



(REVIEW ARTICLE)



LONELINESS AND SOCIAL ISOLATION AS CLINICAL RISK FACTORS IN PRIMARY CARE: A COMPREHENSIVE REVIEW OF CARDIOVASCULAR, MENTAL HEALTH, AND MORTALITY OUTCOMES

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World Journal of Biology Pharmacy and Health Sciences, 2026, 27(02), 168–178

Publication history: Received on 08 July 2026; revised on 25 August 2026; accepted on 27 August 2026

Article DOI: <https://doi.org/10.30574/wjbphs.2026.27.2.0449>

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ABSTRACT

Background: Loneliness and social isolation have emerged as central concerns in contemporary preventive medicine. Once considered predominantly social or psychological phenomena, they are now recognized by the World Health Organization and the United States Surgeon General as pressing public health priorities with measurable biological consequences. Their prevalence has risen sharply in the wake of demographic ageing, family fragmentation, urbanization, and the COVID-19 pandemic, positioning primary care clinicians at the front line of detection and management.

Objective: This review synthesizes contemporary epidemiological, mechanistic, and clinical evidence on loneliness and social isolation as independent risk factors for cardiovascular disease, adverse mental health outcomes, and all-cause mortality, and evaluates the implications for routine primary care practice.

Methods: A structured narrative review was conducted of peer-reviewed meta-analyses, prospective cohort studies, Mendelian randomization analyses, mechanistic laboratory work, and international policy statements published between 2010 and 2025, retrieved from PubMed, the Cochrane Library, and the archives of major cardiology, psychiatry, and public health journals.

Results: Convergent evidence from more than two dozen high-quality investigations indicates that social disconnection independently increases the risk of coronary heart disease by approximately 29%, stroke by 32%, incident heart failure by 15–20%, type 2 diabetes by 20–33%, dementia by roughly 31%, and all-cause mortality by 22–32%, with hazard ratios comparable to those of established risk factors such as smoking, obesity, and physical inactivity [5–10]. Mechanistic work implicates hypothalamic–pituitary–adrenal axis dysregulation, chronic low-grade inflammation, up-regulation of the conserved transcriptional response to adversity, sympathetic overactivation, impaired sleep architecture, and adverse health behaviours. Brief screening tools such as the three-item UCLA Loneliness Scale can be integrated into routine consultations, and structured non-pharmacological interventions, including cognitive-

behavioural therapy and link-worker–delivered social prescribing, demonstrate measurable reductions in loneliness scores.

Conclusion: Loneliness and social isolation warrant recognition as modifiable clinical risk factors in primary care. Their systematic identification, biopsychosocial contextualization, and integration into cardiovascular and mental health risk-reduction pathways constitute an ethical and empirical imperative for the coming decade.

Keywords: Loneliness; Social Isolation; Cardiovascular Disease; Depression; Dementia; Mortality; Primary Care; Social Prescribing.

1 INTRODUCTION

1.1 Framing the problem

Human beings are obligately social creatures, and the quality of their social relationships has long been suspected of shaping their health. What was once an intuitive claim has become, in the past fifteen years, one of the most rigorously documented findings in epidemiology. Landmark meta-analytic work by Holt-Lunstad and colleagues, drawing on more than three million participants, established that deficient social relationships carry a mortality risk on par with smoking fifteen cigarettes a day and exceeding the risks associated with obesity and physical inactivity [5,6]. Building on this foundation, the United States Surgeon General issued a formal advisory in 2023 characterizing loneliness and isolation as a national epidemic, and the World Health Organization established a Commission on Social Connection later that same year, estimating that one in six people worldwide experiences loneliness and that the phenomenon contributes to approximately 871 000 deaths annually [1,2,18].

