Clinical and lifestyle predictors of loneliness: a two-year longitudinal study

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Keywords: Loneliness; Depression; Anxiety; Lifestyle; Physical Activity; Social Relationships.

Introduction

Loneliness is highly prevalent and rising worldwide. A recent systematic review and meta-analysis (Surkalim et al., 2022) with pre-pandemic data from 113 countries or territories showed that loneliness prevalence in adults ranged from 2.9% to 24.2%, depending on the region or age group. Another systematic review with meta-analysis (Ernst et al., 2022) that included longitudinal studies with data before and during the COVID-19 pandemic showed increased loneliness scores and prevalence rates.

These findings reinforce the urgency of addressing loneliness as a public health concern, considering that there is a robust association between loneliness and various negative health outcomes. For instance, loneliness can induce several cardiometabolic changes, such as an increased coronary heart disease risk, increased activation of the hypothalamic-pituitary-adrenal axis (Hodgson et al., 2020), high blood pressure, and increased cholesterol levels (Leigh-Hunt et al., 2017; Lim et al., 2020). Moreover, it is associated with neurological diseases such as stroke (Valtorta et al., 2016), Parkinson's disease (Terracciano et al., 2023), and dementia (Salinas et al., 2022). In

addition, loneliness can increase overall mortality comparable with well-established risk factors for mortality (Holt-Lunstad et al., 2015, 2010). In psychiatry, we have several studies showing loneliness as a predictor of depressive symptoms, anxiety, and suicidality (Antonelli-Salgado et al., 2021; Mann et al., 2022).

Despite the increase in studies of loneliness as a predictor of these various clinical outcomes, the literature still lacks longitudinal studies on predictors of loneliness, especially in low- and middle-income countries and collectivist societies (Luhmann et al., 2023; Surkalim et al., 2022). Collectivist societies are those in which the group's needs are valued over the individuals. Brazil scored 36 on Hofstede's Individualism scale (0 - 100). The score shows a mix of individualistic and collectivist characteristics but is predominately collectivist (Hofstede, 2024).

Therefore, the primary aim of this study is to carry out a longitudinal assessment of clinical factors for the development of loneliness in a sample of adults in Brazil. The secondary objective is to analyze lifestyle factors as a predictor of loneliness.

Methods

Setting, participants, and design

The present study is part of a larger cohort with four temporal waves (baseline, 1, 6, and 24 months). This larger cohort aimed to investigate the impact of the COVID-19 pandemic on specific mental health variables within the Brazilian population across various pandemic phases. Data collection was performed using online questionnaires due to the need to comply with recommendations on social distancing. The inclusion criteria were being at least 18 years old, living in Brazil at the time of data collection, and having access to the Internet. For inclusion in the subsequent waves of data collection, participants needed to provide their email addresses at the end of the baseline questionnaire and agree to receive an email with the specific questionnaires regarding that wave. All online questionnaires were provided to eligible participants using an online platform (*Survey Monkey*) ("Survey Monkey," 2024), and the baseline questionnaire was advertised through social media (Facebook, Instagram, and WhatsApp) to reach participants.

This study is based on this cohort's first and fourth waves of data collection. All predictor variables and covariates were obtained from the first wave (baseline). The outcome (loneliness) was obtained from the fourth wave. We distributed the Wave 1 (W1) questionnaire between May 6 and June 6, 2020, and the Wave 4 (W4) two years after W1. Considering that our study began approximately two months after the confirmation of the first case of COVID-19 in Brazil (Brazilian Ministry of Health, 2022), our baseline refers to an early stage of the pandemic. The research ethics committee of Hospital de Clínicas de Porto Alegre (Rio Grande do Sul, Brazil) approved the study (CAAE: 30222820.4.0000.5327). All participants electronically signed the informed consent form before answering the online questionnaires. After completing each questionnaire, participants were provided information about mental health support centers in Brazil.

This study report follows the STROBE guidelines (von Elm et al., 2007). Table S1 in the supplementary material presents the STROBE checklist.

Measures

Survey instruments

The online questionnaires used during data collection included validated scales and tools to assess loneliness and specific clinical variables. In addition, the questionnaires covered lifestyle and sociodemographic variables.

Loneliness

Loneliness was measured with the 3-item short version of the R-UCLA (Hughes et al., 2004). The scale asks “How often do you feel you lack companionship?”, “How often do you feel left out?”, and “How often do you feel isolated from others?”. Response options for each item are “hardly ever or never”, “some of the time”, or “often” (equating to scores of 1,2, and 3, respectively). Total scores range from 3 to 9, and higher scores indicate greater loneliness (Hughes et al., 2004), with scores ≥ 6 indicating important loneliness (Steptoe et al., 2013). We used Cronbach’s α and McDonald’s ω to test internal reliability (Lucke, 2005; Raykov, 1997), and the analyses and results are described in a previous article (Antonelli-Salgado et al., 2021).

Mental Health

Depressive symptoms were measured with the PHQ-9 (Kroenke et al., 2001). A score equal to or greater than 9 is considered a positive screening result for depression in the Brazilian population (Matias et al., 2016; Santos et al., 2013). Anxiety symptoms were measured using the GAD-7 (Moreno et al., 2016). A positive indicator of signs and symptoms of anxiety disorders is a value equal to or greater than 10. The AUDIT-C was used to evaluate alcohol use (Bush et al., 1998). In men, a score of 4 or more is considered positive; in women, a score of 3 or more is considered positive. The questions about cannabis use were based on the ASSIST (Alcohol, Smoking, and Substance Involvement Screening Test) instrument (WHO ASSIST Working Group, 2002).

