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Loneliness as a Pathway from Social Isolation to Psychological Distress: A Cross-Sectional Mediation Study in Portuguese Adults

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Abstract

Social disconnection has become a public-health concern, but it remains unclear whether mental-health symptoms are more closely related to limited social contact or to the subjective experience of loneliness. This cross-sectional study examined 632 self-selected adults living in Portugal, recruited online, and explored whether loneliness helps explain the association between social isolation and psychological distress across small, medium, and large cities. Participants completed self-report measures of loneliness, social isolation, depression, anxiety, stress, and positive and negative affect. Loneliness was a salient experience: the mean score was close to the scale midpoint, and 36.2% of participants scored above it. Higher loneliness was associated with greater psychological distress, greater social isolation, lower positive affect, and higher negative affect. When loneliness was considered together with social isolation, the direct link between isolation and distress became minimal, suggesting that distress was more closely connected to how social disconnection was experienced than to contact frequency alone. This pattern was similar across city sizes, and average levels of loneliness, isolation, distress, and affect did not meaningfully differ between small, medium, and large cities. Overall, the findings are consistent with loneliness as a candidate target for mental-health promotion in this sample of Portuguese adults, although longitudinal studies are needed to clarify causal pathways.

Keywords: loneliness; social isolation; psychological distress; negative affect; Portugal

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1. Introduction

Loneliness and social isolation are now recognized as public-health priorities. The EU Loneliness Survey, conducted in 2022 [1], found that 13% of adults aged 16 years or older felt lonely most or all of the time, and approximately 35% reported feeling lonely at least some of the time. The size of the associated health effect is comparable to established behavioral risks: meta-analytic evidence places the mortality risk of loneliness, social isolation, and living alone at increases of 26%, 29%, and 32%, respectively, after adjustment

for confounders [2]. Recent proteomic work identified plasma signatures linking these states to inflammation, antiviral responses, and complement systems, with prospective associations to cardiovascular disease, type 2 diabetes, stroke, and mortality [3]. Population-level mental-health policy now treats both constructs as legitimate targets of intervention.

Loneliness and social isolation are conceptually distinct. Loneliness is the subjective perception that one's social relationships are inadequate in number or quality, whereas social isolation is the objective absence of social ties or contact [4,5]. This definition follows the cognitive discrepancy model, which locates loneliness in the gap between desired and achieved relationships and treats that gap, rather than the objective level of contact, as the proximal correlate of distress [6]. In this framework, loneliness arises when achieved relationships are appraised as falling short of the standards a person holds for their number or quality, so the same objective social condition can be experienced very differently across individuals [6]. The model therefore motivates the mediational structure tested here, in which the subjective evaluation of the social condition, rather than contact frequency itself, is expected to carry the association with distress. The two constructs typically correlate only modestly to moderately. Having few contacts and feeling alone are not the same experience, and a person can rate high on one and low on the other. The implication for mental-health research is mechanistic rather than nominal: does objective isolation harm mental health directly, or is its association with distress accounted for by the subjective interpretation of one's social condition?

Cacioppo and Hawkley [7] argued for the second account. In their model, persistent loneliness is the proximal psychological pathway through which impoverished social conditions are associated with psychological distress. The model rests on the evolutionary argument that humans, as a hyper-social species, depend on a stable social surround to thrive [4]. When that surround is perceived as insufficient, hypervigilance for social threat increases, social cognition shifts toward negative interpretation of ambiguous interpersonal information [8], and downstream physiological and affective consequences follow. Longitudinal evidence converges on this temporal ordering. In five-year cross-lagged analyses of the Chicago Health, Aging, and Social Relations Study, loneliness predicted increases in depressive symptomatology more strongly than the reverse, after adjusting for social support and a wide set of demographic and health covariates [9]. Santini et al. [10], in a longitudinal mediation analysis of the National Social Life, Health, and Aging Project across three waves spanning a decade, replicated the same ordering in older adults and showed that perceived isolation mediated the association between social disconnectedness and both depression and anxiety. Meta-analytic evidence on intervention effects converges on the same logic: programs that address maladaptive social cognition outperform programs that only increase opportunities for contact [11].

Despite this accumulating support, three gaps motivate the present study. First, formal mediation testing of the isolation–loneliness–distress chain has been conducted predominantly on Anglo and Northern-European samples, with limited replication in Portuguese-language adult populations using bootstrap confidence intervals on the indirect effect. Within Europe, loneliness is more prevalent in Southern and Eastern countries [1,12], which makes Portugal a substantively informative setting for this test. Second, cross-sectional applications of the model dominate the empirical literature, even though Maxwell and Cole [13] and Maxwell et al. [14] have shown that cross-sectional mediation estimates can be substantially biased relative to longitudinal parameters, including in directions opposite to the true longitudinal effect. Robust cross-sectional tests therefore require explicit comparison with reverse-direction models, sensitivity to the operationalization of the predictor, and acknowledgment that the resulting estimates are atemporal associations rather than evidence of temporal mechanism. Third, although prior research has examined

urbanization as a main exposure for mental-health outcomes [15–17], few studies have asked whether the structural paths of the loneliness pathway are invariant across cities of different size. Theory does not specify a strong direction for this moderation, and the empirical literature is mixed: Keller et al. [18], pooling 69,136 individuals across European cohorts, found no association between rural-versus-urban residence and loneliness, while smaller country-specific studies have reported either urban-elevated or rural-elevated patterns depending on the local context. Whether population size modulates the structural relations connecting isolation to distress at the individual level, rather than only mean loneliness levels, is the question we ask here.