1.2 Relevance to primary care

Primary care occupies a strategic position in the response to this crisis. General practitioners, family physicians, and community nurses see the majority of at-risk patients — older adults living alone, bereaved spouses, chronically ill persons with mobility limitation, socially anxious adolescents, and displaced populations — often long before overt cardiovascular or psychiatric disease develops [3,19]. Yet loneliness remains inconsistently recognized in routine consultations, seldom coded in electronic records, and rarely addressed within structured care pathways [20]. This omission is clinically consequential: patients experiencing chronic loneliness present with higher symptom burdens, poorer adherence to prescribed regimens, and greater healthcare utilization for functional complaints [21,22].

1.3 Aim and scope

This review pursues three interrelated aims. First, it clarifies the conceptual and operational distinctions between loneliness and social isolation, both of which are essential for accurate clinical screening. Second, it synthesizes the epidemiological literature linking these exposures to three principal outcome domains — cardiovascular disease, mental health disorders, and all-cause mortality — while examining mechanistic pathways that render these associations biologically plausible. Third, it appraises the practical instruments and interventions available to primary care clinicians, with particular attention to social prescribing models that have been formally embedded within national health systems in the United Kingdom and elsewhere [15,17].

2 CONCEPTUAL FRAMEWORK AND DEFINITIONS

2.1 Loneliness as a subjective experience

Loneliness is best conceptualized as a subjective, distressing experience arising from a perceived mismatch between the social relationships an individual desires and those they actually possess. This formulation, rooted in the work of Perlman and Peplau, emphasizes that loneliness is a cognitive-affective state rather than a headcount of social contacts [23]. A person surrounded by acquaintances may feel intensely lonely, while another with a small but meaningful network may not. Contemporary neuroscience situates loneliness within the phylogenetically ancient signalling systems that alert an organism to threats against its social body, closely paralleling the physiological signature of physical pain [11,12].

2.2 Social isolation as an objective state

Social isolation, by contrast, refers to the objective condition of having few social contacts, limited participation in social roles, and infrequent engagement with community structures [24]. It is typically assessed through indicators such as living arrangements, marital status, network size, and frequency of contact. The correlation between loneliness and

isolation is real but modest — commonly reported in the range of 0.20 to 0.40 — meaning that clinicians who screen only for one will miss a substantial proportion of at-risk patients [23,24].

2.3 Related constructs

Additional constructs used in the literature include living alone, low social support, and social disconnection, an umbrella term embraced by the United States Centers for Disease Control and Prevention that encompasses both objective isolation and subjective loneliness [25]. The Cacioppo Evolutionary Theory of Loneliness offers an integrative interpretive framework: loneliness evolved as an aversive signal encouraging the repair of social bonds, but when chronic — as it increasingly is in modern societies — its allostatic burden becomes pathogenic [11,12].

3 EPIDEMIOLOGY AND CONTEMPORARY BURDEN

3.1 Global prevalence

Prevalence estimates depend on the instrument used, the cut-off applied, and the population sampled, but converge on the conclusion that loneliness is widespread. A systematic review encompassing 113 countries reported pooled adolescent prevalences ranging from 9.2% in South-East Asia to 14.4% in the Eastern Mediterranean, with substantial regional variation [26]. Among older adults, meta-analytic estimates cluster near 26–30%, with institutionalized elders exceeding 50% [27]. In the United States, the Centers for Disease Control and Prevention reported in 2024 that more than one in three adults experience loneliness and one in four lack adequate social and emotional support [25]. The WHO estimated in 2025 that one in six people worldwide is lonely, translating into approximately 100 lonely deaths every hour globally [2].

3.2 Age and gender patterns

Contrary to persistent stereotypes portraying loneliness as an old-age phenomenon, contemporary surveys consistently identify adolescents and young adults as the loneliest cohorts, with rates in the 18–24 age band approaching or exceeding one in two in several high-income countries [4,28]. Older adults nonetheless remain vulnerable, particularly following bereavement, functional decline, or residential relocation. Gender patterns are heterogeneous: women more frequently report loneliness on standardized scales, whereas men more often exhibit objective social isolation and lower rates of help-seeking, which may explain the stronger loneliness–mortality association observed in men in some longitudinal analyses [8,29].