Lifestyle/Social

Lifestyle measures were assessed in Likert scale format but analyzed dichotomously. Physical activity was separated into two groups, using the cutoff point of 150 min/week, based on recommendations from the World Health Organization (WHO, 2022). The variables Sleep quality, Family relationship, and Friendship relationship were divided into Poor/Average or Good/Excellent.

Covariates

To adjust our results, we chose several sociodemographic factors that were already related to loneliness in previous studies, such as age, gender, sexual orientation, income, education, and race (Buczak-Stec et al., 2023; Lim et al., 2020; Lin, 2023; Luhmann et al., 2023; Solmi et al., 2020). The supplemental material includes a Portuguese (original version) and an English-translated version of the questions used in this study (see Method S1).

Statistical analysis

We only analyzed participants who completed all questions related to the variables of interest in this study. Descriptive analyses were reported as means or absolute and relative frequencies. We filtered the data with subjects that presented valid values for UCLA (UCLA Loneliness Scale 3-item version) in the first and fourth

waves and evaluated just those that did not have loneliness (UCLA score < 6) at baseline (W1). Then, we divided participants into two groups based on UCLA's total score at W4: absent and incident cases of loneliness. In the fourth-wave assessment, UCLA scores greater or equal to 6 were considered incident cases (positives), and scores less than 6 were coded as absent cases (negatives).

First, we used chi-squared with Rao & Scott's second-order correction or Mann–Whitney U test to analyze demographic and clinical variables between these two groups. Afterward, we used hierarchical multi-predictor Poisson regression analysis and allocated the variables in three different levels: (i) Sociodemographic; (ii) Lifestyle; and (iii) Clinical. We then calculated risk ratios (RR) and respective confidence intervals (95% CI) for each domain using bivariate analysis, considering p-values below 0.20 statistically significant. The RR is the ratio of the cumulative incidences in the exposed and unexposed groups, and provides a useful measure for comparing the risks for each group. The variables within the threshold were allowed to integrate the sequence of multi-predictor analysis (Poisson regression), starting from the most distal level to the most proximal ones (sociodemographic → lifestyle → clinical). The variable was retained if the subsequent level analysis calculated a p-value < 0.10. At each of the following levels, the Poisson regression model was adjusted with the corresponding level variables and the previous groups' statistically significant variables. The final model was composed of the variables of the level that presented a p-value <0.05 and the other variables of the previous levels in the same condition. Hierarchical regression is a type of regression model in which the independent variables are entered in blocks. Each block represents one step. The order (or which independent variable is entered into which block) was determined by the researchers based on theory.

Missing data at follow-up were addressed using inverse probability weighting (IPW) (Seaman and White, 2013). Age, region, gender, skin color, income, education, marital status, living alone, unemployment, physical activity, history of psychiatric diagnosis, anxiety symptoms (GAD-7), and AUDIT-C score were included in the

regression model to predict attrition. IPW was trimmed to the 5th and 95th percentiles. We also calculated survey weights to account for demographic representation at the national level. This procedure applies iterative post-stratification to match population margins to the survey sample proportions, which can approximate the demographic characteristics of the sample to the Brazilian population. We weighted our sample using Brazilian population margins regarding sex at birth, age groups, the region of residency, race/ethnicity, and household income according to the last Brazilian census (Instituto Brasileiro de Geografia e Estatística, 2010). The survey weight was trimmed up to 20. The final weights were calculated as the product of IPW and survey weights and were used in all regressions to minimize bias due to attrition and sample representation.

The generalized linear models were fitted within the *glm* R function from *stats* package. Survey weights were calculated using the packages survey in R (Lumley, 2020) (rake function). All analyses were performed using the R programming language (version 4.3.2). The following additional R packages were used: *dplyr* (version 1.1.4), *huxtable* (version 5.5.3), *tidyr* (version 1.3.0) and *gtsummary* (version 1.7.2). All statistical estimates were performed using survey weight.

Results

Sample size, descriptive results and bivariate analysis

We included 473 participants in our sample. The participant selection flowchart and reasons for dropouts in all waves are shown in Figure S1 (supplementary material). The mean age of the participants was 38.7 (SD: 12.1) years and 87.1% identified as females. Based on data from the last national census, our weighted sample closely represents the Brazilian population. The incidence of loneliness at W4 was 26.42%, corresponding to 125 out of 473 responses. Table 1 presents the weighted demographic and personal characteristics of our included sample and the comparison between participants with and without loneliness through the combination of all weighings. Tables S3, S4, and S5 present in the supplementary material provide this comparison with each type of weight used. The results of the bivariate Poison regression are presented in Table 2.

Multi-predictor analysis

The hierarchical Poisson regression model identified several clinical variables as significant risk factors associated with the incidence of loneliness. Specifically, depressive symptoms (RR: 1.21; 95%CI: 1.08–1.366; p=0.001), anxiety symptoms (RR: 1.19; 95%CI: 1.049–1.35; p=0.007), severe risk for alcohol abuse (RR: 1.579; 95%CI: 1.32–1.88; p<0.001) and cannabis use (RR: 1.75; 95%CI: 1.25–2.40; p<0.001) were considered risk factors.

