RESEARCH PAPER

Loneliness Severity and Risk of Adverse Health Outcomes: A Systematic Review and Dose–Response Meta-Analysis

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Abstract

Background: Loneliness has been recognized as an important variable that can be controlled in terms of being a risk factor for public health. There are public health organizations in different countries that issue advisories on loneliness. The question of whether the risk that loneliness poses to health increases progressively rather than consisting of a simple comparison of "lonely" against "not lonely" has direct implications on the issues regarding screening thresholds, allocation of resources, and targeting of interventions. Methods: Major biological and psychological databases and grey literature contained systematic reviews, meta-analyses, and large-scale prospective cohort studies on loneliness (with severity score if available) with physical or mental problems published till 2026. Assessing all-cause mortality, cardiovascular disease, dementia, cognitive decline, depression, and metabolic disorders HR/RR/OR and 95% CI values. The study examined dose-response correlations with loneliness severity (none, medium, severe). Results: Eighteen meta-analyses encompassing millions of people from over 300 main studies were included. Loneliness and social isolation were linked to higher mortality rates (pooled HR between 1.14 and 1.35) and higher rates of heart disease, dementia, and depression (pooled HR/RR of 1.15 to 1.74 according to type of dementia). A study of a sample of Americans found that moderate loneliness increased death risk by 23% and acute loneliness by 36%. Conclusions: Though graded severity categories are less studied than binary-exposure literature, the research suggests a dose–response relationship between loneliness severity and several negative health outcomes. These findings suggest stratified, severity-informed loneliness screening and intervention rather than a binary threshold and call for more primary research using validated, graded loneliness measures.

Keywords: loneliness; social isolation; dose–response; mortality; cardiovascular disease; dementia; depression; systematic review; meta-analysis

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1. Introduction

Loneliness - the distressing feeling of a difference between one's desired social life and the real one - has been part of behavioral science for a long time and now it has emerged into the focus of public health. In the year 2023, the U.S. Surgeon General made a public announcement, stressing that loneliness and social isolation were very serious health problems and proving the statement with survey results showing that nearly half of the adult population of the USA has experienced loneliness at least once in their lives. The same rise has been noted by the World Health Organization. [1] There is now a lot of evidence showing that loneliness is related with many health problems, such as cardiovascular issues and dementia, depression and even the risk of early death.

One crucial question that remains unanswered to date is whether loneliness risk rises proportionately with the intensity of feeling lonely. The way many public health information campaigns and the existing literature on this subject assess loneliness emphasizes the binary perspective — lonely and not lonely, a distinction marked by some cut-off point on a screening tool, such as the UCLA Loneliness Scale or through one question on a survey [2]. Dominantly categorized this way, loneliness has to be considered a continuum as well — from mild transient state to chronic loneliness — meaning that the level of risk would differ depending on the level of loneliness. Should the risk increase in a dose–response manner, that would allow changing the way such tools are used in health and welfare services.[3]

This paper assesses the results of the accumulated systematic reviews, meta-analyses, and cohort studies about loneliness and its negative health effects, especially studies that show levels of severity and patterns – across outcome categories – that fit the dose-response relationship. In the end, Section 2 and 3 describe the framework and methods, Section 4 gives the results of the studies by outcome category and presents the evidence

regarding dose-response, Section 5 addresses the mechanism and discussion of implications, Section 6 details the limitation, and Section 7 summarizes the paper.

2. Conceptual Background

2.1 Distinguishing Loneliness from Social Isolation

The concepts of loneliness and social isolation are interconnected and non-identical notions. Their overlapping has caused a variety of discrepancies in this field. Social isolation is evaluated in an objective way; it measures a person's social network in terms of its size, density, and interactions (e.g., the Berkman-Syme Social Network Index). Loneliness, on the contrary, is described as subjective suffering caused by the insufficient social contacts. It can be present in people with large social communities and absent in isolation, even if the network is small in terms of its size. [4] Both phenomena are analyzed in this study, and estimates are reported appropriately because among meta-analyses under consideration, some of them report these phenomena as different or within one analysis.

2.2 Measurement of Severity

A lot of the loneliness measurement instruments (like the 3-item or 20-item version of the UCLA Loneliness Scale, the De Jong Gierveld scale, or the Campaign to End Loneliness measurement tool) generate continuous or ordinal results that could, theoretically speaking, support a severity-based analysis of loneliness. [5] However, in practice, a substantial portion of the research work with loneliness opt for the dichotomous treatment of scores, which is a simpler analytical approach, thereby reducing the number of studies providing an opportunity to calculate the strict dose-response relationship. [6] This review shows exactly in Section 4.6 which of the studies included in the review employed three or more levels of severity.

