

The impact of anhedonia on physical health and somatic diseases: an exploratory literature review

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ABSTRACT

Anhedonia, or the lack of interest and pleasure, is a transdiagnostic feature of mental health disorders with emerging links to physical health. This exploratory literature review investigated evidence of anhedonia's association with physical health and somatic diseases. A citation chaining approach was applied to 20 papers identified through targeted searches conducted from September to October 2024 on PubMed and Google/Google Scholar. Studies published in English and reporting outcomes in adults with anhedonia were included. Quality assessments were performed using the Centre for Evidence-Based Medicine critical appraisal tool for prognostic studies. Data on study characteristics, assessment and definition of anhedonia, and clinical outcomes were extracted. 41 publications on 40 unique studies were included. Most studies included patients with cardiac conditions, and 14 reported a psychiatric diagnosis, predominantly depression. Anhedonia was significantly associated with all-cause mortality, risk of major adverse cardiovascular events and worse physical health-related quality of life. Moreover, high positive affect was correlated with lower risk of functional decline, reduced inflammatory biomarkers and protective effects against conditions like diabetes and hypertension, compared with low positive affect. To our knowledge, this is the first exploratory review to gather evidence that anhedonia, whether occurring as a symptom of depression, another psychiatric disorder, or a somatic condition, may be associated with poorer health and somatic disease outcomes. Conversely, positive affect may confer protective benefits. These insights emphasise the need to prioritise development of treatment modalities that have proven impacts on hedonic tone.

Introduction

There is growing recognition that mental health is a dual-continua model where negative mental health and positive mental health

(PMH) operate on two distinct levels (Iasiello et al., 2020). PMH encompasses several facets of wellbeing—including happiness, hedonic tone (valence or pleasure) and positive affect—comprising activated (joy and enthusiasm) and de-activated (relaxation) emotions (Fredrickson

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2001; Lim 2016), which significantly shape patients' experiences of depression (Zisook, et al. 2025). Anhedonia is a multifaceted symptom characterised by a reduced ability to experience pleasure, loss of interest in activities that were previously enjoyable and emotional and motivational deficits impacting daily functioning and quality of life (Cooper, et al. 2018; Gorwood 2008; Wong, et al. 2024). Anhedonia consists of anticipatory (less motivation or interest) and consummatory (reduced pleasure) aspects affecting sensory and interpersonal experiences and is sometimes defined as low positive affect (Beames, et al. 2025). Whilst the underlying mechanisms of anhedonia are not well known, they are thought to be related to reward processing pathways, such as failure to activate reward associations, as well as related to inflammation and metabolic dysfunction (Moreira, et al. 2019; Nogo, et al. 2021; Serretti 2023; Whitton and Pizzagalli 2022). These mechanisms converge as risk factors for somatic diseases such as cardiovascular disease, diabetes and cancer (Bekhhbat, et al. 2022).

Anhedonia is a core symptom of major depressive disorder (MDD), with a prevalence of approximately 70% in patients with MDD, as compared with 15% in the general healthy population (Cao, et al. 2019; Cutler et al., 2026; Roberts-West, et al. 2023; Serretti 2023). For patients with depressive disorders, anhedonia is associated with greater disease severity and persistence, suggesting it may index treatment resistance and poor functional outcomes (McIntyre, et al. 2023; Serretti 2023; Wong, et al. 2024). Anhedonia may also persist in patients in clinical remission as a residual symptom of depression (Nierenberg 2015). Additionally, it has been reported as having a more substantial impact on functioning than sleep disturbances, anxiety and physical symptoms (Demyttenaere, et al. 2021; Nierenberg 2015). Studies have implicated anhedonia as a risk factor for suicidality and suicidal ideation for patients with depressive disorders (Gillissie, et al. 2023; Serretti 2023).

Beyond depression, anhedonia is recognised as a transdiagnostic symptom in a variety of mental health disorders, including schizophrenia and bipolar disorder, and is included in key diagnostic frameworks, demonstrating the prevalence and burden within these patient populations (Culig and Belzung 2016; McIntyre, et al. 2020; Whitton and Pizzagalli 2022). The frameworks include the Diagnostic and Statistical Manual of Mental Disorder, 5th edition (DSM-5), the Research Domains Criteria (RDoC) and the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) (American Psychiatric Association 2022; Cuthbert 2022; World Health Organization 2016). Whereas earlier research has focused on the effect of anhedonia on mental health outcomes, its recognition as a transdiagnostic symptom has increased interest in its impact on physical health. For example, it has been linked with a range of conditions, including diabetes and obesity, whereby reduced motivation can result in decreased physical activity and increased metabolic dysregulation (Carter and Swardfager 2016; Hwang, et al. 2025; Ibrahim, et al. 2016; Mansur, et al. 2019). Anhedonia frequently leads to problems with sleep, which have been linked to cognitive impairment and suicidal ideation (Choi, et al. 2025; Zhao, et al. 2024). In addition, anhedonia may be associated with increased immune responses, including elevated cytokine levels and has been reported to be more prevalent in patients with chronic pain than healthy populations (Garland, et al. 2020; Kudina, et al. 2020; Mallorquí, et al. 2022). However, while existing evidence indicates the complex effects of anhedonia on multiple interacting domains of physical health, considering each study in isolation makes it difficult to gain a thorough understanding of the role of anhedonia in physical health and somatic diseases.

