or (3) not in education, employment, or training (NEET) status (self-report, assessed at 14-23 and 18-28 years). Well-being was assessed with the Short Warwick-Edinburgh Mental Well-being Scale (SWEMWBS) (Tennant et al., 2007). Further details are in the supplementary material (page 4, Table S5).

2.4 Statistical analysis

2.4.1 Confirmatory factor analysis

Confirmatory factor analysis was used to evaluate if loneliness aggregates to other depressive symptoms in the sMFQ and to binarize the item "I felt lonely", to distinguish a normative feeling from a clinical indicator, compatible with DAWBA-based depression items. Details of these variables are described in the supplementary material (page 6, Tables S5-S6).

2.4.2 Network Analysis

Network analysis evaluated symptom centrality based on sMFQ responses, with each item treated as a node and edges representing regularized partial correlations estimated via graphical least absolute shrinkage and selection operator (GLASSO). Model selection used the Extended Bayesian Information Criterion (EBIC) with a γ tuning parameter of 0.5 to favor parsimony (Foygel and Drton, 2010); missing data were handled with listwise deletion. Each item of the sMFQ was treated as a node in a network, and the relationships between these nodes were determined based on the pattern of responses. The strength of the connections between symptoms (nodes) was measured using partial correlation coefficients, controlling for other symptoms in the network. We computed expected influence, strength, betweenness, and closeness to identify key symptoms, focusing on expected influence for its robustness to negative edges (Robinaugh et al., 2016). Edge-weight accuracy and the significance of edge-weight and strength differences were estimated via non-parametric bootstrapping ($n = 1000$) (Epskamp and Fried, 2018). Centrality stability was assessed with case-dropping bootstrapping ($n = 1000$) and summarized by the correlation stability coefficient (CS-coefficient), which reflects the proportion of data that can be dropped while maintaining a correlation of at least 0.7 with the original estimates, at 95% certainty. This coefficient should ideally exceed 0.5, and at minimum exceed 0.25. Analyses used the bootnet and qgraph packages in R (Version 4.3.1).

2.4.3 Regression models: depressive symptoms and clinical groups

Clinical groups were examined in cross-sectional and longitudinal regression analyses to determine whether MDD with loneliness was independently associated with the clinical validators, using MDD without loneliness as the reference group. We regressed the life-threatening, poor life chances (and their components) and well-being validators on the clinical groups at 14-23 and 18-28 years. Analyses were adjusted for covariates and sampling weights.

3. Results

3.1 Loneliness as part of the depression construct and clinical operationalization

The unidimensional sMFQ showed good fit (Table S6), with additional details provided in the supplementary material (page 7). Participants scoring 2 ("True") on the loneliness item were classified as positive for loneliness in subsequent regression analyses.

3.2 Network analysis

Figure 1 shows the sMFQ symptom network, with 68 of 78 possible non-zero edges. "I felt lonely" had a strong partial correlation with "I thought nobody really loved me", "I cried a lot", and "I felt miserable or unhappy", and was the most central symptom according to Expected Influence (Figure 2; Table S7). Bootstrap analyses supported the robustness of these findings, showing that the relation between "I felt lonely" and "I felt miserable or unhappy" was significantly stronger than most other edges and that "I felt lonely" remained a significantly stronger node compared to almost all other nodes, except node 5 ("I felt I was no good anymore") and node 8 ("I hated myself") (Figures S1–S4; CS-coefficient = 0.75).

[Figure 1 here]

[Figure 2 here]

3.3 Loneliness as severity indicator - Sample characteristics and regressions by clinical groups

Sample characteristics by clinical groups are described in Table 1 (proportions were weighted for attrition and representativeness). At both 14-23 and 18-28 years, females were more prevalent across clinical groups, particularly among participants with MDD and loneliness. Porto Alegre included a higher proportion of participants with MDD without loneliness, whereas São Paulo had more participants with MDD and loneliness. As expected, sMFQ scores were highest in the groups reporting loneliness (groups 2 and 4).

[Table 1 here]

Table 2 shows associations between clinical groups and the life-threatening, poor life chances, and well-being validators, using participants with MDD without loneliness as the reference group. The full regression

output, including covariate associations, is available in the supplementary material (Table S8). Cross-sectionally, participants with MDD and loneliness had higher odds of life-threatening outcomes (OR: 3.963, 95% CI: 2.571–6.177) and lower well-being (B: -2.100, 95% CI: -3.096 to -1.104) than those with MDD alone. No differences were observed for participants with loneliness without MDD. Longitudinally, the MDD with loneliness group showed lower well-being (B: -1.477, 95% CI: -2.420 to -0.534), but not life-threatening or poor life chances outcomes. Analyses of individual validator components are presented in Tables S9–S17; death and criminal conviction were not analyzed separately because of the small number of events.