Regarding lifestyle variables, the model identified protective factors for the incidence of loneliness. More than 150 min/week of physical activity (RR: 0.177; 95%CI: 0.078- 0.348; p<0.001) and good/excellent quality of family relationships (RR: 0.730; 95%CI: 0.609- 0.875; p<0.001) and sleep (RR: 0.483; 95%CI: 0.390- 0.594; p<0.001) were protective factors. The number of people living in the same household also has a protective tendency, though statistical significance was not sustained after adjusting for all factors (RR: 0.968; 95%CI: 0.913- 1.024; p=0.262).

Lastly, when analyzing the association between sociodemographic variables and the incidence of loneliness, several risk factors were recognized: female gender (RR: 1.719; 95%CI: 1.393-2.119; p<0.001), non-heterosexual orientation (RR: 1.518; 95%CI: 1.227- 1.872; p<0.001), middle (RR: 1.388; 95%CI: 1.094-1.743; p=0.006) and upper (RR: 1.361; 95%CI: 1.062- 1.735; p=0.014) socioeconomic status. The same model also identified higher education as a protective factor, with significance observed for college education (RR: 0.684; 95%CI: 0.551–0.851; p<0.001) and master's or PhD education (RR: 0.705; 95%CI: 0.556–0.893; p=0.004). Furthermore, a quadratic terms analysis revealed that both extremes of age were associated with an increased risk of loneliness (RR: 2.849; 95%CI: 1.881- 4.287; p<0.001).

All these results from the multi-predictor poison analysis, including those that were not statistically significant, are shown in table 3. A comparison of the effect size of the predictors of loneliness is shown in Figure S2 (supplementary material).

Discussion

This is the first longitudinal study to evaluate clinical and lifestyle predictors of loneliness in adults from a low- or middle-income country with collectivist society characteristics. After adjustment for multiple confounding variables, clinical factors

such as depressive symptoms, anxious symptoms, alcohol abuse, and cannabis use were risk factors for loneliness.

Our findings are in line with the scientific literature that points to a bidirectional relationship between loneliness and symptoms of depression and anxiety; that is, depressive and anxious symptoms can increase the risk of developing loneliness, but also have a greater chance of developing among individuals with loneliness. A recent study (Chen et al., 2023) conducted a meta-analysis (37 studies and 39,511 participants) using a cross-lagged approach to examine the reciprocal relations between loneliness and depressive symptoms. They showed that loneliness and depressive symptoms reciprocally predicted each other over time with similar effect sizes ($\beta = 0.18$). Depression can alter social decision-making capacity, leading to greater social avoidance. Depressed people may have significantly less positive (happiness) and more negative (shame, guilt, disappointment) feelings about social activities (Fernández-Theoduloz et al., 2019).

The relationship between loneliness and depressive symptoms is complex and some studies point to another possibility. Loneliness as part of the symptoms of a depressive disorder (Gijzen et al., 2021; Manfro et al., 2023; Mullarkey et al., 2021, 2019). In this sense, the loneliness that precedes depressive disorder could not be a risk factor but rather a prodrome. In this same understanding, loneliness after depressive disorder would be a residual symptom of this disorder.

Another recent meta-analysis (Gabarrell-Pascuet et al., 2023) of cross-sectional data that included 73 studies (1,020,461 participants) during the COVID-19 Pandemic showed the association of loneliness with symptoms of depression ($r = 0.49$), but also symptoms of anxiety ($r = 0.40$). A two-year follow-up study (Domènech-Abella et al., 2019) including data from 5,066 adults aged 50 years and older in Ireland, showed that loneliness and anxiety are bidirectional. Anxiety predicts loneliness (OR = 1.60), which can predict loneliness (OR = 1.24). This increased risk of loneliness due to anxiety reinforces previous findings that show anxiety and depression are associated with worse psychosocial functioning (social connectedness, quality of social relationships) (Cowden et al., 2021).

The association between loneliness and alcohol or cannabis misuse has been reported previously in the literature. According to a cross-sectional population-based study from Canada (n = 3772) that investigated factors associated with loneliness during the COVID-19 pandemic, severe loneliness (according to the UCLA-3) was

significantly associated with past month cannabis use (OR of 1.47) and past-month binge drinking (OR of 1.39 for binge drinking at least once a month, and OR of 1.70 for binge drinking at least once a week) (Lin, 2023). In addition, according to a longitudinal study from the US (n = 210), with data collected before the COVID-19 pandemic, participants with moderate and severe loneliness at baseline presented a significantly higher frequency of cannabis and alcohol use at follow-up in adjusted models (Gutkind et al., 2022). Even though substance misuse may be a potential consequence of loneliness (representing a potential maladaptive coping mechanism) (Gutkind et al., 2022; Lin, 2023), our study also suggests it as a potential risk factor, which may be contributing to the worsening of feelings of loneliness.

As described in the literature, our study also found physical activity as a protective factor for loneliness (Vancampfort et al., 2019). Links between social relationships and physical activity may be particularly important, since sustained physical activity is associated with a range of beneficial outcomes, including reduced stress and anxiety symptoms, improved sleep quality, reduced levels of depressive symptoms, and prevention and reduced mortality from chronic diseases such as high blood pressure and diabetes, as well as providing socialization and quality of life (Schrempft et al., 2019). A study carried out during the covid 19 pandemic among 7,203 young university students demonstrated that less physically active students were more likely to experience loneliness than students who were more physically active (Wenig et al., 2023). We did not find studies in the literature that relate the amount of time spent doing physical activity to loneliness. Our study found that above 150 minutes would be a protective factor. We hypothesize that longer time is related to more frequent activities, consequently bringing greater benefits in terms of physical health and socialization.