The concept that anhedonia can affect both mental and physical domains of health and quality of life has been receiving greater attention in recent years, expanding its relevance to physicians working in general clinical settings or with specialisms outside of psychiatry. Emerging evidence of a link between anhedonia, somatic diseases and physical health indicates an opportunity to develop treatments that target both causes and symptoms comprehensively, improving patient outcomes. The objective of this review was to identify and synthesise published

evidence on the association between anhedonia and physical health and somatic diseases.

Experimental procedures

Given the anticipated limited evidence on this topic, we chose to conduct an exploratory literature review rather than a systematic literature review (SLR). We implemented a citation chaining method (also known as snowballing), as described by Wohlin (2014). This allowed for a more specific search approach, capturing relevant publications that would have been difficult to identify through an SLR.

Eligibility criteria

Studies were included if they reported outcomes for adult patients with anhedonia, where anhedonia was due to or related to mental disorders, but not somatic diseases. Outcomes of interest included health-related quality of life (HRQoL) and patient-reported outcomes (PROs) associated with physical health and functioning, incidence and prevalence of somatic disease and physical health, management and treatment of chronic conditions, and mortality. All studies published prior to when the searches were conducted were eligible for inclusion. Full eligibility criteria are reported in Table 1.

Search strategy

Citation chaining was used to find relevant publications (Fig. 1) (Wohlin 2014). An initial set of 20 publications was identified by performing time-limited, targeted searches on PubMed and Google/Google Scholar from September to October 2024, and through consultations with the authors. Search strings were formed of three terms, combining key words related to the condition (e.g., anhedonia, lack of positive affect, negative affect), somatic diseases and physical health (e.g., somatic or physical disease, disorder, health or symptoms) and quality of life (e.g., quality of life or QoL). Iterations of backward and forward chains were then conducted on the initial set to find additional relevant studies. Backward chains involved examining the reference lists of the initial set of papers, while forward chains involved inspecting the articles that had cited the initial set. In both cases, relevant titles were identified and the abstracts and potentially relevant full-text articles were reviewed against the eligibility criteria.

Titles and abstracts were evaluated by one reviewer, and the full text of any potentially relevant studies was screened by the same reviewer. A second reviewer independently verified 10% of the article decisions and any decisions where the original reviewer was uncertain. Any relevant records were included in the review and incorporated into the citation chaining process. Searches were conducted until 10 days had been spent searching. The citation chaining process was carried out using Semantic Scholar (2025). Due to the higher volume of evidence identified than anticipated, studies with at least 100 participants were prioritised. There were no notable differences in baseline characteristics, countries or outcomes reported (with regard to somatic and psychiatric diseases) between the studies that were included and those that were deprioritised.

Data extraction

Data extraction was performed in line with the University of York Centre for Reviews and Dissemination (CRD) guidance (Centre for Reviews and Dissemination 2008). For each included study, one reviewer extracted the relevant data and a second reviewer verified that the data were accurate and complete. Discrepancies or omissions were resolved through discussion, with a third reviewer arbitrating where required.

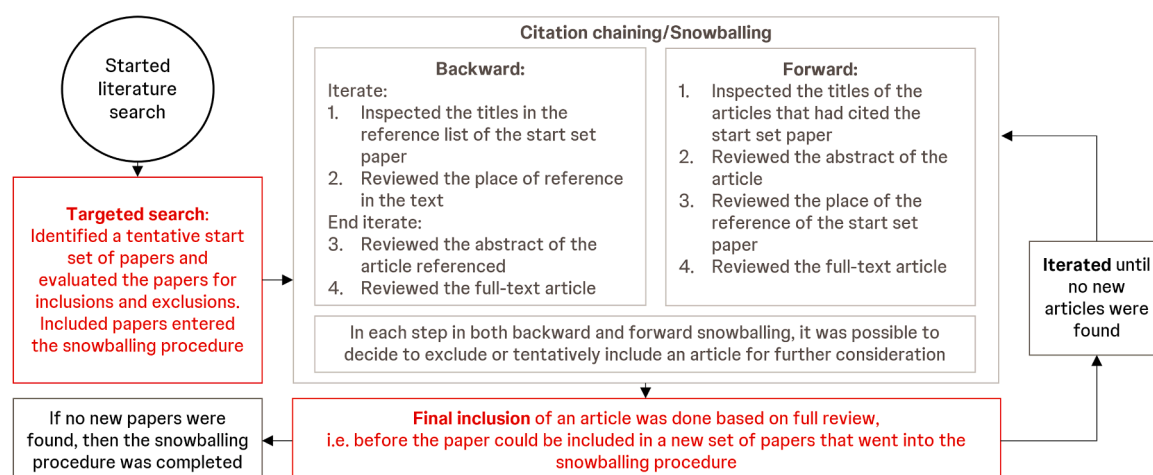
The following key information was extracted into a pre-designed data extraction table: study characteristics, patient population