We frame the present study as a test of a psychological mediation hypothesis about mental health, not as a comprehensive account of loneliness as a socially situated phenomenon; relational and community determinants such as perceived social support, relationship quality, and neighborhood cohesion lie outside the present measurement and are treated as boundary conditions in the Discussion [6,19]. We pursued three aims in a Portuguese adult sample. The first was to estimate the indirect statistical effect of objective social isolation on psychological distress through perceived loneliness, with bootstrap-based inference. The second was to test, exploratorily, whether the structural paths of the model are invariant across small, medium, and large cities in Portugal. The third was to compare the indirect effects via loneliness and immediate negative affect in a parallel-mediator framework, to estimate how much of the loneliness pathway is captured by acute affective reactivity. Three hypotheses were tested. H1: perceived loneliness statistically mediates the cross-sectional association between objective social isolation and psychological distress, with a non-significant direct path. H2: The structural paths of the model do not differ across city-size groups. H3: The indirect effect through loneliness is at least as large as the indirect effect through negative affect, indicating that loneliness is not reducible to immediate affective reactivity. Throughout the manuscript, including its title, the term "pathway" is used in a statistical sense, to denote the decomposition of a cross-sectional association into direct and indirect components, and not as a claim about causal mechanism.

2. Materials and Methods

2.1. Design

We conducted a cross-sectional self-report study, delivered online via Google Forms to adults aged 18 years or older resident in cities of varying sizes distributed across the regions of Portugal. Reporting follows the STROBE recommendations for cross-sectional research.

2.2. Participants

Participants were recruited between 6 July 2025 and 1 December 2025 through two complementary strategies: targeted paid advertising campaigns on social media platforms (e.g., Meta) and email invitations disseminated through institutional networks and partner organizations. The survey link directed interested individuals to the anonymous online questionnaire, which they completed at the time and location of their choice. Because recruitment was open and non-probabilistic, the number of individuals reached by the campaigns could not be determined; a response rate therefore cannot be computed and repeat participation cannot be formally ruled out. Inclusion criteria were: residence in Portugal for at least one year, age 18 years or older, signed informed consent, and access to the internet and a device adequate for completing an online questionnaire. Exclusion corresponded to non-fulfillment of any inclusion criterion. The a priori sample-size target was at least 592 participants for the primary mediation analysis (small-to-medium effect, $\alpha = 0.05$, power = 0.99, two-tailed; [20]); the realized sample exceeded this target. Power

for the multi-group invariance test was lower than for the main mediation, given that interaction tests typically detect only larger effects, and effects with $\eta^2p \approx 0.01$ or below could escape detection at this sample size.

Three indicators of data quality were combined to address careless responding and multivariate outliers. Within-person response variability (IRV) was computed across all items of the DASS-21, UCLA-LS v3, SIS, and PANAS-VRP scales, flagging participants with overly homogeneous response patterns. Repeated personal reliability (RPR) was computed across semantically paired UCLA-LS v3 items, alongside mean differences between synonymous and antonymous item pairs, to identify incoherent response patterns. Mahalanobis distance was computed on the total scores of the five scales, with multivariate outliers defined by values exceeding the χ^2 criterion at $p < 0.001$. A composite quality index excluded participants whose responses met two or more of these criteria. From an initial sample of 639 participants, four were excluded based on these criteria (one for not meeting the minimum-age requirement, one for low-quality responses, and two for failing two or more of the multivariate criteria), yielding a working sample of 635. For the analyses reported here, the pre-computed composite quality flag in the source dataset and an additional minimum-age verification were jointly applied, excluding three further cases: one with an inconsistent age value (11 years), incompatible with other reported indicators (postgraduate education, independent living, partnered status) and suggesting a data-entry error, and two flagged by the composite quality index at the strictest threshold. The final analytic sample comprised 632 adults. Of these, 626 reported information on city size and were included in the city-size stratified analyses (small city, $n = 178$; medium city, $n = 206$; large city, $n = 242$).

Portugal does not use a single official threshold-based classification of city size; the European Commission Urban Audit and Eurostat DEGURBA frameworks rely on density typologies rather than discrete population thresholds [21]. The thresholds used here capture three meaningful tiers within the Portuguese urbanization gradient: peripheral and rural-adjacent localities (≤20,000), district capitals and mid-sized regional centers (20,001–75,000), and the larger urban centers including the metropolitan areas of Lisbon and Porto (>75,000). The thresholds are compressed by international standards, in that the largest stratum here would not be classified as "large" in countries with multi-million-inhabitant cities. We revisit this constraint when interpreting the moderation null.

Sociodemographic characteristics of the analytic sample are presented in Table 1.

Table 1. Sociodemographic characteristics of the analytic sample ($N = 632$).