4. Discussion

This study replicated previous findings that loneliness is part of the latent depressive construct and a central depressive symptom in young people, while extending this evidence by examining its role as a severity indicator for MDD. Individuals with MDD and loneliness showed greater cross-sectional severity, including higher odds of life-threatening outcomes and lower well-being, than those with MDD without loneliness. Prospectively, this group also exhibited poorer well-being, supporting the role of loneliness as a marker of greater depression severity.

CFA allowed us to operationalize loneliness as a clinical symptom, distinguishing it from normative loneliness, and compare it with the nine DSM symptoms of MDD. Although loneliness is not a DSM criterion, diagnostic criteria should not be equated with the disorders they index (Kendler, 2016), and evaluating symptoms beyond those included in the DSM may improve clinical characterization (Kendler, 2017). Consistent with qualitative evidence (Viduani et al., 2024), our findings suggest that loneliness captures clinically meaningful information related to adverse outcomes in depressed young people.

Consistent with previous network studies (Gijzen et al., 2021; Manfro et al., 2021; Mullarkey et al., 2019), loneliness emerged as one of the most central depressive symptoms. Notably, the loneliness–sadness edge was among the strongest in the network, reinforcing the close relation between loneliness and a core DSM depressive symptom. This finding is also consistent with qualitative evidence showing loneliness as one of the most prominent features of the lived experience of depression in young people (Viduani et al., 2024).

Our findings suggest that loneliness is a central associate symptom and a marker of MDD severity. Cross-sectionally, individuals with MDD and loneliness had higher odds of life-threatening outcomes and lower well-being than those with MDD without loneliness. In addition, both the MDD with loneliness group and the loneliness without MDD group had higher odds of concurrent suicide attempt or self-harm than participants with neither MDD nor loneliness (Table S9), consistent with previous evidence linking loneliness to suicidal behaviors (McClelland et al., 2020). Longitudinally, loneliness remained associated with poorer well-being, but not with the broader life-threatening or poor life chances composites. Importantly, participants with MDD and loneliness had higher odds of subsequent psychiatric inpatient admission (Table S11). This is particularly relevant because, unlike many medical conditions, psychiatric disorders lack objective biomarkers of severity and therefore rely on clinical measures (Bentley et al., 2014; Kroenke et al., 2001; Zimmerman et al., 2018). The DSM defines severity according to the number and intensity of symptoms without considering the contribution of specific symptoms. Our findings suggest that assessing loneliness

may improve the characterization of depression severity by identifying individuals at greater current clinical risk and poorer future well-being.

Our study has several strengths, including a large prospective cohort with five years of follow-up and the evaluation of loneliness independently from social isolation. Nonetheless, some limitations should be acknowledged. First, the use of mixed evaluation tools (i.e, sMFQ and DAWBA) limited the direct evaluation of loneliness as a diagnostic criterion. Future studies should develop structured interviews that formally assess loneliness as a cardinal or conditional symptom of MDD. Regarding DAWBA, it assumes that other symptoms are zero if none of the skip questions are positive, which is not always true but it is a limitation of this semi-structured interview to generate diagnostic status. Second, loneliness was measured using a single dichotomized sMFQ item, which may not fully capture the multidimensional nature of the construct. Third, some outcomes differed across waves in their assessment, temporality, and severity. Although harmonized into broader clinical validators, these differences may have affected comparability. However, our aim was not to infer causality but to determine whether loneliness and depressive symptoms captured clinically relevant information regarding vulnerability and functioning, an approach supported by previous evidence (Aaltonen et al., 2024; Lund et al., 2018). Finally, the findings may not generalize beyond young people or outside the Brazilian context and should be replicated in other populations.

In conclusion, our findings support loneliness as a central component of depressive symptomatology in youth and a marker of MDD severity. Individuals with MDD and loneliness showed greater clinical severity than those with MDD without loneliness. Future studies should formally operationalize loneliness as a phenotypic feature of depression within a single structured instrument, evaluating whether it functions as a cardinal or conditional symptom and whether its inclusion improves the identification of clinically meaningful depressive presentations. At minimum, our findings support considering loneliness as a severity criterion in depressed youth, with the potential to improve clinical characterization and help identify those at greater risk of impairment and poorer future functioning.