Table 1
Eligibility criteria.

Study parameter	Inclusion criteria	Exclusion criteria
Patient population	Adults (≥ 18 years) with anhedonia ^a which may be due to or related to mental disorders	Children (< 18 years) Anhedonia due to somatic diseases
Outcomes	HRQoL measured by an appropriate scale and PROs related to physical health and functioning, including but not limited to: Severity of somatic symptoms Functional impairment Incidence and prevalence of somatic diseases and physical health (e.g., cardiovascular diseases, metabolic disorders, neurological disorders, cognitive disorders, gastrointestinal disorders, inflammatory disorders, pain disorders) Mortality, in relation to suicide or natural causes Management/treatment of chronic conditions Any other relevant outcomes of interest ^b	Studies where outcomes are not reported separately for the population of interest
Study design	RCTs Non-randomised interventional studies (e.g., single arm trials) Observational studies SLRs/MAs/NMAs Narrative reviews	In vivo/animal studies Editorials Guidelines Commentaries
Other considerations	English language Human participants Any geography	No abstract or full text published in the English language

^a Anhedonia was defined using broad terminologies including “lack of positive affect”, “lack of pleasure/interest/enjoyment”, “amotivation” and “lack of happiness/meaningless life”.

^b The link between anhedonia and longevity (lifespan) was of interest and was captured in the outcomes. HRQoL: health-related quality of life; MDD: major depressive disorders; (N)MA: (network) meta-analysis; PRO: patient-reported outcome; RCTs: randomised controlled trials; SLR: systematic literature review.

**Fig. 1.** Citation chaining procedure (often referred to as snowballing), adapted from Wohlin (2014).

characteristics, assessment and definition of anhedonia, and incidence and prevalence of somatic diseases. For the purpose of reporting the findings of this review, studies were categorised by condition (cardiac, diabetes, gastrointestinal, mental health), type of care received (primary care) or other (general, adults aged ≥ 65 , mixed [various chronic illnesses] and other [patients with or at risk of symptomatic knee osteoarthritis]).

Quality assessment

The quality of the extracted studies was evaluated using the Centre for Evidence-Based Medicine (CEBM) tool for prognostic studies (Centre for Evidence-Based Medicine, 2024). The assessment was performed by one reviewer and verified by a second reviewer. Any disagreements were resolved through discussion with a third reviewer.

Results

Included studies

In the initial targeted search, 360 records were identified, of which 51 were eligible for citation chaining (Fig. 2). Following title, abstract and full-text review, a total of 41 publications on 40 unique studies were included, comprising 27 prospective cohort studies, 10 cross-sectional studies, two retrospective cohort studies and one prospective ecological momentary assessment.

The key characteristics of the included studies are described in Table 2. These studies spanned 13 countries and reported data on over 200,000 patients from 1978 to 2019. Over half of the studies had a sample size of greater than 500 ($n = 23/40$). Most of the studies were conducted in Europe ($n = 19/40$) and the United States ($n = 17/40$). The most commonly reported follow-up period was 2–5 years ($n = 8/40$).

Studies including patients with cardiac conditions were the most common ($n = 18/40$), followed by general ($n = 7/40$), adults aged ≥ 65 years ($n = 4/40$) and primary care ($n = 3/40$). Lack of positive affect was