Characteristic	Category	*n*	%
Age (years)	M = 37.65, SD = 15.47, range = 18–86	626	—
Gender	Women	401	63.4
	Men	219	34.7
	Non-binary or other	11	1.7
Sexual orientation	Heterosexual	509	80.5
	Bisexual	68	10.8
	Gay	28	4.4
	Lesbian	14	2.2
	Pansexual	7	1.1
	Other	5	0.8

Table 1. *Cont.*

Characteristic	Category	*n*	%
Education	Secondary or below	134	21.2
	Bachelor (in progress or complete)	297	47.0
	Postgraduate or higher	201	31.8
Marital status	Single, no partner	205	32.4
	Single, with partner	175	27.7
	Married or cohabiting	163	25.8
	Divorced or separated	76	12.0
Living arrangement	With family members	224	35.4
	With romantic partner	184	29.1
	Alone	138	21.8
	With friends	54	8.5
	Other	32	5.1
Religion	Catholic	329	52.1
	Agnostic	121	19.1
	Atheist	115	18.2
	Other	67	10.6
Economic vulnerability	No	569	90.0
	Yes	46	7.3
	Prefer not to say	16	2.5
City size	Small (≤20,000)	178	28.2
	Medium (20,001–75,000)	206	32.6
	Large (>75,000)	242	38.3
	Not reported	6	0.9

Note. Age statistics include only participants who reported their age (n = 626). Percentages are computed over the full analytic sample (N = 632) and may not sum to 100 due to rounding and missing values for a small number of variables.

2.3. Measures

2.3.1. Sociodemographic Questionnaire

A purpose-built questionnaire collected age, nationality, gender, sexual orientation, racial–ethnic self-identification, marital status, occupation, religion, household composition, and economic vulnerability.

2.3.2. UCLA Loneliness Scale, Version 3 (UCLA-LS v3)

The UCLA-LS v3 [22] (Portuguese version [23]) is a 20-item measure of perceived loneliness, with items rated on a 4-point Likert scale (1 = "never" to 4 = "always"). Total scores range from 20 to 80; higher values indicate greater loneliness, with a theoretical median of 50. The Portuguese validation reports excellent internal consistency (α = 0.91). In the present sample, α = 0.94. In this administration, item 19 was worded in the loneliness direction and scored directly, whereas the validated Portuguese version words this item in the non-lonely direction and reverse-keys it. The scale used here is therefore a slightly adapted version of the Portuguese UCLA-LS v3 rather than the validated instrument in its

exact form, a deviation that qualifies comparisons with the Portuguese validation norm (see Sections 4.4 and 4.5).

2.3.3. Depression, Anxiety and Stress Scale–21 (DASS-21)

The DASS-21 [24] (Portuguese version [25]) comprises 21 items rated on a 4-point Likert scale (0 = "did not apply to me at all" to 3 = "applied to me most of the time"), distributed across three subscales (Depression, Anxiety, Stress). The total score ranges from 0 to 63; higher scores indicate greater psychological distress. In the present sample, $\alpha = 0.95$ for the total score.

2.3.4. Social Isolation Scale (SIS)

The SIS [26] (Portuguese version [27]) comprises six items distributed across two dimensions: Objective Connectedness, indexing the actual frequency of in-person contact with family, friends, and neighbors, and Subjective Sense of Belonging, indexing perceived integration in social ties and community activities. Total scores range from 6 to 36; lower scores indicate greater isolation. The Portuguese validation reports a composite reliability of 0.71 in older adults. In the present sample, internal consistency was $\alpha = 0.75$ for the total score, $\alpha = 0.71$ for the Objective Connectedness subscale, and $\alpha = 0.61$ for the Subjective Sense of Belonging subscale. Because the Subjective Sense of Belonging subscale shares conceptual surface with the loneliness mediator, the Objective Connectedness subscale alone was used as the predictor in a planned sensitivity analysis (see Section 2.5).

2.3.5. Positive and Negative Affect Schedule, Reduced Portuguese Version (PANAS-VRP)

The PANAS-VRP [28] (based on [29,30]) comprises ten items, five for Positive Affect and five for Negative Affect, rated on a 5-point Likert scale (1 = "very slightly or not at all" to 5 = "extremely"). Mean-of-items scoring (range 1 to 5) was used. In the present sample, $\alpha = 0.86$ for Positive Affect and $\alpha = 0.84$ for Negative Affect.

2.4. Procedure and Ethics

The Ethics Committee for Research with Human Subjects of the Graduate Program in Clinical and Health Psychology at the Faculty of Social and Human Sciences, University of Beira Interior, approved the study on 15 October 2024 (approval number CE-UBI-Pj-2024-086-ID2760). The informed consent form appeared on the opening page of the online protocol, and only participants who gave electronic consent continued to the questionnaires. Participation was voluntary and anonymous: the protocol recorded no names or contact details and collected no direct identifiers, so individual responses could not be traced back to participants. The present study is part of a broader research program on social and psychological correlates of mental health; the analyses, sample, and instruments reported here are specific to this article.

2.5. Data Analysis

Analyses were conducted in R 4.5.2 with packages lavaan (mediation, multi-group SEM), and psych (descriptive statistics, internal consistency). E-values for sensitivity to unmeasured confounding were computed with the closed-form approximation of VanderWeele and Ding [31]. The mediation model specified objective social isolation as the predictor (SIS reversed: sis_iso = 36 − SIS_total, so that higher values indicate greater isolation), perceived loneliness as the mediator, and the DASS-21 total score as the outcome. Direct, indirect (a × b), and total effects were estimated by maximum likelihood within a path-analytic decomposition and are reported with unstandardized and standardized coefficients and 95% bootstrap percentile confidence intervals from 5000 resamples. Structural invariance across the three city-size groups was tested by comparing a configural

multi-group model (paths free across groups) with a constrained model (paths equal across groups) using the chi-square difference test, complemented by ΔR^2 estimates of slope heterogeneity and pairwise z tests for individual path differences [32].