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Author Contributions:

João Villanova do Amaral: Study design, data curation, formal analysis, investigation, methodology, project administration, validation, visualization, writing – original draft, and writing – review & editing. **Gabriele dos Santos Jobim:** methodology, writing – review & editing. **Christian Kieling:** methodology, writing – review & editing. **João Pedro Gonçalves Pacheco:** Investigation, methodology, writing – review & editing. **Lucas Toshio Ito:** Methodology; writing - review & editing; data curation. **Rafaella Ormond:** Methodology; writing - review & editing; data curation. **Marcos Leite Santoro:** Methodology; writing - review & editing; Funding acquisition; Data curation; Data collection. **Síntia Iole Nogueira Belangero:** Methodology; Writing – review & editing; Funding acquisition; Data curation; Data collection. **Ary Gadelha:** Writing – review & editing, funding acquisition, data curation, study design and data collection. **Eurípedes Constantino Miguel:** Writing – review & editing, funding acquisition, data curation, study design and data collection. **Rodrigo Affonseca Bressan:** Writing – review & editing, funding acquisition, data curation, study design and data collection. **Pedro Mario Pan:** Writing – review & editing, data curation, study design and data collection. **Luis Augusto Rohde:** Conceptualization, writing – review & editing, funding acquisition, data curation, study design and data collection. **Giovanni Abrahão Salum:** Funding acquisition, data curation, study design, data collection, supervision, and writing – review & editing. **Maurício Scopel Hoffmann:** Conceptualisation, supervision, data curation, study design, data collection, investigation, writing – original draft, and writing – review & editing. **João Villanova do Amaral** and **Maurício Scopel Hoffmann** directly accessed and verified the underlying data reported in the manuscript. All authors read and approved the final version of the manuscript and had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Data Sharing

Data dictionary is available at <https://osf.io/ktz5h/wiki/Data%20Dictionaries/> and <https://osf.io/w3jr4> to direct download. Individual-level data is available upon request to the Brazilian High-Risk Cohort Study

research committee, by following the instructions and filling the research form available at <https://osf.io/ktz5h/wiki/home/>. Study design and ethical details can be found elsewhere (Salum et al., 2025).

References

1. Aaltonen K, Sund R, Hakulinen C, Pirkola S, Isometsä E (2024) Variations in Suicide Risk and Risk Factors After Hospitalization for Depression in Finland, 1996–2017. *JAMA Psychiatry* 81:506. <https://doi.org/10.1001/jamapsychiatry.2023.5512>
2. Abdellaoui A, Nivard MG, Hottenga J-J, Fedko I, Verweij KJH, Baselmans BML, Ehli EA, Davies GE, Bartels M, Boomsma DI, Cacioppo JT (2018) Predicting loneliness with polygenic scores of social, psychological and psychiatric traits. *Genes Brain Behav* 17:e12472
3. Abdellaoui A, Verweij KJH (2021) Dissecting polygenic signals from genome-wide association studies on human behaviour. *Nat Hum Behav* 5:686–694. <https://doi.org/10.1038/s41562-021-01110-y>
4. Achterbergh L, Pitman A, Birken M, Pearce E, Sno H, Johnson S (2020) The experience of loneliness among young people with depression: a qualitative meta-synthesis of the literature. *BMC Psychiatry* 20:415
5. American Psychiatric Association (2022) Diagnostic and Statistical Manual of Mental Disorders, DSM–5-TR. ed. American Psychiatric Association Publishing. <https://doi.org/10.1176/appi.books.9780890425787>
6. Angold A, Costello EJ, Messer SC, Pickles A (1995) Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. *Int J Methods Psychiatr Res* 5:237–249
7. Bentley KH, Gallagher MW, Carl JR, Barlow DH (2014) Development and validation of the Overall Depression Severity and Impairment Scale. *Psychol Assess* 26:815–830. <https://doi.org/10.1037/a0036216>
8. Bryan BT, Thompson KN, Goldman-Mellor S, Moffitt TE, Odgers CL, So SLS, Uddin Rahman M, Wertz J, Matthews T, Arseneault L (2024) The socioeconomic consequences of loneliness: Evidence from a nationally representative longitudinal study of young adults. *Soc Sci Med* 116697
9. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA (1998) The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med* 158:1789–1795
10. Epskamp S, Fried EI (2018) A tutorial on regularized partial correlation networks. *Psychol Methods* 23:617–634
11. Fleitlich-Bilyk B, Goodman R (2004) Prevalence of Child and Adolescent Psychiatric Disorders in Southeast Brazil. *J Am Acad Child Adolesc Psychiatry* 43:727–734. <https://doi.org/10.1097/01.chi.0000120021.14101.ca>