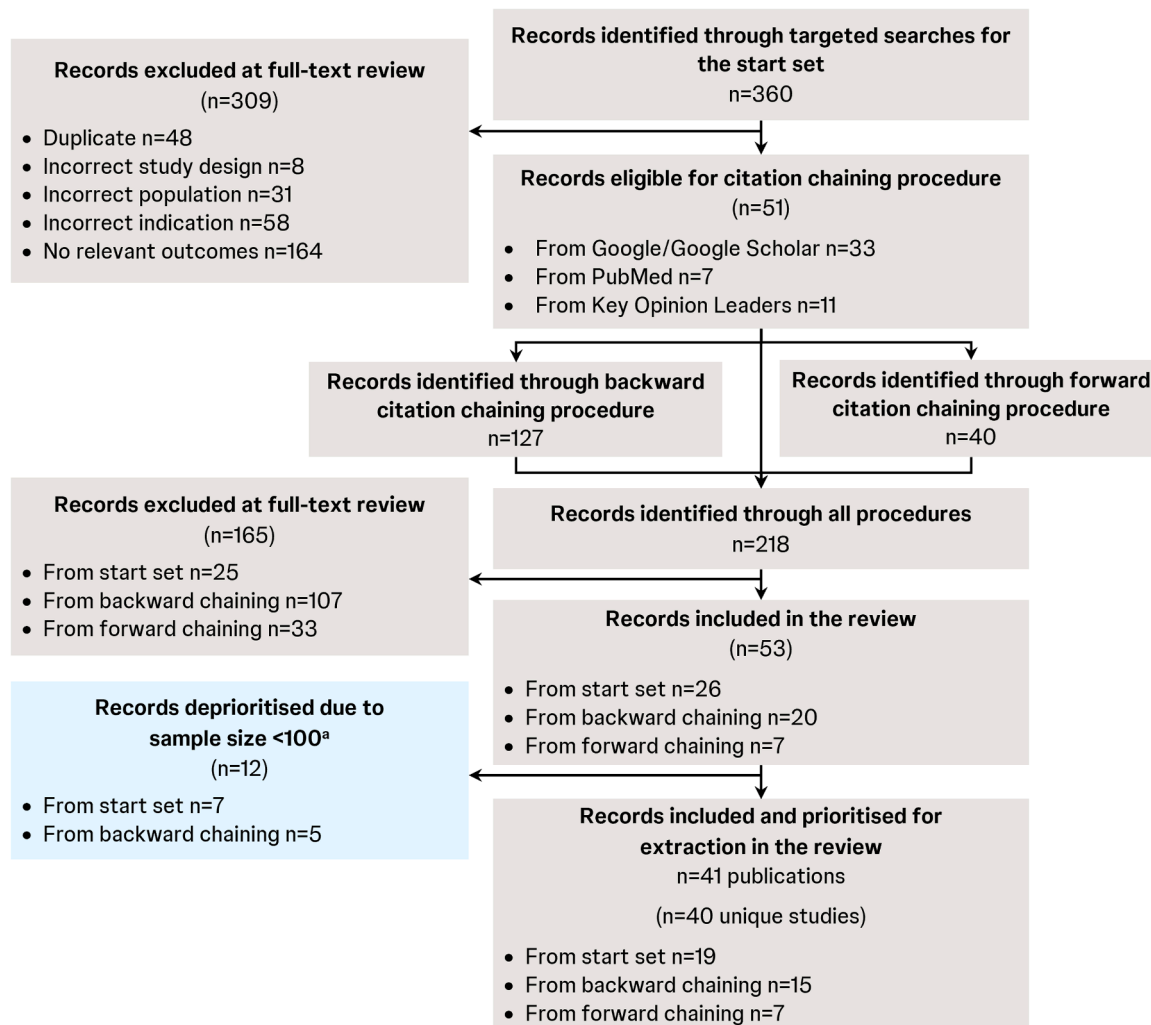


Fig. 2. Flowchart of studies included and excluded in the review process.

^aStudies involving <100 patients were deprioritised due to limited representation of anhedonic cohorts, lack of new data on somatic and psychiatric diseases, lower study quality, and unclear participant recruitment. Of the 12 studies, 8 were conducted in the USA, while Canada, Germany/Austria, the Netherlands, and the UK each conducted 1 study.

the most common definition of anhedonia, used in 21 of the included studies, while 11 studies only used the term ‘anhedonia’. For the purpose of this review, we have only reported outcomes related to negative affect from studies that also included positive affect and/or general anhedonia ($n = 17$). Although it is not considered a definition of anhedonia, we propose that outcomes associated with negative affect are relevant to patients with anhedonia and depression when combined with findings associated with positive affect. As such, results from three studies have henceforth been excluded from this report (Charles and Almeida 2006; Leger, et al. 2018; Leventhal, et al. 1996).

Baseline characteristics

The baseline characteristics of the included studies are summarised in Table 3. A total of 29 studies reported mean age; the widest mean age range was observed in studies reporting on primary care patients (42.5 [$n = 1055$]–66.1 [$n = 386$]). The youngest patients were involved in a study investigating mental health disorders (mean [standard deviation (SD)] age of patients with mood disorders: 28.7 [9.7] years; $n = 80$).