Four sensitivity analyses were planned. First, the model was re-estimated with the SIS Objective Connectedness subscale alone as a non-overlapping predictor. Second, a reverse-direction mediation was specified to address the symmetry of cross-sectional decomposition [13,14]. Third, a parallel-mediator model was estimated with loneliness and immediate negative affect as simultaneous mediators of the isolation–distress association. Fourth, the main mediation was re-estimated with sociodemographic covariates (age, gender, education, income, and sexual-minority status) entered on all paths. Two exploratory robustness checks were also conducted: Harman's single-factor test for common method bias [33] and E-values for unmeasured confounding [31]. Bivariate associations among the core variables were summarized by Spearman correlations, given the ordinal nature of the underlying items. The reproducibility seed was 20260430, and the significance level was $\alpha = 0.05$ for two-tailed tests.

3. Results

3.1. Descriptive Statistics and Reliability

Descriptive statistics and internal-consistency estimates are presented in Table 2. Mean perceived loneliness was close to the theoretical midpoint of the UCLA-LS v3, with a small but identifiable proportion of the sample scoring in the elevated range. Distress scores were moderate and skewed toward the lower end of the DASS-21. On the SIS, the observed mean was above the theoretical midpoint, indicating low average objective isolation in this sample (lower scores correspond to greater isolation). Internal consistency was good to excellent for all scales, except the SIS Subjective Sense of Belonging subscale ($\alpha = 0.61$), the marginal value of which is interpreted in the limitations and is the reason for the planned predictor-sensitivity analysis.

Table 2. Descriptive statistics and internal consistency of study variables.

Scale	Items	Range	Theor. Median	M	SD	95% CI	α	% >midpt.
UCLA-LS v3	20	20–80	50	45.87	12.30	[44.91, 46.83]	0.94	36.2
DASS-21 (total)	21	0–63	31.5	21.34	15.02	[20.17, 22.51]	0.95	26.6
SIS (total)	6	6–36	21	26.22	5.98	[25.75, 26.68]	0.75	—
Positive Affect	5	1–5	3	3.53	0.80	[3.46, 3.59]	0.86	72.3
Negative Affect	5	1–5	3	2.60	0.94	[2.53, 2.68]	0.84	29.6

Note. M = mean; SD = standard deviation; 95% CI = 95% confidence interval; α = Cronbach's alpha; % >midpt. = percentage of participants scoring above the theoretical midpoint (mean-of-items metric for affect; raw total otherwise). Lower SIS scores indicate greater objective isolation. Percentages above the theoretical midpoint are reported as descriptive reference points, not validated clinical cutoffs.

3.2. Bivariate Associations

Spearman correlations among the core variables in the full sample are reported in Table 3. Loneliness correlated positively with distress and negative affect, and negatively with positive affect and the SIS total. Because lower SIS scores indicate greater isolation, the negative correlation between loneliness and SIS indicates that greater loneliness was associated with greater objective isolation. The loneliness–SIS correlation was the strongest in the matrix and was the largest single association observed across the three city-size strata in supplementary stratified analyses.

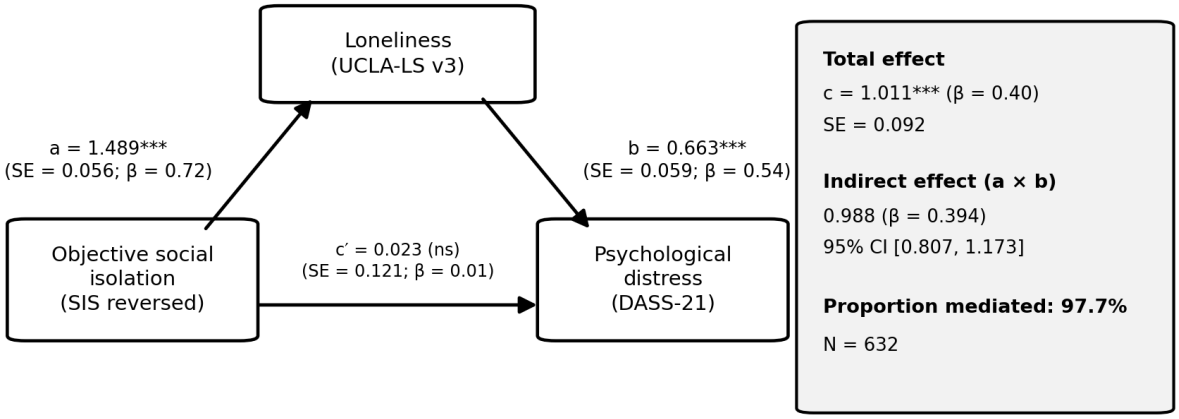
Table 3. Spearman correlations among study variables (N = 632).

Variable	1	2	3	4	5
1. Loneliness (UCLA-LS v3)	—				
2. Distress (DASS-21)	0.56 ***	—			
3. Social Isolation (SIS, total)	−0.71 ***	−0.42 ***	—		
4. Positive Affect	−0.45 ***	−0.37 ***	0.38 ***	—	
5. Negative Affect	0.41 ***	0.66 ***	−0.28 ***	−0.24 ***	—

Note. Lower SIS scores indicate greater objective isolation. *** $p < 0.001$ (two-tailed).