Concerning the connection between loneliness and sleep, our study found an association between loneliness and quality of sleep, similar to results found in other studies (Guerra-Balic et al., 2023). A meta-analysis correlated loneliness with higher self-reported sleep disturbance, defined as impaired sleep quality and insomnia symptoms. Loneliness was also associated with sleep inadequacy and dissatisfaction, but not sleep duration (Griffin et al., 2020). McLay et al. (2021), in a large sample of 95,045 older adults (> 65 years of age), showed that loneliness, social isolation, and health concerns are related and may produce sleep disorders, especially in women. A propensity-score-matched case-control study with 11,696 participants found that

loneliness was associated with extended sleep latency, increased nocturnal awakenings, and reduced subjective sleep quality and daytime function but was not associated with sleep behavior, including sleep onset and offset timings (Peng et al., 2021). As our study only addressed general sleep quality, we are unable to differentiate these issues. Note that the majority of the studies present in the literature demonstrate loneliness as a risk factor for sleep quality and not the opposite relationship. We have few studies (Christiansen et al., 2016; Segrin and Domschke, 2011) examining sleep disturbance and loneliness, being cross-sectional studies. Longitudinal research identified sleep disturbance as a partial mediator of the connection between loneliness and self-reported health, thereby uncovering sleep disturbance as a treatment target to mitigate the potential effect of loneliness on health (Griffin et al., 2021).

Our study showed that better quality of family relationships and higher education was a protective factor. The following covariates: female gender, non-heterosexual orientation, higher socioeconomic status, and extremes of age (in a U-shape way) were associated with an increased risk of loneliness. An umbrella review (Solmi et al., 2020) of observational studies (795 studies and 746,706 participants) about loneliness-related factors supported these findings. According to this review, factors cross-sectionally associated with loneliness included poor quality of social contacts, female sex, and age (in a U-shape way). However, contrary to our results, loneliness was associated with low socioeconomic status. We believe that our findings reflect the nuances of a country with collectivist characteristics. Usually, people from birth are integrated into cohesive groups (especially represented by the extended family; including uncles, aunts, grandparents, and cousins) (Hofstede, 2024). People with low socioeconomic status commonly live in communities with a large number of people living in small spaces. Brazil has more than 10 thousand favelas and urban communities, where 16.6 million people live (8% of the Brazilian population) (IBGE, 2022). In this context, greater social dependence exists to meet basic survival needs. This can encourage greater and better social connection and reduce the feeling of loneliness. Regarding sexual orientation, several other studies have also shown that non-heterosexuals have a higher risk of loneliness (Buczak-Stec et al., 2023; Luhmann et al., 2023). Finally, a higher level of education is also a protective factor in other studies in the literature (Lim et al., 2020; Lin, 2023).

Even though our study presents limitations, we implemented some strategies to mitigate them. First, we conducted an online self-report survey and there may be

variations in how participants interpret some questions. To reduce this risk, we used scales validated for our country or carried out psychometric tests. Second, we have a sampling bias when inviting participants via social media, and there was a significant loss of participants over the two-year follow-up. However, we used weights that brought our sampling closer to the characteristics of the Brazilian demographic census and weighted for loss to follow-up. Even with the adjustments, we need to be cautious when interpreting the rates as a representative prevalence of the Brazilian population. Third, we use a reduced version of the UCLA scale; because of this, we are unable to analyze different categories of loneliness, such as emotional and social.

In addition to some strengths already presented to minimize the limitations highlighted above, this study has other strengths to highlight. First, the study has a longitudinal design that allows for a better understanding of the cause-and-effect relationship between predictors and outcomes. Second, our national sample recruited individuals covering all 27 Brazilian federative units. Third, the sample size allowed us to analyze a wide range of variables and thus corrected our results for several confounding factors.

In summary, our study showed that after two years of follow-up and adjustment for multiple confounding variables, clinical factors such as depressive symptoms, anxiety symptoms, alcohol abuse, and cannabis use were risk factors for loneliness. Among lifestyle factors, more than 150 min/week of physical activity, good/excellent family relationship quality, and good/excellent sleep quality were associated with a lower incidence of loneliness. Therefore, addressing such predictors may be essential for preventing loneliness.

References

Antonelli-Salgado, T., Monteiro, G.M.C., Marcon, G., Roza, T.H., Zimerman, A., Hoffmann, M.S., Cao, B., Hauck, S., Brunoni, A.R., Passos, I.C., 2021. Loneliness, but not social distancing, is associated with the incidence of suicidal ideation during the COVID-19 outbreak: a longitudinal study. J. Affect. Disord. 290, 52–60. https://doi.org/10.1016/j.jad.2021.04.044

Brazilian Ministry of Health, 2022. Painel Coronavírus [WWW Document]. URL https://covid.saude.gov.br/ (accessed 1.20.21).