Almost all studies reported sex ($n = 36/37$). The proportions of males and females included in studies of patients with cardiac and general conditions were well balanced. Race was reported in 15/37 studies, and Black and Hispanic patients were underrepresented in over half of the

studies. The proportion of Black patients was highest in primary care studies (52.1% [$n = 386$]–92.1% [$n = 1055$]).

Overall, 25 studies reported comorbidities and at least one psychiatric diagnosis was reported in 14 studies, with depression being the most frequently reported ($n = 11/14$). Other diagnoses reported included post-traumatic stress disorder, panic disorder and anxiety; however, these were rarely reported. Although not a diagnosis, Type-D personality, defined by the tendency to both experience negative emotions and inhibit their expression, was also reported and was assessed using the Type D scale (DS14) (Pelle, et al. 2009). Outcomes related to Type-D personality were only reported when the diagnosis was associated with low positive affect.

HRQoL and PROs related to physical functioning

Overall, 10 studies reported outcomes that affected HRQoL or PROs related to physical functioning (Table 4). For patients with mood disorders (most with a unipolar mood disorder diagnosis of MDD/dysthymia or MDD in partial remission), more severe anhedonia was significantly correlated with worse physical HRQoL (Whitton, et al. 2023). In a cohort of patients with cardiac disorders, low positive affect was independently associated with issues in self-care and usual activities (Versteeg, et al. 2009), while high positive affect was

Table 2
Characteristics of included studies.

Author(s), Year	Study design	Study location	Study period	Duration of follow-up	Measure of anhedonia	Assessment method	Outcomes reported
Bekendam et al. 2018	Prospective cohort (TWeesteden mild STenosis [TWIST])	Netherlands	2009–2015	Mean $\pm$ SD: 3.4 $\pm$ 1.4 years	Positive affect and negative affect	Positive affect was assessed with the validated GMS, comprising of two 10-item subscales (0–4 range), measuring positive affect and negative affect	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality Physical health
Brouwers et al. 2013	Prospective cohort	Netherlands	2006–NR	12 and 18 months	Positive affect: reversed scoring of the HADS positive affect scale so that higher scores indicate higher positive affect, aligning it with the GMS and PANAS scales Anhedonia/mood and hopelessness	Positive affect was assessed by positive affect items of the GMS, the positive items of the PANAS and the positive affect dimension of the HADS	Mortality Physical health
Byrne et al. 2018	Prospective cohort	Australia	2001–2014	Mean $\pm$ SD: 4.7 $\pm$ 3.1 years Median: 6.7 years	High scores on SHAPS represent a reduction of hedonic tone; a score of 3 or more allows a categorical definition of anhedonia	CDS	Mortality
Carpinelli et al. 2019	Cross-sectional	Italy	2017	-	High scores on SHAPS represent a reduction of hedonic tone; a score of 3 or more allows a categorical definition of anhedonia	SHAPS, obtained by a psychologist	Physical health
Charles and Almeida (2006)	Prospective ecological momentary assessment (Midlife in the United States Survey [MIDUS])	USA	1995–1997	8 days	SNA and TNA	SNA used a 6-item questionnaire with a 5-point scale; TNA was assessed in the MIDUS survey using a short form of neuroticism with a 5-point scale	Physical health
Cooper et al. 2002	Retrospective cohort (Medicare)	USA	1998–2000	2 years	Felt sad for 2 weeks or more, which includes the feeling of dysphoria or lack of interest or pleasure in usual activities, anhedonia	Survey	Mortality
Damen et al. 2013	Prospective cohort (Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital [RESEARCH] registry)	Netherlands	2001–2009	7 years	Reduced positive affect; score ≤ 7 on the positive affect scale of HADS (i.e. one SD below the mean)	HADS	Mortality
Davidson et al. 2010a	Prospective cohort	USA	2003–NR	1, 3, 6 and 18 months	Self-reported anhedonia	Self-report measure of depressive symptom severity (BDI). The presence of depressed mood and anhedonia was determined for patients according to the standard criteria used in psychiatric interviews – that the symptom be clinically impairing and present for at least 2 weeks, most of the day, nearly every day	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality
Davidson et al. 2010b	Prospective cohort (Canadian Nova Scotia Health Study)	Canada	1995–NR	10 years	Positive affect is a rating of the degree to which the participant expresses positive emotions, whether verbally or in behaviour or tone of responses	The Expanded Structured Interview is a 12-minute, interpersonally stressful interview designed to assess anger expression and stress reactions by asking participants about their characteristic responses to a variety of different situations	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality
Denollet et al. 2008	Prospective cohort (follow-up, Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital [RESEARCH] registry)	Netherlands	2001–2003 (calculated)	2 years	Positive affect and negative affect, each based on four items of HADS	HADS	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality

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Table 2 (continued)