3.3. Mediation Pathway and Structural Invariance

The single-mediator path model decomposed the total effect of objective isolation on distress into a direct path and an indirect path through perceived loneliness (Figure 1). The indirect effect was substantial and statistically nonzero, accounting for nearly all the total association; the direct path was indistinguishable from zero. The pattern is consistent with H1 (full or near-full statistical mediation in the cross-sectional model). Coefficient values, bootstrap confidence intervals, and percentage mediated are reported in Figure 1 and, for reference and the multi-group decomposition, in Table 4.



*Note. Coefficients are unstandardized; β = standardized coefficient. Bootstrap percentile CI from 5,000 resamples. *** $p < 0.001$; ns = not significant.*

Figure 1. Single-mediator path model linking objective social isolation to psychological distress through perceived loneliness (N = 632). Values are unstandardized coefficients with standardized coefficients in parentheses. Bootstrap percentile confidence intervals are based on 5000 resamples. *** $p < 0.001$.

The same mediation structure was estimated separately for the three city-size groups in a configural multi-group model (Table 4). The indirect effect was substantial and statistically nonzero in every group, with overlapping bootstrap confidence intervals and structurally similar coefficient patterns. In the small-city group the percentage mediated exceeded 100% because the direct path was small and opposite in sign to the total effect, a pattern of inconsistent mediation (statistical suppression) rather than an estimation error. The omnibus chi-square difference test for simultaneous invariance of all three structural paths supported invariance, $\Delta\chi^2(6) = 3.11$, $p = 0.795$; pairwise z tests for differences in individual paths returned no significant differences across groups (all $|z| \leq 1.22$, $p \geq 0.221$); and adding city-size interactions to the structural model contributed near-zero variance

(ΔR^2 = 0.0009 for path a, 0.0002 for path b). The mediation structure was statistically equivalent across small, medium, and large cities, supporting H2.

Table 4. Multi-group mediation coefficients by city size (configural model).

Group	*n*	a (β)	b (β)	c′ (β)	a × b	95% CI [LL, UL]	% Mediated
Small city	178	1.575 (0.78)	0.784 (0.64)	−0.250 (−0.10)	1.235	[0.840, 1.666]	125.3
Medium city	206	1.422 (0.70)	0.623 (0.48)	0.065 (0.02)	0.886	[0.586, 1.180]	93.2
Large city	242	1.460 (0.70)	0.639 (0.55)	0.121 (0.05)	0.933	[0.655, 1.216]	88.5
Pooled (full sample)	632	1.489 (0.72)	0.663 (0.54)	0.023 (0.01)	0.988	[0.807, 1.173]	97.7

Note. Path a = effect of objective social isolation (SIS reversed) on loneliness (UCLA-LS v3); path b = effect of loneliness on distress (DASS-21 total), controlling for isolation; path c′ = direct effect of isolation on distress, controlling for loneliness. Standardized coefficients (β) appear in parentheses. 95% CIs for indirect effects are bootstrap percentile intervals (5000 resamples). Omnibus invariance test of the three structural paths: $\Delta\chi^2(6) = 3.11$, $p = 0.795$. Pairwise z tests across groups [32]: all $p \geq 0.221$. ΔR^2 for city-size interactions: 0.0009 (path a), 0.0002 (path b).

Three pre-specified sensitivity analyses tested the robustness of these conclusions. First, because the SIS total combines objective contact frequency with a subjective sense-of-belonging component that overlaps conceptually with the loneliness mediator, the model was re-estimated using only the Objective Connectedness subscale as the predictor. The substantive pattern was preserved: a direct path indistinguishable from zero, a substantial and statistically nonzero indirect effect through loneliness (a × b = 1.117, 95% CI [0.925, 1.315]), and the same structural conclusion. Second, a reverse-direction mediation specifying distress as the predictor and isolation as the outcome also produced a non-trivial indirect effect (a × b = 0.158, 95% CI [0.135, 0.183]). This symmetry is expected from cross-sectional decomposition and does not provide evidence for the reverse direction; it underlines that cross-sectional mediation cannot adjudicate causal direction [13,14], which we revisit in the Discussion. Third, when loneliness and immediate negative affect were specified as parallel mediators, both carried statistically nonzero indirect effects of comparable magnitude (loneliness: a × b = 0.577, 95% CI [0.425, 0.734]; negative affect: a × b = 0.374, 95% CI [0.273, 0.484]). The bootstrap CI for the difference between the two indirect effects was [0.002, 0.400], marginally excluding zero. H3 was therefore supported, though only weakly: loneliness carried an indirect effect at least as large as that of negative affect, and marginally larger; given the narrow margin, the two pathways are best read as comparable in magnitude. Adjusting the main model for age, gender, education, income, and sexual-minority status left the indirect effect essentially unchanged (a × b = 0.982, 95% CI [0.801, 1.168]), as did adjustment of the Objective Connectedness model (a × b = 1.107, 95% CI [0.918, 1.310]). A fully adjusted model that additionally included partnership status (partnered versus unpartnered, collapsed from marital status) and living arrangement, estimated on complete cases (n = 614), also left the indirect effect essentially unchanged (a × b = 0.985, 95% CI [0.799, 1.168]).

3.4. Robustness to Common Method Bias and Unmeasured Confounding

Two exploratory robustness checks supported the substantive conclusions. Harman's single-factor test on the 57 items of the five scales returned a first unrotated factor accounting for 34.0% of the variance, below the conventional concern threshold of 50% [33]; common method bias is unlikely to account for the observed associations. Following VanderWeele and Ding [31], the E-values for the standardized paths of the main mediation model were 3.28 for path a, 2.66 for path b, and 2.24 for the total effect. An unmeasured confounder

would need to be associated with both the exposure and the outcome of each path by risk ratios of these magnitudes, after adjustment for measured covariates, to fully explain away the observed associations, a level of confounding that indicates moderate robustness rather than implausibility.