12. Foygel R, Drton M (2010) Extended Bayesian Information Criteria for Gaussian Graphical Models
13. Fusar-Poli P, Estradé A, Stanghellini G, Esposito CM, Rosfort R, Mancini M, Norman P, Cullen J, Adesina M, Jimenez GB, da Cunha Lewin C, Drah EA, Julien M, Lamba M, Mutura EM, Prawira B, Sugianto A, Teresa J, White LA, Damiani S, Vasconcelos C, Bonoldi I, Politi P, Vieta E, Radden J, Fuchs T, Ratcliffe M, Maj M (2023) The lived experience of depression: a bottom-up review co-written by experts by experience and academics. *World Psychiatry* 22:352–365
14. Gariépy G, Honkaniemi H, Quesnel-Vallée A (2016) Social support and protection from depression: systematic review of current findings in Western countries. *Br J Psychiatry* 209:284–293
15. Gijzen MWM, Rasing SPA, Creemers DHM, Smit F, Engels RCME, De Beurs D (2021) Suicide ideation as a symptom of adolescent depression. a network analysis. *J Affect Disord* 278:68–77
16. Goodman R, Ford T, Richards H, Gatward R, Meltzer H (2000) The Development and Well-Being Assessment: Description and initial validation of an integrated assessment of child and adolescent psychopathology. *J Child Psychol Psychiatry* 41:645–655
17. Hodgson S, Watts I, Fraser S, Roderick P, Dambha-Miller H (2020) Loneliness, social isolation, cardiovascular disease and mortality: a synthesis of the literature and conceptual framework. *J R Soc Med* 113:185–192
18. Hoffmann MS, Pine DS, Georgiades K, Szatmari P, Miguel EC, Pan PM, Gadelha A, Rohde LA, Merikangas KR, Milham MP, Satterthwaite TD, Salum GA (2024) Comparing mental health semi-structured diagnostic interviews and symptom checklists to predict poor life outcomes: an 8-year cohort study from childhood to young adulthood in Brazil. *Lancet Glob Health* 12:e79–e89
19. Holt-Lunstad J (2022) Social connection as a public health issue: The evidence and a systemic framework for prioritizing the social in social determinants of health. *Annu Rev Public Health* 43:193–213
20. Holt-Lunstad J, Perissinotto C (2023) Social Isolation and Loneliness as Medical Issues. *N Engl J Med* 388:193–195
21. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D (2015) Loneliness and Social Isolation as Risk Factors for Mortality: A Meta-Analytic Review. *Perspect Psychol Sci* 10:227–237
22. ICD–11 for Mortality and Morbidity Statistics [WWW Document] URL <https://icd.who.int/browse/2024-01/mms/en> (accessed 11.11.24)
23. Kendler KS (2017) DSM disorders and their criteria: how should they inter-relate? *Psychol. Med* 47:2054–2060
24. Kendler KS (2016) The Phenomenology of Major Depression and the Representativeness and Nature of DSM Criteria. *Am J Psychiatry* 173:771–780
25. Kieling C, Buchweitz C, Caye A, Silvani J, Ameis SH, Brunoni AR, Cost KT, Courtney DB, Georgiades K, Merikangas KR, Henderson JL, Polanczyk GV, Rohde LA, Salum GA, Szatmari P (2024) Worldwide Prevalence and Disability From Mental Disorders Across Childhood and Adolescence: Evidence From the Global Burden of Disease Study. *JAMA Psychiatry* 81:347. <https://doi.org/10.1001/jamapsychiatry.2023.5051>