Author(s), Year	Study design	Study location	Study period	Duration of follow-up	Measure of anhedonia	Assessment method	Outcomes reported
Doyle et al. 2012 Ehrmann et al. 2017	Prospective cohort Cross-sectional	Ireland ^a Germany	- -	8 years -	- -	HADS Patients completed the CES-D questionnaire which contains 20 items assessing the frequency of depressive symptoms. A total score (all 20 items) and mean item scores for the “affective,” “somatic,” and “anhedonic” subtypes were calculated	death) Mortality Mortality Physical health
Hawkins et al. 2014	Prospective cohort	USA	1991–2006	13–16 years	Lack of positive affect (items 4, 8, 12 and 16 on CES-D)	CES-D	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death)
Hu and Gruber (2008)	Cross-sectional	USA	-	-	Positive affect and negative affect	Positive affect and negative affect were measured using PANAS, where each item is rated on a 5-point scale. Total scores are computed for each scale, with lower scores representing lower affect levels	Mortality HRQoL/PROs Somatic disease/ chronic illness
Lawrence et al. 2015	Prospective cohort (General Social Survey-National Death Index [GSS-NDI])	USA	1978–2008	6–30 years (calculated)	General happiness	GSS question: “Taken all together, how would you say things are these days – would you say that you are very happy, pretty happy, or not too happy?”	Mortality
Leger et al. 2018	Prospective cohort (MIDUS II)	USA	-	10 years (approximate)	Negative affect; lingering negative affect is the degree to which the stressor-related negative affect from the day before is still present the day after a stressor occurs	5-point score on 13 items over the past 24 h, across 8 days	HRQoL/PROs Somatic disease/ chronic illness
Leroy et al. 2010	Prospective cohort	France	-	3 years	Lack of ability to experience pleasure (severity of anhedonia is PAS greater than or equal to 23 or 29)	PAS: a 61-item self-rating scale evaluating sensorial and physical pleasures. Each item is scored 0 or 1, with a total score ranging from 0 to 61. The scale evaluated a lifelong characterological defect in the ability to experience pleasure (anhedonia-trait)	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death)
Leveille et al. 1992	Prospective cohort (Group Health Cooperative of Puget Sound)	USA	-	1 year	Positive affect	Positive affect was obtained from a 10-item scale with items adapted from Veit and Ware (1985)(Veit and Ware 1983)	Mortality HRQoL/PROs
Leventhal et al. 1996	Prospective cohort	USA	1985–NR	6 months	Negative affect	Original study: Ratings on six 5-point scales reflecting depressive affect (depressed/sad/hopeless; DA) and anxious affect (anxious/afraid/worried; AA) experienced the day before the interview were summed to create a negative affect score Replication study: Two scales assessed trait depression and trait anxiety. The first consisted of six items reported as having the highest factor loadings in the depression and anxiety scales of the Beck CCL. The affective components of anxiety and depression were also measured, using six DA and six AA adjectives selected from the Profile of Mood States and the Pregnancy Mood Checklist.	HRQoL/PROs

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Table 2 (continued)