Buczak-Stec, E., König, H.-H., Hajek, A., 2023. Sexual Orientation and Psychosocial Factors in Terms of Loneliness and Subjective Well-Being in Later Life. Gerontologist 63, 338–349. https://doi.org/10.1093/geront/gnac088

Bush, K., Kivlahan, D.R., McDonell, M.B., Fihn, S.D., Bradley, K.A., 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. https://doi.org/10.1001/archinte.158.16.1789
Chen, Z., Song, X., Lee, T.M.C., Zhang, R., 2023. The robust reciprocal relationship between loneliness and depressive symptoms among the general population: Evidence from a quantitative analysis of 37 studies. J. Affect. Disord. 343, 119–128. https://doi.org/10.1016/j.jad.2023.09.035
Christiansen, J., Larsen, F.B., Lasgaard, M., 2016. Do stress, health behavior, and sleep mediate the association between loneliness and adverse health conditions among older people? Soc. Sci. Med. 152, 80–86. https://doi.org/10.1016/j.socscimed.2016.01.020
Cowden, R.G., Chapman, I., Houghtaling, A., 2021. Additive, Curvilinear, and Interactive Relations of Anxiety and Depression With Indicators of Psychosocial Functioning. Psychol. Rep. 124, 627–650. https://doi.org/10.1177/0033294120918809
Domènech-Abella, J., Mundó, J., Haro, J.M., Rubio-Valera, M., 2019. Anxiety, depression, loneliness and social network in the elderly: Longitudinal associations from The Irish Longitudinal Study on Ageing (TILDA). J. Affect. Disord. 246, 82–88. https://doi.org/10.1016/j.jad.2018.12.043
Ernst, M., Niederer, D., Werner, A.M., Czaja, S.J., Mikton, C., Ong, A.D., Rosen, T., Brähler, E., Beutel, M.E., 2022. Loneliness before and during the COVID-19 pandemic: A systematic review with meta-analysis. Am. Psychol. 77, 660–677. https://doi.org/10.1037/amp0001005
Fernández-Theoduloz, G., Paz, V., Nicolaisen-Sobesky, E., Pérez, A., Buunk, A.P., Cabana, Á., Gradin, V.B., 2019. Social avoidance in depression: A study using a social decision-making task. J. Abnorm. Psychol. 128, 234–244. https://doi.org/10.1037/abn0000415
Gabarrell-Pascuet, A., García-Mieres, H., Giné-Vázquez, I., Moneta, M.V., Koyanagi, A., Haro, J.M., Domènech-Abella, J., 2023. The Association of Social Support and Loneliness with Symptoms of Depression, Anxiety, and Posttraumatic Stress during the COVID-19 Pandemic: A Meta-Analysis. Int. J. Environ. Res. Public Health 20. https://doi.org/10.3390/ijerph20042765
Gijzen, M.W.M., Rasing, S.P.A., Creemers, D.H.M., Smit, F., Engels, R.C.M.E., De Beurs, D., 2021. Suicide ideation as a symptom of adolescent depression. a network analysis. J. Affect. Disord. 278, 68–77. https://doi.org/10.1016/j.jad.2020.09.029
Griffin, S.C., Mladen, S.N., Williams, A.B., Dautovich, N.D., Lageman, S.K., Dzierzewski, J.M., Perrin, P.B., Rybarczyk, B.D., 2021. Sleep Disturbance Mediates the Association Between Loneliness and Health in Older Americans. Int. J. Behav. Med. 28, 64–72. https://doi.org/10.1007/s12529-020-09897-2
Griffin, S.C., Williams, A.B., Ravyts, S.G., Mladen, S.N., Rybarczyk, B.D., 2020. Loneliness and sleep: A systematic review and meta-analysis. Health Psychol Open 7, 2055102920913235. https://doi.org/10.1177/2055102920913235
Guerra-Balic, M., González-González, C.S., Sansano-Nadal, O., López-Dóriga, A., Chin, M.-K., Ding, K., Yang, J., Durstine, J.L., 2023. Impact of COVID-19 lockdown on physical activity, insomnia, and loneliness among Spanish women and men. Sci. Rep. 13, 2912. https://doi.org/10.1038/s41598-023-30173-2
Gutkind, S., Gorfinkel, L.R., Hasin, D.S., 2022. Prospective effects of loneliness on frequency of alcohol and marijuana use. Addict. Behav. 124, 107115. https://doi.org/10.1016/j.addbeh.2021.107115
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. https://doi.org/10.1177/0141076820918236
Hofstede, 2024. Country Comparison Tool [WWW Document]. Hofstede Insights. URL https://www.hofstede-insights.com/country-comparison-tool (accessed 24).
Holt-Lunstad, J., Smith, T.B., 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. https://doi.org/10.1177/1745691614568352