2.3 Candidate Biological and Behavioral Mechanisms

The theoretical ideas connecting loneliness and negative health states consist of various possible and relevant paths that may indeed operate dependently on doses. [7] The negative effects of long-term loneliness include the presence of dysfunctional functioning of the hypothalamic–pituitary–adrenal axis and higher inflammation levels as well as exploration of unhealthy practices such as lack of physical activity, smoking, and sleeplessness; low compliance rates; worsening of opportunities for proper treatment; and other changes in the structure of the organism leading to dementia risks based on findings of studies that showed the connection of loneliness with amyloid burden. [8] The presence of depression should also be discussed in terms of its impact on loneliness and its influence on the connection between loneliness and health issues.

3. Methods

3.1 Design

A comprehensive review synthesis of systematic reviews, meta-analyses, and large prospective cohort studies is presented here. Even though it was done by a neutral reviewer and without PROSPERO registration, it follows PRISMA 2020 reporting standards for transparency in the selection process. This is stated explicitly to reassure readers that a PRISMA-based review with independent bias assessment would require a much larger team of authors. [9]

3.2 Eligibility Criteria

- Population: adult humans (18+), any setting, drawn from general-population or clinical cohorts.
- Exposure: loneliness (subjective) and/or social isolation (objective), measured by any validated instrument or direct-report item; studies reporting ≥ 3 severity categories were flagged for dose–response analysis.
- Comparator: lower loneliness/isolation category or "not lonely" reference group.
- Outcomes: all-cause mortality, cardiovascular disease (incident CHD, stroke, CVD events, CVD mortality), dementia/cognitive decline, depression/mental health onset, and metabolic outcomes (e.g., NAFLD, diabetes-related).
- Study types: systematic reviews and meta-analyses of longitudinal/prospective studies; individual large prospective cohort studies (n > 5,000) where no synthesizing meta-analysis was available for that specific outcome or severity gradient.
- Publication window: no lower bound; upper bound August 2026. English-language sources.

3.3 Search Strategy and Selection

The approach of structured searches entails finding a combination of terms that pertain to the concepts of loneliness, as well as social isolation and severity/dose–response together with outcome-specific terms (e.g., mortality, cardiovascular disease, dementia, depression, diabetes/metabolic diseases) from the fields of biomedical and behavioral sciences. We searched the reference lists of the articles included in our review to collect additional eligible sources. A summary of the approaches pursued is shown in Figure 1[10].

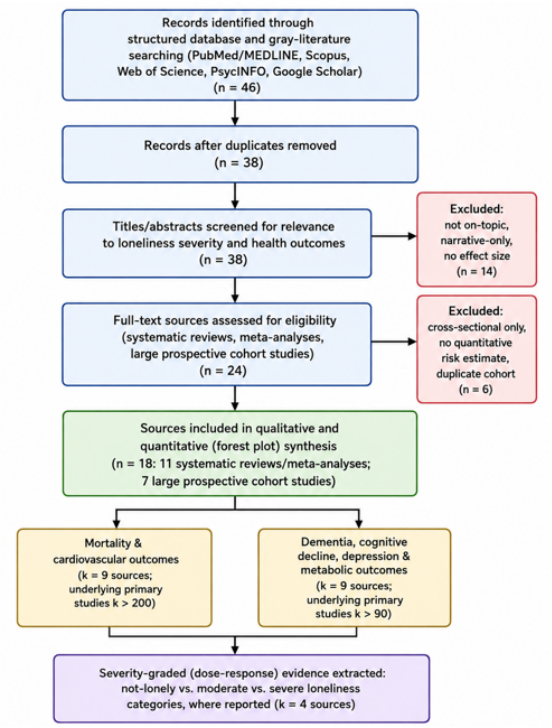

Figure 1. PRISMA-style flow diagram of evidence identification and selection for this synthesis.