Author(s), Year	Study design	Study location	Study period	Duration of follow-up	Measure of anhedonia	Assessment method	Outcomes reported
Lin et al. 2018	Cross-sectional (Grady Trauma Project)	USA	2009–2014	-	Positive affect and negative affect	The two depression scale scores (CCL and mood) were summed to yield a trait measure of depressive affect PANAS	HRQoL/PROs Physical health Physical health
Luong et al. 2016	Cross-sectional (Multi-Method Ambulatory Assessment [MMAA])	Germany	2013–NR	-	Positive affect and negative affect	Negative affect valuation was assessed by how frequently participants appraised each of three negative emotions (anger, nervousness, and downcast) with respect to four facets: pleasantness (2 items), utility (2 items), appropriateness (2 items), and meaningfulness (2 items)	
Meyer et al. 2015	Prospective cohort	Switzerland	2004–2010	3.4 years	Positive affect and negative affect	The GMS comprising 20 items yielding a negative affect and a positive affect subscale (typical items are “insecure”, “helpless”, “feeble”, or “weakened” under the negative affect subscale and “cheerful”, “lively”, “active”, or “dynamic” under the positive affect subscale). Rating (0, not at all, to 4, extremely) on a five-point Likert scale Bradburn affect balance scale: 10 items, five of which assess positive affect. Responses were on a four-point Likert type scale from 0 (not at all) to 3 (a great deal). Scores for each subscale range from 0 to 15; higher scores indicate higher positive affect or higher negative affect	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality
Nabi et al. 2008	Prospective cohort (Whitehall II)	UK	1985–NR	Mean ± SD: 12.5 ± 3.8 years	Positive affect	Bradburn affect balance scale: 10 items, five of which assess positive affect. Responses were on a four-point Likert type scale from 0 (not at all) to 3 (a great deal). Scores for each subscale range from 0 to 15; higher scores indicate higher positive affect or higher negative affect	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality Mortality
Nefs et al. 2016	Prospective cohort (Diabetes, Depression, Type D personality Zuidoost-Brabant [DiaDDZoB])	Netherlands	2005–2010	Mean ± SD: 1878 ± 306 days Range: 26–1964 days	Two items in EPDS (e.g., I have looked forward with enjoyment to things)	Total EPDS score over the past 7 days (originally for post-partum depressive symptoms but validated for male and female samples, including people with T2D in primary care)	Mortality
Ostir et al. 2001	Prospective cohort (North Carolina Established Population for the Epidemiologic Study of the Elderly [EPESE])	USA	1986–1992	6 years	Increasing CES-D scores (0–20) indicate poorer emotional wellbeing	CES-D (modified) 16-item negative affect structure Remaining 4 items make up the positive affect structure	Mortality
Ostir et al. 2006	Cross-sectional (Hispanic EPESE)	USA	1993/4–NR	-	Positive emotion	CES-D Single positive emotion factor consisting of 4 CES-D items Responses scored on a four-point scale (0–3) Summing the responses, the positive emotion scale had a potential range of 0–12 Remaining 16 CES-D items used to calculate depressive symptoms	Physical health
Pelle et al. 2009	Prospective cohort	Netherlands	2001–2007	12 months	Positive affect	GMS Positive affect sub-scale consisted of 10 mood items These items were scored on a five-point Likert scale ranging from 0 (false) to 4 (true)	HRQoL/PROs Somatic disease/ chronic illness
Pelle et al. 2011	Prospective cohort (Cardiac Rehabilitation Program at the Rotterdam	Netherlands	2004–2005	3 months	Lack of positive affect defined as a score ≤7 on the positive affect scale	HADS: the positive affect scale was computed by summing up four items	HRQoL/PROs

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Table 2 (continued)

Author(s), Year	Study design	Study location	Study period	Duration of follow-up	Measure of anhedonia	Assessment method	Outcomes reported
Petrie et al. 2018	Organization for Cardiac Rehabilitation [CAPRI] Prospective cohort	Norway (Hordaland Health)	1997–2016	14 years	Decreased positive affect and increased negative affect	GMS to cross-validate positive affect and negative affect PANAS (total 5-point scores on 20-item questionnaire with positive affect and negative affect subscales) CES-D scale	Mortality
Rathbun et al. 2020	Prospective cohort Osteoarthritis Initiative [OAI]	USA	-	4 years	General anhedonia	CES-D scale	Somatic disease/ chronic illness
Richman et al. 2005	Cross-sectional	USA	2-year period	1 year	Positive emotion (curiosity, hope) and negative emotion (anxiety and anger)	Measures of hope and curiosity were derived from two established scales, trait hope and trait curiosity Negative emotions (anger and anxiety) were assessed using the trait measures of the State-Trait Personality Inventory DISH and BDI-1	Somatic disease/ chronic illness
Sanchez et al. 2023	Prospective cohort (Prescription Use, Lifestyle & Stress Evaluation [PULSE])	USA	2009–2013	1, 6 and 12 months	Anhedonia defined by DISH and for sensitivity analysis by BDI-1; a loss of interest or pleasure in most activities for at least a few days and up to most days for more than 2 weeks on the DISH	DISH and BDI-1	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality HRQoL/PROs
Spindler et al. 2009	Cross-sectional	Denmark	-	-	Positive affect and negative affect, each determined by ten items in the GMS	GMS	Physical health
Stebenne et al. 2017	Cross-sectional (Mechanisms and Longitudinal Outcomes of Silent Myocardial Ischemia [MOSMI])	Canada	2005–2006	-	Positive affect and negative affect	PANAS-X (Expanded)	Physical health
Sullivan et al. 2001	Prospective cohort (Group Health Cooperative of Puget Sound)	USA	1991–NR	5 years (between 1- and 6-year timepoints)	Positive affect and negative affect	PANAS	HRQoL/PROs
Tully et al. 2015	Prospective cohort	Australia	2007–NR	5 years; median: 4.6 years	General anhedonia and negative affect	MASQ – 30-item to measure anhedonia, anxious arousal, anhedonia/low positive affect and general negative affect	Somatic disease/ chronic illness (results presented under mortality as endpoint includes death) Mortality HRQoL/PROs
Van Oudenhove et al. 2011	Cross-sectional	Belgium	2002–2009	-	Positive affect and negative affect	PANAS: two 10-item mood scales for positive affect and negative affect over the past 2 weeks	HRQoL/PROs
Versteeg et al. 2009	Prospective cohort	Netherlands	2005–2006	12 months	Positive affect and negative affect	GMS, with terms rated on a 5-point Likert scale	HRQoL/PROs
Whitton et al. 2023	Prospective cohort	USA	-	3 and 6 months	-	MASQ, which allows dissociation of symptoms of anhedonia from non-anhedonic symptoms of depression and anxiety	HRQoL/PROs
Willame et al. 2022	Retrospective cohort	Belgium	2017–2019	-	State anhedonia, determined by the BDI-II Anhedonia subscale; trait anhedonia, determined by the Temporal Pleasure Experience Scale	BDI-II Anhedonia subscale (for state anhedonia) and Temporal Pleasure Experience Scale (for trait anhedonia)	Somatic disease/ chronic illness