3.5. Secondary Descriptive Analysis: City-Size Effects on Means

For descriptive completeness, one-way ANOVAs compared mean levels across small, medium, and large cities on each core variable. No statistically significant differences emerged on any of the five outcomes (all $p \geq 0.171$, all $\eta^2 \leq 0.006$). The result complements the multi-group invariance test: city size differentiated neither the means nor the structure of the relations among variables in this sample.

4. Discussion

This study tested three hypotheses about loneliness as a candidate proximal pathway from social isolation to psychological distress in a self-selected, digitally recruited sample of Portuguese adults. We also asked whether the paths of that pathway hold equally across cities of different sizes, and whether loneliness can be empirically distinguished from acute negative affect as a mediator. The sections below place those patterns against the existing literature, asking which converging findings strengthen our reading and which qualify it.

4.1. Loneliness as a Candidate Proximal Pathway

Hawkley and Cacioppo [4] argued that persistent loneliness is the proximal psychological pathway from impoverished social conditions to mental-health symptoms. Two people with the same objective social network can experience very different levels of distress, depending on how they perceive their relationships. Infrequent contact, on its own, need not track mental-health symptoms once we hold the subjective interpretation of those contacts constant. Both claims are testable here.

Our indirect effect is larger than what comparable studies have reported. Wang et al. [34] pooled five prospective cohort studies across 24 countries and found that loneliness mediated only about 5–6% of the link between socioeconomic status and depression in older adults. Santini et al. [10], in a longitudinal NSHAP analysis, reported substantial but partial mediation. Several features of our sample plausibly push the effect upward. The sample skews younger and more educated than the general population, which tends to come with higher psychological literacy and more articulated self-report. Social-media recruitment has also been shown to over-select younger, more educated, and more digitally engaged participants [35], who tend to report more social-cognitive concerns. Two robustness checks held nonetheless: the non-overlapping predictor specification and the common method bias check both supported the original estimate. Because restricting the predictor to objective contact did not reduce the indirect effect, conceptual overlap between the belonging component and loneliness is an unlikely explanation for the near-complete mediation, although shared method variance cannot be fully excluded. The most defensible reading is that, in a digitally engaged Portuguese adult sample, perceived loneliness is the cognitive-evaluative state most strongly associated with the cross-sectional link between self-reported social conditions and self-reported psychological distress; the mediated share is larger here than in older, probability-sampled cohorts using broader social-isolation measures. The magnitude itself, however, should be treated as a finding to be replicated in probability-sampled designs rather than as a pooled population parameter; we frame it as the upper end of plausible cross-sectional estimates given the demographic and methodological profile of this sample.

The clearest longitudinal benchmark for our pattern is Santini et al. [10], who used three waves of the National Social Life, Health, and Aging Project to document bidirectional pathways between social disconnectedness and depression. Perceived isolation carried a substantial mediating role. The bidirectionality is informative: loneliness predicts later depression and anxiety, but depression and anxiety also predict later loneliness. Misiak et al. [36], using a cross-lagged panel network of Polish adults assessed about seven months apart, confirmed that the longitudinal architecture is bidirectional rather than unidirectional, and that emotional loneliness in particular shows the strongest reciprocal links with distress. Our cross-sectional model cannot adjudicate between unidirectional and bidirectional accounts. What it adds is a robustly estimated atemporal association in a Portuguese sample, plus evidence that the pattern survives sensitivity tests that longitudinal benchmarks do not always implement.

Recent biological evidence converges on the same logic. Shen et al. [3] identified plasma proteomic signatures linking both isolation and loneliness to inflammation, cardiovascular disease, type 2 diabetes, and mortality. Their Mendelian-randomization analyses provided causal evidence for several of those proteins specifically through loneliness rather than through isolation. The clinical implication is testable. Programs targeting only the quantity of social interaction tend to produce smaller effects than programs that address relational quality and social cognition [11,37], though reviews of psychological interventions also report heterogeneous effects, definitional inconsistency, and limited evidence on long-term outcomes [37]; our cross-sectional pattern is consistent with, but cannot establish, the value of targeting the loneliness construct. Cognitive-behavioral approaches that restructure social-information-processing biases [8] target the construct that carries the cross-sectional indirect effect. Whether they do so with the predicted impact on distress is a question for randomized trials.

4.2. Loneliness and Negative Affect as Parallel Pathways

The third hypothesis used negative affect as a comparison mediator. If loneliness is the proximal cognitive-evaluative pathway described by Cacioppo and Hawkley [7], its indirect effect should exceed that of more immediate affective reactivity. The prediction received only partial support, and the rough equivalence of the two pathways is open to two readings that are not mutually exclusive.