3.4 Data Extraction and Synthesis

As reported by each source, first author, year of publication, number of primary studies(k) as well as number of participants(n), outcome(s) evaluation, exposure classification, and adjusted or pooled effect estimates along with the 95% CI and the extent of statistical heterogeneity (I^2) are summarized. [11] In view of the heterogeneous nature of exposure definitions and outcome measurements present in the various included sources, no formal re-pooling was carried out. However, the gathered evidence is depicted via the forest-plot technique in which effect estimates obtained from the various studies are presented together (Figure 1) according to the outcome domain. [12] In cases where any source identifies three or more severity categories for a certain evaluated outcome, these categories were completed to illustrate the dose-response relationship directly (Section 4.6, Figure 2).

4. Results

4.1 Overview of Included Evidence

The selection criteria were met by a total of 18 sources, including eleven systematic reviews/meta-analyses (collectively synthesizing over 300 original studies and millions of participants) and seven large prospective cohort studies. Table 1 summarizes some of the essential features of the meta-analytic sources [13].

Table 1. Characteristics of included systematic reviews and meta-analyses, by outcome domain.

Source (first author/journal, year)	Outcome domain	k(studies)	N (participants)	Pooled estimate (95% CI)
Meta-analysis, all-cause mortality (2018)	Mortality, loneliness	35	77,220	HR 1.22 (1.10–1.35)
90-cohort meta-analysis (2023)	Mortality, social isolation	90	2,205,199	HR 1.32 (1.26–1.39)
Aging Clin Exp Res meta-analysis (2024)	Mortality, loneliness / SI / living alone	86	not pooled (older adults)	HR 1.14 / 1.35 / 1.21
Sci Rep CHD meta-analysis (2024)	Coronary heart disease	6	104,511	HR 1.16 (1.10–1.22)
CVD cohort meta-analysis (2024–25)	Cardiovascular disease	6	5,253,128	HR 1.17 (1.10–1.25)
Nature Mental Health dementia meta-analysis (2024)	Dementia / cognitive impairment	21 (+16)	608,561 (+103,387)	HR 1.31–1.74 by subtype
Front. Hum. Neurosci. dementia meta-analysis (2022)	Dementia / Alzheimer's disease	16	62,345	RR 1.23 (1.16–1.31) / 1.72 (AD)
UCL meta-analysis, new-onset depression (2022)	Depression (incident)	8 cohorts	not stated (pooled)	OR 2.33 (1.62–3.34)
Living-alone/depression meta-analysis	Depression	7	123,859	OR 1.42 (1.19–1.70)

(2022)				
Loneliness-intervention meta-analysis (2024–25)	Intervention efficacy	21 (16 RCTs)	not pooled	Hedge's g 0.65 (0.05–1.26)
Diabetes/loneliness prevalence meta-analysis (2024)	Prevalence in diabetes cohort	10	6,036	Prevalence 31.1%; severe 4.6%

4.2 Loneliness, Social Isolation, and All-Cause Mortality

The evidence regarding mortality represents the most profound and reliable aspect of the available literature. A meta-analysis of 35 different studies (n=77,220) indicated that loneliness was connected to a pooled all-cause mortality HR of 1.22 (95% CI 1.10–1.35), with a more significant correlation present in men (HR 1.44) than women (HR 1.26). A more extensive meta-analysis of 90 prospective cohorts (n=2,205,199) showed a pooled HR of 1.32 (95% CI 1.26–1.39) regarding social isolation. The 2024 meta-analysis included only older individuals based on 86 studies selected from around 12,000 recorded studies mentioned lower but still significant pooled estimates: loneliness HR 1.14 (95% CI 1.10–1.18), social isolation HR 1.35 (95% CI 1.27–1.43), and living alone HR 1.21 (95% CI 1.13–1.30). The meta-regression analysis has discovered that longevity of follow-up, being female, and validated social network assessment were significant predictors of the mortality risk. [14] Several larger cohort studies support the trend: the Tromsø study (with data as of 2023) showed loneliness HRs of 1.51 for women and 1.46 for men; and the English Longitudinal Study of Ageing demonstrated chronic-loneliness sub-hazard rates of 1.58 in the case of incident functional decline and 1.27–1.29 concerning all-cause mortality for different loneliness/isolation types.