Holt-Lunstad, J., Smith, T.B., Layton, J.B., 2010. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 7, e1000316. https://doi.org/10.1371/journal.pmed.1000316
Hughes, M.E., Waite, L.J., Hawkley, L.C., Cacioppo, J.T., 2004. A Short Scale for Measuring Loneliness in Large Surveys. Research on Aging. https://doi.org/10.1177/0164027504268574
IBGE, 2022. Censo 2022 [WWW Document]. IBGE. URL https://censo2022.ibge.gov.br/?localidade=BR (accessed 22).
Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. 16, 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x
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. https://doi.org/10.1016/j.puhe.2017.07.035
Lim, M.H., Eres, R., Vasan, S., 2020. Understanding loneliness in the twenty-first century: an update on correlates, risk factors, and potential solutions. Soc. Psychiatry Psychiatr. Epidemiol. 55, 793–810. https://doi.org/10.1007/s00127-020-01889-7
Lin, S.L., 2023. The “loneliness epidemic”, intersecting risk factors and relations to mental health help-seeking: A population-based study during COVID-19 lockdown in Canada. J. Affect. Disord. 320, 7–17. https://doi.org/10.1016/j.jad.2022.08.131
Lucke, J.F., 2005. The α and the ω of congeneric test theory: An extension of reliability and internal consistency to heterogeneous tests. Appl. Psychol. Meas. 29, 65–81.
Luhmann, M., Buecker, S., Rüsberg, M., 2023. Loneliness across time and space. Nat Rev Psychol 2, 9–23. https://doi.org/10.1038/s44159-022-00124-1
Lumley, T., 2020. Survey: analysis of complex survey samples.
Manfro, P.H., Pereira, R.B., Rosa, M., Cogo-Moreira, H., Fisher, H.L., Kohrt, B.A., Mondelli, V., Kieling, C., 2023. Adolescent depression beyond DSM definition: a network analysis. Eur. Child Adolesc. Psychiatry 32, 881–892. https://doi.org/10.1007/s00787-021-01908-1
Mann, F., Wang, J., Pearce, E., Ma, R., Schlief, 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. https://doi.org/10.1007/s00127-022-02261-7
Matias, A.G.C., Fonsêca, M. de A., Gomes, M. de L. de F., Matos, M.A.A., 2016. Indicators of depression in elderly and different screening methods. Einstein 14, 6–11. https://doi.org/10.1590/S1679-45082016AO3447
Moreno, A.L., DeSousa, D.A., Souza, A.M.F.L.P., Manfro, G.G., Salum, G.A., Koller, S.H., Osório, F. de L., Crippa, J.A. de S., Others, 2016. Factor structure, reliability, and item parameters of the brazilian-portuguese version of the GAD-7 questionnaire. Temas em Psicologia 24, 367–376.
Mullarkey, M.C., Marchetti, I., Beevers, C.G., 2019. Using Network Analysis to Identify Central Symptoms of Adolescent Depression. J. Clin. Child Adolesc. Psychol. 48, 656–668. https://doi.org/10.1080/15374416.2018.1437735
Mullarkey, M.C., Marchetti, I., Bluth, K., Carlson, C.L., Shumake, J., Beevers, C.G., 2021. Symptom centrality and infrequency of endorsement identify adolescent depression symptoms more strongly associated with life satisfaction. J. Affect. Disord. 289, 90–97. https://doi.org/10.1016/j.jad.2021.02.064
Peng, A., Tang, Y., He, S., Ji, S., Dong, B., Chen, L., 2021. Association between loneliness, sleep behavior and quality: a propensity-score-matched case–control study. Sleep Med. 86, 19–24. https://doi.org/10.1016/j.sleep.2021.08.008
Raykov, T., 1997. Scale Reliability, Cronbach’s Coefficient Alpha, and Violations of Essential Tau-Equivalence with Fixed Congeneric Components. Multivariate Behav. Res. 32, 329–353. https://doi.org/10.1207/s15327906mbr3204_2
Salinas, J., Beiser, A.S., Samra, J.K., O’Donnell, A., DeCarli, C.S., Gonzales, M.M.,

Aparicio, H.J., Seshadri, S., 2022. Association of Loneliness With 10-Year Dementia Risk and Early Markers of Vulnerability for Neurocognitive Decline. Neurology 98, e1337–e1348. https://doi.org/10.1212/WNL.0000000000200039

Santos, I.S., Tavares, B.F., Munhoz, T.N., de Almeida, L.S.P., da Silva, N.T.B., Tams, B.D., Patella, A.M., Matijasevich, A., 2013. Sensibilidade e especificidade do Patient Health Questionnaire-9 (PHQ-9) entre adultos da população geral. Cadernos de Saúde Pública. https://doi.org/10.1590/s0102-311x2013001200006

Schrempft, S., Jackowska, M., Hamer, M., Steptoe, A., 2019. Associations between social isolation, loneliness, and objective physical activity in older men and women. BMC Public Health 19, 74. https://doi.org/10.1186/s12889-019-6424-y

Seaman, S.R., White, I.R., 2013. Review of inverse probability weighting for dealing with missing data. Stat. Methods Med. Res. 22, 278–295. https://doi.org/10.1177/0962280210395740

Segrin, C., Domschke, T., 2011. Social support, loneliness, recuperative processes, and their direct and indirect effects on health. Health Commun. 26, 221–232. https://doi.org/10.1080/10410236.2010.546771

Solmi, M., Veronese, N., Galvano, D., Favaro, A., Ostinelli, E.G., Noventa, V., Favaretto, E., Tudor, F., Finessi, M., Shin, J.I., 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. https://doi.org/10.1016/j.jad.2020.03.075

Steptoe, A., Shankar, A., Demakakos, P., Wardle, J., 2013. Social isolation, loneliness, and all-cause mortality in older men and women. Proc. Natl. Acad. Sci. U. S. A. 110, 5797–5801. https://doi.org/10.1073/pnas.1219686110

Surkalim, D.L., 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. https://doi.org/10.1136/bmj-2021-067068

Survey Monkey [WWW Document], 2024. . SurveyMonkey Inc. URL pt.surveymonkey.com (accessed 1.24).