3.3 The pandemic amplifier

The COVID-19 pandemic constituted a natural experiment in enforced social disconnection. Longitudinal data indicate a small but statistically significant increase in the prevalence of loneliness during 2020–2022, superimposed on already rising trends, together with a 25% global increase in anxiety and depressive disorders in the pandemic's first year [30,31]. Older adults, adolescents, and individuals with pre-existing mental disorders sustained disproportionate impact, and residual effects on social connectivity are still being characterized [4,31].

4 CARDIOVASCULAR OUTCOMES

4.1 Coronary heart disease and stroke

The most comprehensively documented physical consequences of loneliness and isolation are cardiovascular. The seminal systematic review and meta-analysis by Valtorta and colleagues, published in *Heart* in 2016, pooled sixteen prospective observational studies encompassing 181 006 adults and reported a 29% increase in incident coronary heart disease (pooled relative risk 1.29, 95% confidence interval 1.04–1.59) and a 32% increase in incident stroke (RR 1.32, 95% CI 1.04–1.68) among individuals reporting loneliness or isolation, independent of conventional risk factors [7]. These estimates have subsequently been endorsed and elaborated by the American Heart Association's 2022 scientific statement on the effects of social isolation and loneliness on cardiovascular and brain health [8].

4.2 Heart failure and cardiovascular mortality

Beyond incident disease, social disconnection worsens prognosis in established cardiovascular illness. A large analysis of the UK Biobank cohort demonstrated that both social isolation and loneliness independently increase the risk of hospitalization or death from heart failure by 15% to 20%, even after adjustment for baseline cardiometabolic status [32]. Perceived social isolation is associated with elevated 90-day rehospitalization rates in patients discharged with heart failure, contributing to the growing recognition that discharge planning must attend to social context as rigorously as to medication reconciliation [33]. A 2024 meta-analysis of nineteen studies confirmed a pooled increase in incident cardiovascular disease and cardiovascular mortality across diverse populations [34].

4.3 Type 2 diabetes and cardiometabolic risk

Loneliness independently predicts incident type 2 diabetes. In an analysis of the English Longitudinal Study of Ageing, Hackett and colleagues followed 4 112 initially diabetes-free adults for twelve years; loneliness at baseline was associated with a 46% higher incidence of type 2 diabetes independent of depression, health behaviours, and cardiometabolic risk factors [35]. Meta-analytic pooling published in 2025 reported a 33% increase in type 2 diabetes risk for lonely individuals and 20% for those socially isolated [36]. Loneliness has also been linked to accelerated microvascular complications among patients already living with diabetes, highlighting its relevance across the disease continuum [37].

4.4 Hypertension and blood pressure trajectories

Longitudinal studies by Hawkey and Cacioppo demonstrated that loneliness predicts accelerated increases in systolic blood pressure over time in middle-aged and older adults, with cumulative differences of up to 30 mm Hg between the loneliest and least lonely quintiles across a five-year window [13,38]. Because these effects are dose-dependent and independent of baseline blood pressure, age, sex, ethnicity, and depressive symptomatology, they support a direct pathophysiological role for chronic loneliness in vascular ageing.

4.5 Causal inference: evidence from Mendelian randomization

Traditional observational studies are vulnerable to residual confounding and reverse causation. Mendelian randomization studies, which exploit random inheritance of genetic variants to approximate a natural experiment, have recently provided more robust causal support. Analyses using large-scale genome-wide association data have documented causal associations between genetically predicted loneliness or isolation and higher risk of coronary heart disease, atrial fibrillation, and heart failure, strengthening the case that these exposures are not merely markers of poor health but drivers of it [39,40].