26. Kroenke K, Spitzer RL, Williams JB (2001) The PHQ–9: validity of a brief depression severity measure. *J Gen Intern Med* 16:606–613
27. Leigh-Hunt N, Bagguley D, Bash K, Turner V, Turnbull S, Valtorta N, Caan W (2017) An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health* 152:157–171
28. Lund C, Brooke-Sumner C, Baingana F, Baron EC, Breuer E, Chandra P, Haushofer J, Herrman H, Jordans M, Kieling C, Medina-Mora ME, Morgan E, Omigbodun O, Tol W, Patel V, Saxena S (2018) Social determinants of mental disorders and the Sustainable Development Goals: a systematic review of reviews. *Lancet Psychiatry* 5:357–369
29. Manfro PH, Pereira RB, Rosa M, Cogo-Moreira H, Fisher HL, Kohrt BA, Mondelli V, Kieling C (2021) Adolescent depression beyond DSM definition: a network analysis. *Eur. Child Adolesc. Psychiatry*
30. Mann F, Wang J, Pearce E, Ma R, Schlieff M, Lloyd-Evans B, Ikhtabi S, Johnson S (2022) Loneliness and the onset of new mental health problems in the general population. *Soc Psychiatry Psychiatr Epidemiol* 57:2161–2178
31. McClelland H, Evans JJ, Nowland R, Ferguson E, O'Connor RC (2020) Loneliness as a predictor of suicidal ideation and behaviour: a systematic review and meta-analysis of prospective studies. *J Affect Disord* 274:880–896. <https://doi.org/10.1016/j.jad.2020.05.004>
32. Mullarkey MC, Marchetti I, Beevers CG (2019) Using Network Analysis to Identify Central Symptoms of Adolescent Depression. *J Clin Child Adolesc Psychol* 48:656–668
33. Patel V, Saxena S, Lund C, Thornicroft G, Baingana F, Bolton P, Chisholm D, Collins PY, Cooper JL, Eaton J, Herrman H, Herzallah MM, Huang Y, Jordans MJD, Kleinman A, Medina-Mora ME, Morgan E, Niaz U, Omigbodun O, Prince M, Rahman A, Saraceno B, Sarkar BK, De Silva M, Singh I, Stein DJ, Sunkel C, Unützer Jü., 2018. The Lancet Commission on global mental health and sustainable development. *Lancet* 392, 1553–1598. [https://doi.org/10.1016/S0140-6736\(18\)31612-X](https://doi.org/10.1016/S0140-6736(18)31612-X)
34. Perlman D, Peplau LA (1981) Toward a social psychology of loneliness. *Pers Relatsh* 3:31–56
35. Robinaugh DJ, Millner AJ, McNally RJ (2016) Identifying highly influential nodes in the complicated grief network. *J Abnorm Psychol* 125:747–757
36. Rosa MMT (2018) and Feelings Questionnaire (MFQ) – Versão Longa [Dissertação De Mestrado, Universidade Federal Do Rio Grande Do Sul]. Universidade Federal do Rio Grande do Sul, Tradução E Validação Da Escala Mood
37. Salum GA, de Giusti C, Souza L, Juk J, Costa R, Sugaya L, Caye A, Simioni A, Rocha PB, Manfro GG, Ito LT, Da Silva F Jr, Duarte I, Esper N, Anés M, Damiano RF, Satterthwaite TD, Carvalho CM, Bado P, Pan PM (2025) Cohort profile: Brazilian high-risk cohort for mental health conditions (BHRC). *Int J Epidemiol* 54(6). <https://doi.org/10.1093/ije/dyaf192>
38. Sbarra DA, Ramadan FA, Choi KW, Treur JL, Levey DF, Wootton RE, Stein MB, Gelernter J, Klimentidis YC (2023) Loneliness and depression: bidirectional mendelian randomization analyses using data from three large genome-wide association studies. *Mol. Psychiatry*
39. Solmi M, Veronese N, Galvano D, Favaro A, Ostinelli EG, Noventa V, Favaretto E, Tudor F, Finessi M, Shin JI, Smith L, Koyanagi A, Cester A, Bolzetta F, Cotroneo A, Maggi S, Demurtas J, De Leo D, Trabucchi M

- (2020) Factors Associated With Loneliness: An Umbrella Review Of Observational Studies. *J Affect Disord* 271:131–138
40. Surkalim DL, Luo M, Eres R, Gebel K, van Buskirk J, Bauman A, Ding D (2022) The prevalence of loneliness across 113 countries: systematic review and meta-analysis. *BMJ* 376, e067068
 41. Tennant R, Hiller L, Fishwick R, Platt S, Joseph S, Weich S, Parkinson J, Secker J, Stewart-Brown S (2007) The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes* 5:63
 42. Tucker J (2016) Improving Children's Life Chances. Child Poverty Action Group
 43. Viduani A, Arenas DL, Benetti S, Wahid SS, Kohrt BA, Kieling C (2024) Systematic Review and Meta-Synthesis: How Is Depression Experienced by Adolescents? A Synthesis of the Qualitative Literature. *J. Am. Acad. Child Adolesc. Psychiatry*
 44. Viduani A, Benetti S, Martini T, Buchweitz C, Ottman K, Wahid SS, Fisher HL, Mondelli V, Kohrt BA, Kieling C (2021) Social isolation as a core feature of adolescent depression: a qualitative study in Porto Alegre, Brazil. *Int. J. Qual. Stud. Health Well-being*. 16
 45. Wang F, Gao Y, Han Z, Yu Y, Long Z, Jiang X, Wu Y, Pei B, Cao Y, Ye J, Wang M, Zhao Y (2023) A systematic review and meta-analysis of 90 cohort studies of social isolation, loneliness and mortality. *Nat Hum Behav*
 46. Wang J, Mann F, Lloyd-Evans B, Ma R, Johnson S (2018) Associations between loneliness and perceived social support and outcomes of mental health problems: A systematic review. *BMC Psychiatry* 18
 47. Zachar P, Kendler KS (2017) The Philosophy of Nosology. *Annu Rev Clin Psychol* 13:49–71
 48. Zimmerman M, Balling C, Chelminski I, Dalrymple K (2018) Understanding the severity of depression: Which symptoms of depression are the best indicators of depression severity? *Compr. Psychiatry* 87:84–88