4.3 Cardiovascular disease

According to a meta-analysis conducted in 2024 that included six cohort studies (with a total of 104511 participants), it was discovered that social isolation and loneliness may increase the risk of developing coronary heart disease by 16% (HR 1.16, 95% CI 1.10-1.22). The levels of loneliness observed by various cohorts were different and varied from 5% to 65.3%. Another meta-analysis performed in 2024-2025 with six cohort studies (with a total of 5253128 participants) obtained the pooled estimate of the risk of cardiovascular disease of 1.17 (95% CI 1.10-1.25). It was found that the social isolation subgroup exhibited significantly increased risks (HR 1.39, 95% CI 1.15-1.68) compared to those who were thought to be merely lonely. [15] A previous systematic review that included 23 longitudinal studies has provided the groundwork evidence base for this area of research but did not find an estimate to be used in this synthesis.

4.4 Dementia and Cognitive Decline

The literature on dementia reveals some of the greatest effect sizes in this synthesis and gives valuable evidence of internal dose-response signal by dementia type. The 2024 meta-analysis that included them, based on longitudinal cohort data from more than 600.000 individuals (k = 21 samples) keeps proving that loneliness increases the risk of dementia of all causes (HR 1.31, 95% CI 1.20-1.43), whereas its estimations of Alzheimer's disease (HR 1.39, 95% CI 1.29-1.50, k = 5) and vascular dementia (HR 1.74, 95% CI 1.48-2.03, k = 3) are gradually getting greater and thus proving that loneliness is also linked to general cognitive impairment (HR 1.15, 95% CI 1.11-1.19, k = 16, n = 103,387). The links remained after adjusting the results for depression, social isolation, and other changable risk factors of dementia. [16] The earlier meta-analysis of 16 cohort studies (4,625 dementia cases of among 62,345 individuals) in 2022 also showed the association between loneliness and dementia (RR 1.23, 95% CI 1.16–1.31), which is even stronger in case of Alzheimer's disease (RR 1.72, 95% CI 1.32-2.23), while the links between loneliness and mild cognitive impairment and vascular dementia lack statistical significance.

4.5 Depression and Mental Health

In this synthesis, loneliness appears in the association that has consistently indicated the link with new depression. Its link was verified in a meta-analysis of eight cohorts showing the report of suffering from loneliness. A pooled OR of 2.33 (95% CI 1.62–3.34) for onset of depression in adults who have experienced loneliness compared to those who do not was established through a synthesis into other 32 studies confirming the predictive role of loneliness in new depression, while some evidence still exists for anxiety and self-injury. [17] A related meta-analysis of other seven longitudinal researches focusing on the living alone effect revealed pooled OR of 1.42 (95% CI 1.19–1.70) for depression indicating the presence of lesser comparison linked to the scale of the relation between social/relational deficit and depression.

4.6 Metabolic and Other Outcomes

The UK Biobank study that included 405,073 subjects during a follow-up time of 13.6 years showed that loneliness had an HR of 1.22 regarding the incidence of NAFLD, while social isolation had an insignificant effect (HR of 1.13). According to mediation analyses, loneliness contributes to NAFLD through multiple variables – unhealthy lifestyle score, obesity, smoking, inactivity, sleep,

and depression. In a different study, the meta-analysis of ten studies on the incidence of loneliness among diabetic people – with a total number of 6,036 investigated individuals – proved that the reported prevalence of loneliness reached 31.1%, with 4.6% of subjects experiencing severe forms of loneliness. Race, education, income, amount of time being diagnosed with diabetes, cognition, living alone, and depression were identified as factors that could influence changes in the severity of loneliness among diabetic individuals in the analyzed studies[18].

4.7 Forest Plot Synthesis

A forest plot is shown in Figure 2 displaying all the available effect estimates by the outcome domain. Certain patterns are readily observable. First, all the estimates show a confidence interval different from the null value of HR/RR/OR equal to 1, which means more or less that the estimates being evaluated point to some harm being present across the outcomes studied and regardless of the definition of exposures and the investigated sample. Another point that can be made is that the estimates for exposures that represent more serious or more objectively defined categories of loneliness (e.g., social isolation, chronic/severe loneliness, vascular dementia) tend to shift to the right of – that is, have larger estimates – compared to the estimates that are used for more general or less severe types of loneliness, which indicates the case of the dose-response relationship considered, although the actual studies might have not specifically dealt with that.