5 MENTAL HEALTH OUTCOMES

5.1 Depression and anxiety

The relationship between loneliness and depression is bidirectional but temporally weighted such that loneliness typically precedes, rather than follows, depressive symptoms. A rapid systematic review conducted by Loades and colleagues during the COVID-19 pandemic synthesized sixty-three studies and concluded that loneliness increases the risk of depression up to nine years later, and possibly of anxiety concurrently [41]. Longitudinal analyses of the Health and Retirement Study confirm that social isolation is associated with a substantial increase in elevated depressive symptoms in older adults [42]. Among adolescents, cohort work by Matthews and colleagues found that children socially isolated at school entry exhibited elevated rates of depression, anxiety, and conduct problems in early adolescence, even after adjustment for prior mental health status [43].

5.2 Suicidal ideation and behaviour

A 2020 systematic review and meta-analysis by McClelland and colleagues examined the prospective association between loneliness and later suicidal ideation and behaviour, concluding that loneliness is a significant predictor of both suicidal ideation and suicidal behaviour, with the association partially — but not fully — mediated by depression [44]. This finding is clinically important: it implies that suicide risk assessment in primary care should incorporate explicit inquiry about social disconnection rather than assuming that loneliness is merely a proxy for depressive illness.

5.3 Cognitive decline and dementia

Loneliness has emerged as an independent modifiable risk factor for late-life cognitive impairment and dementia. The most comprehensive meta-analysis to date, by Luchetti and colleagues in 2024, pooled twenty-one longitudinal studies encompassing more than 600 000 participants and reported that loneliness increased the risk of all-cause dementia by 31% and cognitive impairment by 15% [9,45]. These associations persisted after adjustment for depressive symptoms, education, and comorbidity. Systematic review evidence also indicates that living alone confers an increased risk of incident dementia, with a population-attributable fraction of approximately 8.9% [46]. Because dementia remains largely untreatable once established, identification and mitigation of upstream psychosocial risk factors in midlife represent one of the few high-leverage preventive strategies presently available.

6 ALL-CAUSE MORTALITY

6.1 Meta-analytic evidence

The empirical foundation for the mortality claim rests on two influential meta-analyses. In 2010, Holt-Lunstad and colleagues pooled 148 studies (308 849 participants) and reported that individuals with stronger social relationships had a 50% increased likelihood of survival [6]. A subsequent 2015 meta-analysis by the same research team pooled 70 studies (3 407 134 participants) and reported adjusted odds ratios for mortality of 1.26 for loneliness, 1.29 for objective social isolation, and 1.32 for living alone [5]. These estimates are largely comparable to those associated with well-established cardiovascular risk factors and led to the widely quoted comparison equating chronic social disconnection with smoking approximately fifteen cigarettes per day [47].

6.2 Prospective cohort evidence

Complementary cohort evidence reinforces these findings. Steptoe and colleagues, analyzing the English Longitudinal Study of Ageing, reported that social isolation was independently associated with all-cause mortality in older men and women, with the isolation effect surviving adjustment for baseline health, demographic characteristics, and depressive symptoms; loneliness, by contrast, was largely accounted for by these covariates in that sample [48]. A 2025 comprehensive systematic review and meta-analysis of 90 prospective studies reported that loneliness was associated with a 14% increase in all-cause mortality (hazard ratio 1.14, 95% CI 1.10–1.18) with substantial heterogeneity, and that social isolation and living alone conferred comparable or larger risks [49].

6.3 Cause-specific mortality

Excess mortality among lonely and isolated individuals is not limited to cardiovascular causes. Elevated risks have been documented for cancer mortality, respiratory disease mortality, and death by suicide, with mediation analyses indicating that a substantial fraction of the association with cancer mortality is transmitted through health behaviours such as smoking, physical inactivity, and delayed help-seeking [50].

7 BIOLOGICAL MECHANISMS

7.1 Hypothalamic–pituitary–adrenal axis and allostatic load

Chronic loneliness functions as a persistent social stressor. Longitudinal work has demonstrated that lonely individuals exhibit a flattened diurnal cortisol rhythm, elevated morning cortisol, and impaired feedback regulation of the hypothalamic–pituitary–adrenal (HPA) axis [51,52]. Over years, this pattern contributes to allostatic load — the cumulative wear and tear on physiological systems arising from repeated activation of stress-response machinery — and represents one of the principal biological bridges between subjective loneliness and objective disease [14].