The first interpretation accepts that the two constructs share substantial conceptual variance. The UCLA-LS v3 captures both the cognitive evaluation that one's social ties are inadequate and the affective reaction to that evaluation. The PANAS Negative Affect subscale captures negative-valence affect that is partly a consequence and partly a cause of that cognitive evaluation. Vanhalst et al. [38] showed empirically that uncontrollable rumination both mediates and moderates the loneliness–depression link, and that ruminative processes are themselves part of the cognitive architecture of negative affect. Within that architecture, expecting one mediator to dominate the other in a single cross-sectional decomposition may be theoretically optimistic. Cacioppo and Hawkley's [7] framework treats negative affect as downstream of the loneliness state, not as a parallel mediator, so the rough equivalence we observe is theoretically informative even when not statistically distinguishable. A second interpretation appeals to measurement structure. The UCLA-LS v3 captures global, trait-like loneliness, whereas the PANAS Negative Affect subscale references the past week. The two mediators, therefore, index different temporal windows, and what looks like equal mediating influence may be a composite of slow- and fast-moving affective signals that, together, account for the cross-sectional association. The distress outcome and the negative-affect mediator also overlap empirically (Pearson r = 0.67 in this sample), which further limits how sharply a cross-sectional decomposition can separate the

two indirect paths. A third interpretation, which we cannot rule out, is that our sample's relatively low mean negative affect compresses the variance available to differentiate the two pathways. Whatever the right reading, the breadth of pathways implied here suggests that interventions targeting only acute negative affect would leave the loneliness-related component of the distress association untouched, even though our data do not establish loneliness as the dominant pathway.

4.3. Structural Invariance Across Urban Contexts

The absence of city-size moderation admits two readings of equal weight, which are not mutually exclusive.

The substantive reading is that the loneliness pathway is structurally similar within the Portuguese urbanization gradient. That gradient is comparatively compressed: the "large" stratum (>75,000 inhabitants) is small by international standards, and Portugal lacks the density extremes of multi-million-inhabitant cities. The recent literature on rural–urban differences in loneliness is mixed and supports this reading more than it contradicts it. Keller et al. [18], pooling 69,136 individuals across Danish, French, and UK cohorts during the first pandemic wave, found no association between rural-versus-urban residence and loneliness (odds ratio = 1.06, 95% CI [0.81, 1.38]). Studies that do find a difference report effects that are heterogeneous in direction: urban residents show higher loneliness in some samples, rural residents in others, and the moderating role of loneliness on other outcomes also varies. This is what one would expect if population size were a coarse proxy for the contextual features that matter (neighborhood cohesion, residential duration, public-space quality, social capital), and if those features did not vary systematically with city size. A synthesis of 112 studies similarly reports that subjective neighborhood characteristics, such as cohesion, feeling connected, and neighbor interactions, show stronger and more consistent associations with loneliness than objective or population-size indicators [19]. Hammoud et al. [15], using ecological momentary assessment, made a closely related point: it is overcrowding in the immediate environment, rather than population density at the city level, that predicts moment-to-moment loneliness. Ochnik et al. [16] and the network analyses of van der Wal et al. [17] point in the same direction, identifying granular contextual variables as more promising candidates than crude population-size indicators.

The methodological reading is that path-level moderation tests have inherently lower statistical power than main-effect tests, and small interaction effects could escape detection at this sample size. This reading is genuine, but it is bounded by our finding that the magnitude of heterogeneity was virtually zero. Power affects the detectability of an effect, not its observed magnitude: a power-limited test would have produced a non-significant result with a non-trivial point estimate, whereas ours produced a non-significant result with a near-zero point estimate. Combining both readings, the most defensible conclusion is that within the Portuguese urbanization gradient and at the operationalization we used, urban-size calibration is unlikely to yield substantive gains in population intervention design. We therefore read the null as a negative finding under a population-threshold operationalization, not as evidence that social context is irrelevant to loneliness. Future work that directly measures the contextual features identified by Hammoud et al. and Ochnik et al. would have a better chance of detecting environmental moderators than would a population-size threshold scheme.

4.4. Mean Loneliness Above the 2019 Reference Value

Mean perceived loneliness in this digitally recruited sample was about one-third of a standard deviation above the pooled mean of the Portuguese 2019 validation sample [23].

Three plausible contributors merit consideration. The first is a generational effect. Rebechi et al. [39] tracked five European countries through the pandemic and into the post-acute phase and found that young adults were the most severely affected by loneliness elevations, which have stabilized rather than reverted to pre-pandemic levels. Our sample skews younger than the Portuguese adult population mean, which would produce a higher central tendency on this measure even with no demographic differences from the validation sample. The second is selection from online recruitment. Social-media recruitment in mental-health research has documented systematic selection bias toward younger, more educated, and more digitally engaged individuals [35]; given that those characteristics correlate with reported loneliness in post-pandemic European data, our sample is plausibly enriched for higher loneliness on demographic grounds alone. The third is methodological: the 2019 reference value comes from a psychometric validation sample (the data were collected in 2019 and published in 2023 [23]), not a probability-based national norm, and the comparison between non-equivalent samples cannot adjudicate population-level shifts. The comparison is further qualified by the instrument itself: because item 19 was administered in an adapted form (Section 2.3.2), the total score derives from a slightly adapted version of the Portuguese UCLA-LS v3, and the contrast with the 2019 reference value should be read as approximate rather than exact.

These caveats notwithstanding, the absolute level we observe is substantively meaningful. Within Europe, loneliness is more prevalent in Southern and Eastern countries [1,12]. What survives is that loneliness in our sample is non-trivial and consistent with a European pattern that public-health policy is treating as durable rather than transient.

4.5. Limitations

Seven limitations require explicit discussion. First, the cross-sectional design does not permit causal inference. Maxwell and Cole [13] and Maxwell et al. [14] showed formally that cross-sectional mediation estimates can be substantially biased relative to longitudinal parameters, including in directions opposite to the true longitudinal effect. The reverse-direction model fitted here illustrates this symmetry: a reverse pathway from distress through loneliness to isolation also produced a non-trivial indirect effect. Our framing of the model as isolation → loneliness → distress is grounded in the longitudinal evidence base [9,10], not in the cross-sectional fit itself, and our estimates should be read as atemporal associations rather than as evidence of mechanism.