Terracciano, A., Luchetti, M., Karakose, S., Stephan, Y., Sutin, A.R., 2023. Loneliness and Risk of Parkinson Disease. JAMA Neurol. 80, 1138–1144. https://doi.org/10.1001/jamaneurol.2023.3382

Valtorta, N.K., Kanaan, M., Gilbody, S., Ronzi, S., Hanratty, B., 2016. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. Heart 102, 1009–1016. https://doi.org/10.1136/heartjnl-2015-308790

Vancampfort, D., Lara, E., Smith, L., Rosenbaum, S., Firth, J., Stubbs, B., Hallgren, M., Koyanagi, A., 2019. Physical activity and loneliness among adults aged 50 years or older in six low- and middle-income countries. Int. J. Geriatr. Psychiatry 34, 1855–1864. https://doi.org/10.1002/gps.5202

von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., Vandenbroucke, J.P., STROBE Initiative, 2007. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann. Intern. Med. 147, 573–577. https://doi.org/10.7326/0003-4819-147-8-200710160-00010

Wenig, V., Heumann, E., Stock, C., Busse, H., Negash, S., Pischke, C.R., Heinrichs, K., 2023. Associations of loneliness with mental health and with social and physical activity among university students in Germany: results of the COVID-19 German student well-being study (C19 GSWS). Front Public Health 11, 1284460. https://doi.org/10.3389/fpubh.2023.1284460

WHO, 2022. Physical activity [WWW Document]. URL https://www.who.int/news-room/fact-sheets/detail/physical-activity (accessed 10.19.23).

WHO ASSIST Working Group, 2002. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): development, reliability and feasibility. Addiction. https://doi.org/10.1046/j.1360-0443.2002.00185.x

Table 1. Demographic and personal characteristics of participants

	Not lonely group					Lonely group					
Caracteristic	**n = 348**	**%(n)**	**%(D)**	**%(A)**	**%(C)**	**n = 125**	**%(n)**	**%(D)**	**%(A)**	**%(C)**	***p* value[X]**
Sex											0.079
Male	45	12.9	43.7	18.9	58.7	16	12.8	23.8	18.5	33.3	
Female	303	87.1	56.3	81.1	41.3	109	87.2	76.2	81.5	66.7	
Sexual orientation (heterossexual)	309	88.8	79.1	87.9	77.2	105	84.0	77.9	81.2	70.7	0.7
Skin Color											0.9
Non-White	136	39.1	48.6	44.2	57.0	59	47.2	45.9	55.6	54.7	
White	212	60.9	51.4	55.8	43.0	66	52.8	54.1	44.4	45.3	
Education											0.6
Up to high-school	20	5.7	12.8	8.1	18.0	15	12.0	29.4	17.6	31.1	
Some college education	135	38.8	42.6	42.2	40.8	54	43.2	32.6	43.2	32.9	
Master or doctorate	193	55.5	44.6	49.7	41.1	56	44.8	38.0	39.3	36.0	
Socioeconomic status											0.8
Lower	93	26.7	66.6	32.2	72.5	42	33.6	71.0	39.9	72.3	
Middle	75	21.6	10.7	21.8	8.6	33	26.4	13.9	24.0	11.6	
Upper	180	51.7	22.6	46.0	18.9	50	40.0	15.1	36.0	16.1	
Unemployed	34	9.8	29.5	10.4	34.1	23	18.4	38.1	22.4	42.3	0.7
Social distancing	327	94.0	95.4	93.5	95.9	119	95.2	97.5	95.7	97.7	0.5
Physical activity											<0.001
Less than 150min/week	305	87.6	88.8	89.9	92.7	119	95.2	98.4	96.6	99.0	

More than 150min/week	43	12.4	11.2	10.1	7.3	6	4.8	1.6	3.4	1.0	
Sleep quality											0.004
Better	163	46.8	51.2	45.7	50.4	41	32.8	18.9	29.6	16.7	
Worse	185	53.2	48.8	54.3	49.6	84	67.2	81.1	70.4	83.3	
Marital status (grouped)											0.5
Without Partner	146	42.0	56.8	39.2	56.0	68	54.4	72.2	51.8	65.5	
With partner	202	58.0	43.2	60.8	44.0	57	45.6	27.8	48.2	34.5	
Friendship relationship quality											0.6
Better	231	66.4	66.2	65.2	62.2	72	57.6	55.1	56.4	52.9	
Worse	117	33.6	33.8	34.8	37.8	53	42.4	44.9	43.6	47.1	
Family relationship quality											0.13
Better	263	75.6	78.3	74.0	80.7	79	63.2	65.9	61.0	64.0	
Worse	85	24.4	21.7	26.0	19.3	46	36.8	34.1	39.0	36.0	
Religion	165	47.4	53.9	47.7	56.4	64	51.2	65.1	51.4	63.0	0.7
Alcohol risk zone											0.040
Low risk	253	72.7	82.9	70.6	83.3	92	73.6	59.2	71.5	57.5	
High risk	95	27.3	17.1	29.4	16.7	33	26.4	40.8	28.5	42.5	
Cannabis use	14	4.0	5.4	4.0	4.2	5	4.0	5.2	5.3	6.3	0.7

Weighted characteristics of participants stratified by loneliness incidence. **D.** Weighted by demographics. **A.**Weighted by attrition. **C.** Weighted by demographics and attrition, combined. **X.** Chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey samples applied to the weighted by demographic and attrition data.

Table 2. Bivariate analysis of predictors of the sociodemographic, lifestyle, social and clinical domains.