7.2 Chronic inflammation and the conserved transcriptional response to adversity

A parallel body of work has documented that loneliness is associated with elevated circulating levels of interleukin-6, C-reactive protein, and fibrinogen [52]. At the level of gene expression, chronic social adversity — including loneliness — activates a conserved transcriptional response to adversity (CTRA), characterized by up-regulation of pro-inflammatory genes and down-regulation of antiviral and antibody-related genes [53,54]. The CTRA pattern provides a molecular rationale for the increased vulnerability of lonely individuals to atherosclerosis, metabolic dysfunction, and viral infection.

7.3 Autonomic and cardiovascular reactivity

Loneliness is associated with heightened sympathetic tone and elevated peripheral vascular resistance, contributing to the accelerated blood-pressure trajectories described earlier [13,38]. Impaired parasympathetic recovery from psychological stressors may further amplify cardiovascular risk over time.

7.4 Sleep disruption

Loneliness reliably predicts poorer subjective and objective sleep quality, characterized less by reduced total sleep time than by increased fragmentation and reduced restorative depth [55,56]. Because inadequate sleep is itself a risk factor for hypertension, type 2 diabetes, obesity, and depression, this pathway compounds the direct effects of psychosocial stress.

7.5 Health behaviours as mediators

Loneliness is associated with higher rates of smoking, greater sedentary behaviour, poorer diet quality, reduced adherence to medical regimens, and delayed help-seeking [57,58]. Mediation analyses suggest that health behaviours account for a meaningful — though incomplete — share of the association between social disconnection and mortality, particularly for cancer-related deaths [50].

8 CLINICAL SCREENING IN PRIMARY CARE

8.1 Rationale for routine assessment

Because loneliness and isolation are prevalent, prognostically important, and often unspoken, systematic case-finding within primary care is warranted. Patients rarely raise the topic spontaneously, either because they do not perceive it as a medical matter or because of shame and stigma [1,19]. Structured screening reframes loneliness as a legitimate clinical concern and creates the opportunity for early intervention.

8.2 Instruments

The most extensively validated instruments are the twenty-item Revised UCLA Loneliness Scale and its shorter derivatives. The three-item UCLA loneliness scale (UCLA-3), developed by Hughes and colleagues, offers acceptable sensitivity and specificity, requires less than one minute of consultation time, and is well suited to routine use in general practice [15,59]. The De Jong Gierveld Loneliness Scale, available in six- and eleven-item versions, differentiates emotional from social loneliness, an important clinical distinction because the two dimensions may warrant different interventional emphases [60]. For objective social isolation, brief indices assessing living arrangements, frequency of contact with friends and family, and participation in group activities are commonly used, exemplified by the Berkman-Syme Social Network Index and the Lubben Social Network Scale.

8.3 Practical integration

Integration of screening into pre-visit questionnaires, chronic-disease review templates, and annual wellness visits has been proposed and piloted in several health systems [3,15]. Positive screens should prompt a structured conversation exploring precipitants (bereavement, illness, retirement, migration), current coping strategies, and preferences for further support, rather than triggering an immediate pharmacological response.

9 INTERVENTIONS AND MANAGEMENT

9.1 Psychological interventions

The most rigorous meta-analytic evidence, provided by Masi and colleagues in 2011, indicates that interventions targeting maladaptive social cognition — typically delivered as cognitive-behavioural therapy — produce the largest reductions in loneliness scores, exceeding the effects of interventions focused on enhancing social skills, increasing opportunities for social contact, or providing social support alone [16]. Subsequent trials, including digitally delivered variants, have replicated this finding, reinforcing the recommendation that psychological therapy be considered as a first-line option for entrenched loneliness [61].