Second, the sample was recruited online through social-media networks and over-represents women, participants with higher education, and heterosexual individuals, with the great majority reporting no economic vulnerability (Table 1). All measures were self-report rather than behavioral observation, and the constructs labeled here as "objective social isolation" and "psychological distress" are likewise self-reported indicators of those constructs. In addition, the UCLA-LS v3 yields a single global score; the appraisal, emotional, and relational processes implied by the cognitive discrepancy model were not measured separately and remain unmeasured dimensions in this design. Generalization to older adults, individuals with low digital literacy, men, sexual minorities, or economically vulnerable groups is limited. Findings should be interpreted as describing digitally engaged Portuguese adults with the demographic profile of the sample, not the Portuguese adult population at large.

Third, the SIS Subjective Sense of Belonging subscale showed only marginal internal consistency (Table 2). Two factors plausibly contributed: the subscale is short (three items), and the Portuguese validation sample comprised older adults rather than the broader age range here. The planned sensitivity analysis using the Objective Connectedness subscale alone partially addresses this concern, but our operationalization of objective

contact remains specific to the SIS. Fourth, the mediation was robust to adjustment for the available sociodemographic covariates (age, gender, education, income, and sexual-minority status); partnership status and living arrangement were additionally entered in a fully adjusted model (Section 3.3), which left the indirect effect essentially unchanged, although residual confounding by other unmeasured factors cannot be excluded. Fifth, the study was not pre-registered. We have distinguished pre-specified primary and secondary analyses (mediation, multi-group, predictor sensitivity, reverse-direction, parallel mediator) from exploratory analyses (common method bias, E-values), but the analytic plan was developed concurrently with the dataset, and this distinction is post hoc. Sixth, urban size was operationalized by population thresholds; contextual features such as social cohesion, residential duration, and public-space quality were not directly measured, and the moderation null reported here applies specifically to the population-size operationalization. Because the de-identified analytic dataset does not retain municipality identifiers, the classification could not be re-mapped onto the Eurostat degree-of-urbanization typology.

Seventh, item 19 of the UCLA-LS v3 was administered in an adapted form: its wording was presented in the loneliness direction and the item was scored directly, whereas the validated Portuguese version words this item in the non-lonely direction and reverse-keys it. The loneliness measure used here is therefore a slightly adapted version of the validated Portuguese instrument. To gauge the psychometric consequences of this adaptation, internal consistency was recomputed excluding item 19 ($\alpha = 0.93$, compared with 0.94 for the full scale), and the main mediation model was re-estimated with the 19-item loneliness total, which left the substantive conclusion unchanged ($a \times b = 0.978$, 95% CI [0.798, 1.162]). The adaptation does not affect the internal logic of the mediation analyses, which operate on the observed scores, but it limits the comparability of the sample mean with the Portuguese normative value, and the comparison in Section 4.4 should be read with this qualification.

4.6. Future Directions

Four priorities follow from these findings. The first is a pre-registered longitudinal replication. A three-wave design (per Maxwell and Cole's recommendations), drawn from a probability-based Portuguese adult sample, would test the temporal sequencing implied by the mediation model and discriminate between the unidirectional and bidirectional accounts that cross-sectional decomposition cannot adjudicate. A longitudinal design would also distinguish transient from persistent loneliness, a distinction with prognostic weight, since it is chronic rather than momentary loneliness that most consistently forecasts later depressive symptoms [9]. The second is an experimental test. Pre-registered randomized trials of loneliness-targeted interventions, such as internet-based cognitive-behavioral therapy [40] and social-cognitive retraining aimed at maladaptive social-information-processing biases [8], would provide stronger causal evidence than any correlational mediation can. The third is a finer contextual measurement. Direct assessment of neighborhood cohesion, residential duration, perceived community support, and momentary overcrowding [15,16] is more likely to identify environmental moderators than population-size thresholds alone. The fourth is integration with biological and behavioral markers. The proteomic signatures identified by Shen et al. [3], wearable-derived activity and sleep data, and ecological momentary assessment of social interactions can collectively position loneliness as a phenotype that bridges psychological measurement and physiological consequence.

5. Conclusions

In a cross-sectional self-report study of self-selected, digitally recruited Portuguese adults, perceived loneliness was the cognitive-evaluative state most strongly associated

with the cross-sectional link between social isolation and psychological distress. The pattern was structurally similar across the urbanization gradient sampled and held up against several methodological challenges that typically threaten cross-sectional mediation models. Loneliness and acute negative effect operated as comparable parallel pathways rather than as a single dominant mediator; the equivalence qualifies without contradicting the cognitive-pathway framework, since Cacioppo and Hawkley's account places negative affect downstream of the loneliness state, not in parallel with it. Mean loneliness in this sample sits non-trivially above the 2019 Portuguese reference value, a comparison qualified by the adapted administration of item 19 (Section 4.5), and aligns with European trend data describing post-pandemic elevations that have stabilized rather than reverted. The pattern is consistent with loneliness as a candidate intervention target in this sample, but the cross-sectional design limits causal inference, and pre-registered longitudinal and experimental work is needed before the pathway can be claimed as mechanistic.

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