Tables

Table 1
Sample characteristics by clinical groups

14–23 years					
Characteristic	Neither MDD nor lonely N=892	Loneliness without MDD N = 67	MDD without loneliness N = 102	MDD with loneliness N=89	p-value
Age in years	17.94 (1.96)	17.78 (2.11)	18.55 (1.96)	17.99 (1.79)	0.2
Gender					< 0.001
Female	374 (43%)	41 (59%)	61 (59%)	65 (72%)	
Male	518 (57%)	26 (41%)	41 (41%)	24 (28%)	
Race/ethnicity					0.150
Non-White	363 (41%)	26 (34%)	30 (28%)	31 (43%)	
White	529 (59%)	41 (66%)	72 (72%)	58 (57%)	
Study site					0.040
Porto Alegre (RS)	422 (39%)	33 (53%)	61 (54%)	40 (39%)	
São Paulo (SP)	470 (61%)	34 (47%)	41 (46%)	49 (57%)	
Socioeconomic status					0.075
Class A/B	115 (13%)	7 (9.7%)	13 (12%)	22 (28%)	
Class C	565 (64%)	45 (68%)	59 (57%)	48 (50%)	
Class D/E	212 (23%)	15 (22%)	30 (31%)	19 (22%)	
Total sMFQ Score	3.1 (3.6)	15.2 (4.8)	8.1 (5.5)	19.2 (4.3)	< 0.001
Isolated	107 (12%)	9 (14%)	21 (13%)	16 (13%)	> 0.900
Any life-threatening validator	162 (17%)	38 (57%)	48 (50%)	65 (72%)	< 0.001
Lifetime Suicide Attempt or Self-harm	159 (16%)	38 (57%)	47 (49%)	65 (72%)	< 0.001
Lifetime Psychiatric Inpatient Admission	7 (1.2%)	1 (0.5%)	4 (5.1%)	2 (2.3%)	0.038
Note: Mean (SD); n (unweighted) (% weighted); Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction. *Well-being scores (SWEMWBS raw scores) were transformed into metric scores using the conversion table recommended by the scale developers (Stewart-Brown et al., 2009)					

14–23 years					
Death	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	> 0.900
Any poor life chances validator	705 (79%)	61 (92%)	94 (92%)	85 (95%)	< 0.001
Conviction	36 (4.1%)	0 (0%)	5 (4.3%)	2 (0.6%)	0.200
Lifetime Substance Use	703 (79%)	61 (92%)	93 (91%)	85 (95%)	< 0.001
NEET	134 (16%)	11 (17%)	27 (36%)	18 (11%)	< 0.001
Well Being Score*	21.9 (3.1)	19.4 (3.0)	19.3 (2.9)	17.2 (3.4)	< 0.001
18–28 years					
Any life-threatening validator	94 (11%)	20 (31%)	28 (34%)	42 (42%)	< 0.001
Lifetime Suicide Attempt	81 (9.5%)	19 (29%)	25 (31%)	41 (40%)	< 0.001
Lifetime Psychiatric Inpatient Admission	14 (1.5%)	3 (3.3%)	6 (5.9%)	10 (15%)	< 0.001
Death	3 (0.4%)	1 (0.7%)	0 (0%)	0 (0%)	0.800
Any poor life chances validator	303 (41%)	24 (45%)	39 (46%)	44 (56%)	0.200
Conviction	28 (3.6%)	0 (0%)	4 (5.1%)	1 (0.4%)	0.300
ASSIST Any Moderate/High Risk for Substance Use	194 (26%)	18 (37%)	30 (36%)	38 (44%)	0.026
NEET	127 (18%)	10 (11%)	14 (14%)	13 (16%)	0.600
Well Being Score*	21.8 (3.0)	19.8 (2.9)	20.8 (2.8)	19.1 (2.4)	< 0.001
Note: Mean (SD); n (unweighted) (% weighted); Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction. *Well-being scores (SWEMWBS raw scores) were transformed into metric scores using the conversion table recommended by the scale developers (Stewart-Brown et al., 2009)					