9.2 Social prescribing

Social prescribing, in which primary care clinicians refer patients to non-medical link workers who connect them with community-based activities, has been formally embedded within the English National Health Service since 2019 [17]. A 2022 systematic review by Kiely and colleagues concluded that social prescribing link workers are associated with modest improvements in patient-reported outcomes, including loneliness, quality of life, and mental well-being, although higher-quality randomized trials are still required [17,62]. A national evaluation of the NHS rollout published in 2025 reported small but consistent improvements in patient experience and modest gains for populations with the greatest health inequalities [63].

9.3 Community-based and group interventions

Group activities — including reminiscence groups, exercise classes, choirs, and peer-support programmes — reduce loneliness in some subgroups, particularly among older adults and among women, although effect sizes are heterogeneous. Interventions that afford participants an active role, whether as volunteers, tutors, or hosts, appear more efficacious than passive-attendance formats [16,64].

9.4 Digital interventions

Digital tools, including videoconferencing, structured online communities, and companion robotics, have been evaluated with mixed results. Evidence suggests that digital interventions are more effective when they augment rather than replace in-person contact, and when they are designed with attention to the digital literacy and hardware access of the target population [61,64].

9.5 Pharmacotherapy

There is no pharmacological treatment for loneliness itself. Antidepressant and anxiolytic medications should be reserved for their conventional indications and should not be substituted for psychosocial intervention in patients whose primary complaint is loneliness rather than mood or anxiety disorder [1,16].

10 HEALTH-SYSTEM AND POLICY CONSIDERATIONS

10.1 Economic burden

The economic consequences of loneliness and isolation are substantial. The United States Surgeon General's advisory cites work by Flowers and colleagues estimating that social isolation among older adults accounts for approximately \$6.7 billion in excess Medicare spending each year, primarily driven by longer hospital stays and higher rates of readmission [1,65]. A 2024 systematic review of loneliness-related healthcare utilization identified consistent, though heterogeneous, evidence of elevated primary care and secondary care use, particularly for functional and psychiatric complaints [66].

10.2 Equity considerations

Loneliness and isolation are unevenly distributed. Individuals of lower socioeconomic status, ethnic minorities, migrants, LGBTQ+ persons, people with disabilities, and rural populations experience disproportionately high burdens [1,25]. Interventions delivered without attention to structural determinants — poverty, transport, digital access, safety — risk widening rather than narrowing health inequalities.

10.3 Policy responses

Beyond the United States Surgeon General's 2023 advisory [1] and the WHO Commission on Social Connection [2,18], national strategies have been advanced in the United Kingdom, Japan, Australia, and several European Union member states, typically combining public awareness campaigns, funding for social prescribing infrastructure, and investment in community assets such as libraries, parks, and volunteering programmes.

11 DISCUSSION

11.1 Interpreting the evidence

The convergence of evidence across observational cohorts, meta-analyses, mechanistic studies, and Mendelian randomization analyses provides a level of methodological triangulation rarely achieved for a putative psychosocial risk factor [5,7,8,39,40]. The magnitude of the associations — hazard ratios in the 1.2 to 1.5 range for major cardiovascular, psychiatric, and mortality outcomes — is not merely statistically significant but clinically meaningful, comparable in scale to well-accepted modifiable risk factors. The observation that these associations survive adjustment for depression, health behaviours, and cardiometabolic risk indicates that loneliness and isolation contribute uniquely to disease burden rather than acting solely as proxies for other exposures [7,35].

11.2 Strengths and limitations of the evidence base

Notwithstanding these strengths, several limitations warrant explicit acknowledgment. Most cohort evidence derives from high-income Western populations, and generalizability to low- and middle-income settings remains uncertain despite growing efforts by WHO to address this gap [2]. Measurement heterogeneity — with different studies using different loneliness scales, isolation indices, and cut-points — contributes to residual heterogeneity in meta-analytic estimates [7,49]. Reverse causation cannot be fully excluded in observational designs, although Mendelian randomization and long lag-time cohort work substantially attenuate this concern [39,40]. Randomized intervention data on hard clinical endpoints — cardiovascular events, dementia incidence, mortality — remain sparse; existing trials have largely relied on intermediate outcomes such as loneliness scale scores and quality-of-life measures [16,62].