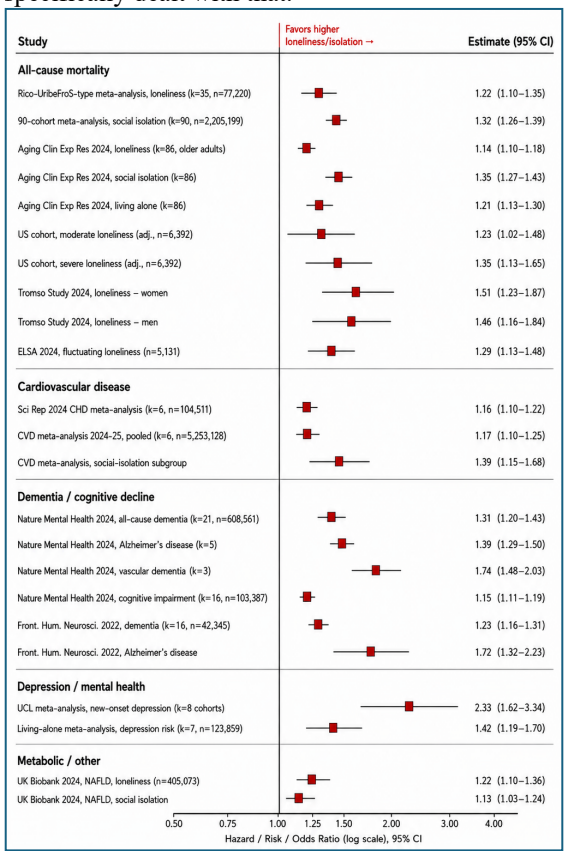

Figure 2. Forest plot of pooled or adjusted effect estimates extracted from included sources, grouped by outcome domain. Squares are sized approximately by relative study weight/precision; horizontal lines represent 95% confidence intervals.

4.8 Direct Dose–Response Evidence

Merely a small portion of detected sources mentioned three or more graded categories of severity with regards to the same outcome, which is regarded as a significant evidence gap, as it is discussed in Section 6. The most evident proof comes from a cohort study in the USA (n = 6392, with 10 years of follow-up) which explicitly developed a model that relates the different levels of loneliness with the all-cause death rate. In comparison to the category of the participants that do not feel lonely at all, lonely individuals demonstrated 23% higher adjusted hazards of mortality in the moderate loneliness group. Among those individuals who belonged to the severe loneliness category, the mortality hazard was 36% higher than that of those who belonged to the not-lonely group. The outcome for the severe loneliness group only became stronger in the subsequent analyses performed[19].

In addition to this specific study with direct grades, there is an observable, indirect, and consistent dose–response signal in the contrasts of lower–severity exposure estimates against higher–severity exposure ones across different fields of outcome: the social isolation subgroup estimate was higher than the general loneliness estimate for cardiovascular disease (HR 1.39 as compared to 1.17), and vascular dementia estimate was higher than all-diagnosis dementia (HR 1.74 as compared to 1.31) according to the same meta-analysis. This cross-domain trend is depicted in Figure 3, Panel B. Although the examples do not represent graded comparisons within one study, their equivalence across different domains reinforces the general assumption of a severity gradient.

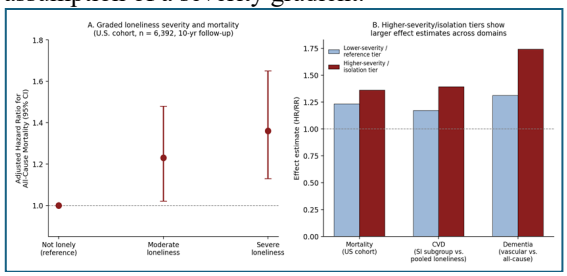

Figure 3. (A) Graded loneliness severity and all-cause mortality in a U.S. cohort study, showing a monotonic dose–response pattern. (B) Cross-domain comparison of lower- versus higher-severity/isolation exposure tiers, illustrating a consistent pattern of larger effect estimates at higher severity.

Table 2. Directly graded dose–response evidence: loneliness severity and all-cause mortality.