Variable	Category	β	SE	RR	RR (lower)	RR (upper)	p-value
Age	-	-0.089	0.033	0.914	0.856	0.976	0.007
Age (quadratic term)	-	-0.053	0.031	0.948	0.892	1.007	0.087
Age (cubic term)	-	-0.028	0.028	0.973	0.920	1.027	0.328
Skin color	White	0.072	0.071	1.074	0.934	1.234	0.314
Education	Some college education	-0.552	0.088	0.576	0.484	0.685	<0.001
	Master or Doctorate	-0.489	0.087	0.614	0.484	0.685	<0.001
Gender at birth	Female	0.804	0.075	2.234	1.930	2.591	<0.001
Heterosexual	No	0.253	0.078	1.288	1.105	1.498	0.001
Household income	Middle	0.220	0.112	1.246	0.995	1.543	0.049
	Upper	-0.122	0.097	0.885	0.995	1.543	0.209
Unemployed	No	-0.263	0.072	0.769	0.669	0.885	0.000
Family relationship	Good/excelent	-0.618	0.074	0.539	0.467	0.623	<0.001
Friend relationship	Good/excelent	-0.287	0.071	0.750	0.653	0.862	<0.001
Physical activity	More than 150min/week	-1.771	0.349	0.170	0.079	0.315	<0.001
Sleep quality	Good/excelent	-1.301	0.095	0.272	0.225	0.327	<0.001
Number of people living in your house	-	-0.146	0.024	0.864	0.824	0.906	<0.001
Anxiety symptoms (z-score)	-	0.531	0.034	1.70	1.591	1.818	<0.001
Depressive symptoms (z-score)	-	0.513	0.029	1.67	1.577	1.769	<0.001
Alcohol risk zone	High risk	0.916	0.072	2.500	2.172	2.875	<0.001
Cannabis use	Yes	0.301	0.146	1.351	1.003	1.778	0.039

The bivariate analyses were performed in order to pre-select the variables that will be used in the multi-predictor Poisson regression. The cut-off point we will use is based on $p < 0.2$. The lower and upper bounds (RR lower and RR upper) were calculated based on a 95% confidence interval (CI).

Table 3. Multi-predictor Poisson regression analysis to evaluate factors associated with loneliness incidence. The table presents the risk ratios and the corresponding 95% CIs with p-values. The columns illustrate the successive introduction of variables in the Poison regression, with each block of variables represented in a separate column. The final column presents the result obtained with the full set of variables.

	Block 1: Sociodemographic	**Block 2: Lifestyle and social**	**Block 3: Clinical**
(Intercept)	**0.258 [0.202, 0.329], p<0.001**	**0.448 [0.325, 0.616], p<0.001**	**0.240 [0.169, 0.341], p<0.001**
Age (z-score)	**0.386 [0.276, 0.547], p<0.001**	0.693 [0.471, 1.029], p=0.066	**0.343 [0.224, 0.529], p<0.001**
Age (quadratic term)	**2.501 [1.790, 3.464], p<0.001**	**1.475 [1.011, 2.133], p=0.041**	**2.849 [1.881, 4.287], p<0.001**
Education (college education)	**0.423 [0.348, 0.514], p<0.001**	**0.567 [0.465, 0.691], p<0.001**	**0.684 [0.551, 0.851], p<0.001**
Education (master or PhD)	**0.458 [0.372, 0.563], p<0.001**	**0.458 [0.368, 0.568], p<0.001**	**0.705 [0.556, 0.893], p=0.004**
Sex (female)	**2.672 [2.265, 3.160], p<0.001**	**2.317 [1.926, 2.795], p<0.001**	**1.719 [1.393, 2.119], p<0.001**
Sexual orientation (non-heterosexual)	**2.203 [1.809, 2.675], p<0.001**	**1.976 [1.612, 2.414], p<0.001**	**1.518 [1.227, 1.872], p<0.001**
Socioeconomic status (middle)	**1.380 [1.088, 1.732], p=0.007**	**1.497 [1.185, 1.871], p<0.001**	**1.388 [1.094, 1.743], p=0.006**
Socioeconomic status (upper)	**1.311 [1.030, 1.660], p=0.026**	**1.432 [1.139, 1.790], p=0.002**	**1.361 [1.062, 1.735], p=0.014**
Number of people living in your house	**0.891 [0.845, 0.939], p<0.001**	**0.902 [0.852, 0.953], p<0.001**	0.968 [0.913, 1.024], p=0.262
Marital status (with partner)	0.924 [0.782, 1.089], p=0.349		
Positive family relationship		**0.689 [0.574, 0.828], p<0.001**	**0.730 [0.609, 0.875], p<0.001**
Positive friendship relationship		0.970 [0.817, 1.151], p=0.725	
Physical activity (more than 150 min/week)		**0.161 [0.074, 0.304], p<0.001**	**0.177 [0.078, 0.348], p<0.001**
Good sleep quality		**0.340 [0.278, 0.414], p<0.001**	**0.483 [0.390, 0.594], p<0.001**
Depressive symptoms (PHQ-9)			**1.214 [1.080, 1.366], p=0.001**

Anxiety symptoms (GAD-7)			**1.191 [1.049, 1.352], p=0.007**
Alcohol risk zone (moderate, high or severe)			**1.579 [1.322, 1.882], p<0.001**
Cannabis use (yes)			**1.750 [1.250, 2.399], p<0.001**
n	473	473	**473**
-2log likelihood	-1793.697	-1678.612	**-1621.319**
AIC	3609.395	3385.223	**3276.637**
BIC	3655.145	3443.450	**3347.342**