Table 2

Regression analysis: clinical groups associated with clinical validators at 14–23 years (cross-sectional) and 18–28 years (longitudinal)

Predictor	Any Life-threatening Validator			Any Poor Life Chances Validator			Well-being Score*		
	OR	95% CI	p	OR	95% CI	p	B	95% CI	p
14–23 years									
Neither MDD nor lonely (vs MDD without loneliness)	0.331	0.243, 0.452	< 0.001	0.246	0.125, 0.438	< 0.001	2.461	1.726, 3.196	< 0.001
Loneliness without MDD (vs MDD without loneliness)	2.057	1.333, 3.188	0.001	0.913	0.386, 2.141	0.833	-0.003	-1.065, 1.059	0.995
MDD with lonely (vs MDD without loneliness)	3.963	2.571, 6.177	< 0.001	2.047	0.803, 5.481	0.138	-2.100	-3.096, -1.104	< 0.001
Observations	1,150			1,150			1,150		
Pseudo R ² / R ²	0.177			0.151			0.197		
18–28 years									
Neither MDD nor lonely (vs MDD without loneliness)	0.283	0.165, 0.493	< 0.001	0.758	0.469, 1.232	0.261	0.791	0.138, 1.443	0.018
Loneliness without MDD (vs MDD without loneliness)	0.931	0.411, 2.067	0.861	0.943	0.453, 1.955	0.875	-0.812	-1.800, 0.175	0.107
MDD with loneliness (vs MDD without loneliness)	1.419	0.678, 2.984	0.353	1.666	0.831, 3.372	0.152	-1.477	-2.420, -0.534	0.002
Note: Models were adjusted for age at domicile evaluation, socioeconomic status, sex, study site, race/ethnicity, and social isolation. Abbreviations: MDD, Major Depressive Disorder; OR, Odds Ratio; CI, Confidence Interval. *Well-being scores (SWEMWBS raw scores) were transformed into metric scores using the conversion table recommended by the scale developers (Stewart-Brown et al., 2009)									

Predictor	Any Life-threatening Validator			Any Poor Life Chances Validator			Well-being Score*		
	OR	95% CI	p	OR	95% CI	p	B	95% CI	p
Observations	1,010			1,004			1,011		
Pseudo R ² / R ²	0.123			0.024			0.125		
Note: Models were adjusted for age at domicile evaluation, socioeconomic status, sex, study site, race/ethnicity, and social isolation. Abbreviations: MDD, Major Depressive Disorder; OR, Odds Ratio; CI, Confidence Interval. *Well-being scores (SWEMWBS raw scores) were transformed into metric scores using the conversion table recommended by the scale developers (Stewart-Brown et al., 2009)									