11.3 Implications for primary care practice

For primary care clinicians, the evidence supports several concrete implications. First, loneliness and isolation should be treated as legitimate targets of clinical assessment, on par with tobacco use or physical inactivity. Second, brief validated screening tools such as the UCLA-3 should be integrated into routine review templates, with appropriate follow-up conversations rather than reflex referrals or prescriptions [15,59]. Third, care pathways for chronic cardiovascular and psychiatric disease should explicitly incorporate psychosocial context, given the demonstrated impact of loneliness on prognosis and rehospitalization [32,33]. Fourth, referral to social prescribing services, where available, should be normalized as a routine component of holistic primary care [17,63].

11.4 Ethical dimensions

Screening for loneliness raises ethical questions that clinicians must navigate with care. The disclosure of loneliness is often accompanied by shame; casual documentation risks compounding stigma. Interventions must respect patient autonomy and preference — some patients value solitude and do not wish to be “treated” for it — and must not medicalize a legitimate emotional response to bereavement, illness, or social change [1,19]. The clinical task is to distinguish transient, situational loneliness from the chronic, pervasive form associated with disease risk and to intervene proportionately.

11.5 Future research priorities

Priority areas for future research include the conduct of adequately powered randomized trials with hard clinical endpoints; the development and validation of screening pathways in low- and middle-income settings; the elucidation of critical developmental windows during which social connection most powerfully shapes lifelong disease trajectories; and the evaluation of health-system-level interventions that address structural determinants of connection. Emerging work on childhood loneliness as a predictor of midlife cognitive decline, for example, hints at intergenerational and life-course dimensions that remain underexplored [67].

RESULTS SUMMARY

Across the outcomes examined in this review, quantitative estimates from high-quality meta-analyses and prospective cohort studies can be summarized as follows. Loneliness and isolation are associated with a 29% increase in incident coronary heart disease and a 32% increase in incident stroke [7]. They are associated with a 15–20% increase in incident heart failure and worse prognosis in established heart failure [32,33]. They are associated with a 20–33% increase in incident type 2 diabetes [35,36] and with accelerated increases in systolic blood pressure over time [13,38]. They are associated with elevated risk of depression up to nine years later [41], with a significant prospective association with suicidal ideation and behaviour [44], and with a 31% increase in all-cause dementia risk [9,45]. They are associated with a 22–32% increase in all-cause mortality, comparable to well-established behavioural risk factors [5,6,49]. Mechanistically, they are associated with HPA-axis dysregulation, chronic low-grade inflammation, up-regulation of the CTRA gene-expression pattern, sympathetic overactivity, impaired sleep, and adverse health behaviours [11–14,51–58]. Brief, valid screening instruments and structured interventions — including cognitive-behavioural therapy and social prescribing — are available and increasingly integrated into primary care [15,16,17,59,62,63].

12 CONCLUSION

Loneliness and social isolation are no longer soft, peripheral concerns of medicine but front-line clinical risk factors with measurable and substantial impact on cardiovascular disease, mental health, and mortality. The scale of the evidence, the coherence of the mechanistic pathways, and the plausibility of causal inference converge on a compelling case for their systematic inclusion in preventive and chronic-disease care. Primary care clinicians occupy the most strategic vantage point for early detection, brief intervention, and referral to community resources, and the emerging infrastructure of social prescribing offers a scalable model for embedding this work within routine practice. Recognizing loneliness as a modifiable clinical risk factor is not a rhetorical flourish but an evidence-based imperative — one that reflects an ancient truth about human beings, now confirmed by contemporary science: we are healthier together, and disconnection wounds the body as surely as it wounds the mind.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgments

The authors gratefully acknowledge all individuals who supported the preparation of this manuscript.

Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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