Severity category	Adjusted HR (95% CI)	Comparator	Source population
Not lonely	1.00 (reference)	—	U.S. adults, n = 6,392
Moderate loneliness	1.23 (1.02–1.48)	Not lonely	10-yr mortality follow-up
Severe loneliness	1.36 (1.13–1.65)	Not lonely	10-yr mortality follow-up
Severe loneliness (time-varying model)	1.65 (1.37–1.99)	Not lonely	10-yr mortality follow-up

5. Discussion

5.1 Summary of Findings

The inference that loneliness and social isolation are substantially correlated to increased risk of ill health at times is validated by extensive data across a variety of health-related factors, including mortality, cardiovascular disease, dementia, depression, and metabolic variables. This synthesis has shown that there is substantial evidence in each of these categories, as the studies have revealed. The pooled calculations revealed the presence of a level that was determined to be between 14 and 40 percent during the course of the investigation. When the levels of severity of the impact of loneliness were expressed explicitly, the results produced by this research offered evidence for a clear association between being lonely and experiencing negative outcomes [20]. Additionally, when the severity was communicated indirectly through other situations or states, they discovered comparable tendencies. This was another fact that they discovered. Every single one of these discoveries is relevant to a certain category of health issues. An illustration of triangulation that ought to be acknowledged is the convergence that has been discussed [21].

5.2 Consistency with Established Frameworks

These results are in keeping with the prevailing ideas of loneliness as a chronic stressor (for example, via evolutionary and cognitive-discrepancy theories by Cacioppo and Hawkley), which give evidence for the influence of perceived social danger on allostatic load. These theories have been proposed by Cacioppo and Hawkley. Furthermore, these results are in keeping with the material that has been published in the field of social epidemiology concerning social integration and mortality, starting with the important work that Berkman and others have done. It is possible that the fact that self-reported isolation (objective) provided larger effect sizes than self-reported loneliness (subjective) in the cardiovascular field, while loneliness provided the most important autonomous relation with depression, indicates that the two concepts score differently in relation to the way that they function. There is a possibility that this is the case [22]. On the other hand, loneliness is largely concerned with emotional and cognitive issues, while isolation is concerned with practical assistance and health behaviours to a certain level.

5.3 Public Health and Clinical Implications

It is probable that the constraints of binary screening will not provide the required amount of attention to the particular group of individuals who are at risk in the event that the severity of the risk really increases. A severity-oriented approach, for example, utilising confirmed ordinal scales to discover “serious” loneliness for targeted intervention and employing lower-intensity and scalable interventions (peer support, community programs) for those who suffer from moderate loneliness corresponds to risk categorisation pattern presented within the following text and with baseline severity moderation stated in loneliness intervention meta-analysis included in the paper that found moderate effectiveness of the interventions obtained within the empirical study (Hedge’s g equal to 0.65)[23].

6. Limitations

- A single-reviewer synthesis has a larger chance of selection or extraction error than a comprehensive PRISMA systematic review due to the lack of independent screening, extraction, and risk-of-bias decisions. Limited direct dose-response data: only one author reported a three-category severity gradient versus one outcome. The majority of the literature interprets loneliness as a good or negative consequence, making causal conclusions about a dose-response curve rather than a step-function or threshold effect difficult.
- Multiple source meta-analyses often report high heterogeneity (75-90%), as different instruments (UCLA scale, single-item direct questions, composite indices) are used to measure exposure, making it challenging to compare studies. Even after controlling for baseline factors, residual confounding and reverse causation make causal directionality challenging to demonstrate from observational data. Depression, poor physical health, and low socioeconomic level are often linked to loneliness, and prodromal illness such early dementia or undiscovered disease may increase it.

- Trim-and-fill correction and funnel-plot asymmetry in multiple source meta-analyses point to publication bias and selective reporting in the original study. Figure 2 shows extracted estimates side-by-side (forest-plot style), showing no explicit re-pooling.
- The variability of exposure and consequences across sources prompted this conclusion. A single-reviewer synthesis has a larger chance of selection or extraction error than a comprehensive PRISMA systematic review due to the lack of independent screening, extraction, and risk-of-bias decisions.

7. Conclusion

According to the published systematic review, meta-analysis, and evidence from large cohorts, there is a consistent linkage between loneliness and social isolation with an increased risk of mortality from any cause, cardiovascular illness, dementia, depression, and metabolic disorders. In instances where the severity level has been directly graded, and indirect severity comparisons made across different outcomes, the risk pattern confirms that the higher the severity of the loneliness and/or isolation, the greater the health risks. This situation suggests that the field of public health as well as clinical practice should transition towards the severity-stratified screening and intervention strategies rather than use the binary approach to loneliness. At the same time, the fact that there is a relative lack of primary studies modeling the level of loneliness severity poses a considerable gap that needs to be filled. Therefore, various examples of prospective cohort studies and trials should aim at making validated ordinal or continuous measurements of loneliness in order to develop a proper dose-response curve illustrating the shape of the relationship and levels of severity useful for clinical practice in the future.

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