Figures

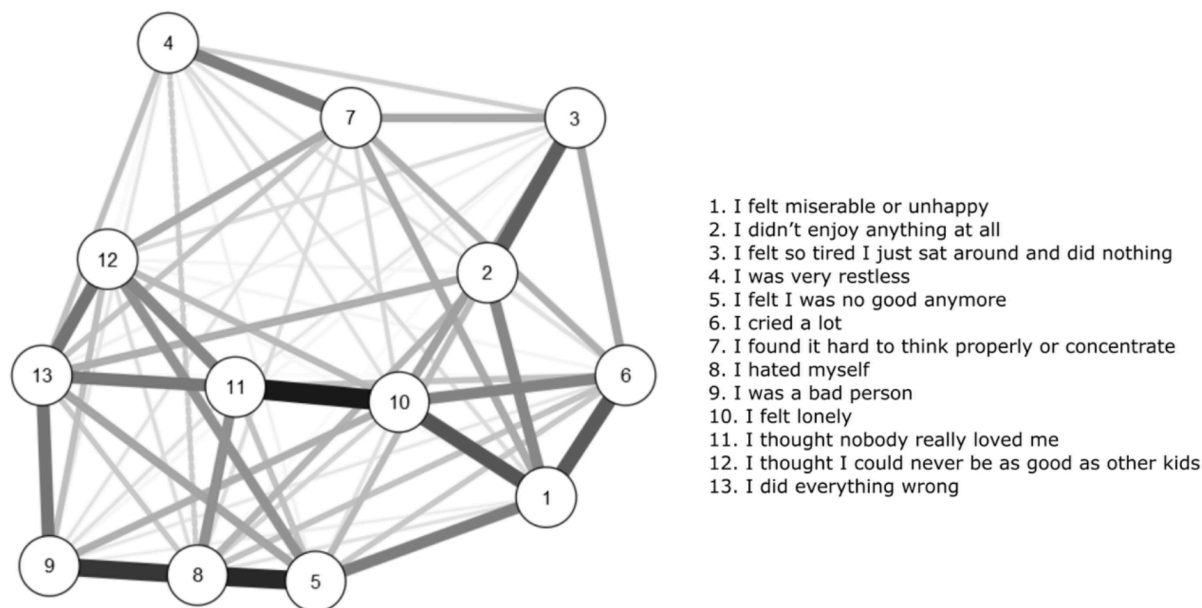


Figure 1

Estimated network structure of sMFQ symptoms.

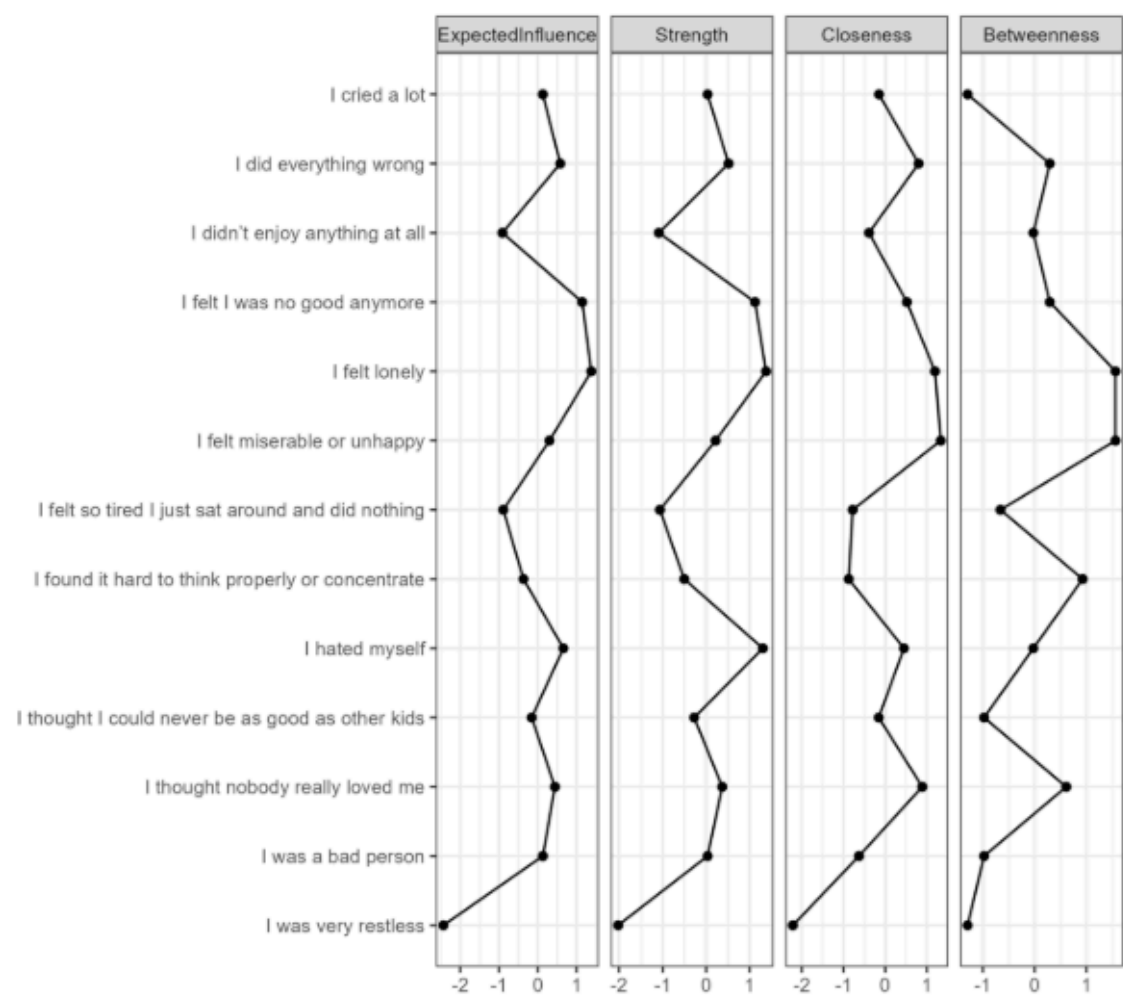


Figure 2

Centrality indices of SMQF items, shown as standardized z-scores.

Supplementary Files

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