^a Study country deduced from author affiliations. AA: anxious affect; BDI: Beck Depression Inventory; CCL: Cognition Checklist; CDS: cardiac depression scale; CES-D: Center for Epidemiologic Studies Depression Scale; DA: depressed affect; DISH: Depression Interview and Structured Hamilton; EPDS: Edinburgh Postnatal Depression Scale; GMS: Global Mood Scale; GSS: General Social Survey; h: hour; HADS: Hospital Anxiety and Depression Scale; HRQoL: health-related quality of life; MASQ: Mood and Anxiety Symptom Questionnaire; MIDUS: Midlife in the United States Survey; NR: not reported; PANAS: Positive and Negative Affect Schedule; PAS: Physical Anhedonia Scale; PID-5: Personality Inventory for the Diagnostic and Statistical Manual of Mental Disorders; PRO: patient-reported outcome; SD: standard deviation; SDS: Symptom Distress Scale; SHAPS: Snaith-Hamilton Pleasure Scale; SNA: state negative affect; TNA: trait negative affect.

positively associated with physical HRQoL (Spindler, et al. 2009). High negative affect was independently associated with problems in all domains of the EuroQoL-5 Dimension (EQ-5D) (Versteeg, et al. 2009) and demonstrated an inverse correlation with HRQoL (Spindler, et al. 2009). Lack of positive affect was reported to be a significant risk factor of low physical HRQoL in a cohort of patients with gastrointestinal disorders (Van Oudenhove, et al. 2011). In adults aged ≥ 65 years, a higher positive affect score was significantly linked to a lower risk of functional decline (Leveille, et al. 1992).

Physical health outcomes

A total of seven studies reported on physical health outcomes (Table 5). Higher visual analogue scale (VAS) scores for abdominal pain were significantly linked with greater anhedonia severity in a cohort of patients with gastrointestinal disorders (Carpinelli, et al. 2019). Positive affect was associated with lower levels of inflammatory biomarkers, including tumour necrosis factor alpha (TNF α), soluble TNF receptor 2 (sTNFr2) and interleukin-6 (IL-6), and therefore less inflammation in patients with chronic heart failure (HF) (Brouwers, et al. 2013). Similar effects were observed in a study on Mexican Americans aged ≥ 65 years, which reported that high positive emotion was significantly associated with lower blood pressure (BP) (Ostir, et al. 2006). In a cohort of patients who presented for cardiac stress testing, patients with higher levels of both negative affect and positive affect were more likely to report chest pain compared with those with higher levels of negative affect but lower levels of positive affect; however, this was not documented in ischaemic patients (Stebenne, et al. 2017).

Somatic disease and chronic illness outcomes

Evidence on somatic disease and chronic illnesses was collected from five studies and is summarised in Table 6. In patients with hypertension and depression, anhedonia was significantly associated with a higher likelihood of having type 2 diabetes (T2D) (Willame, et al. 2022). One study reported that higher levels of hope and curiosity were linked to a reduced likelihood of having diseases such as hypertension and T2D (Richman, et al. 2005). Among patients with non-Type-D personality (individuals without high negative affect and social inhibition), lower levels of health status were reported by patients with low positive affect than patients with high positive affect (Pelle, et al. 2009).

Anhedonia and mortality

Mortality was the most frequently reported outcome across all included studies ($n = 18/40$). In patients with diabetic conditions, anhedonia was significantly associated with all-cause mortality (ACM) (Nefs, et al. 2016). One study reported an association between anhedonia and its role in psychiatric conditions, in relation to physical disease and mortality (Davidson, et al. 2010a). In this study, all patients with acute coronary syndrome completed the Beck Depression Inventory (BDI) and a semi-structured interview to diagnose a major depressive episode based on DSM-5 criteria. Approximately half of anhedonic patients had a major depressive episode. In addition, when both anhedonia and depressed mood were included in the multivariable adjusted model, anhedonia was the only significant predictor of major adverse cardiovascular events (MACE)/(ACM; adjusted hazard ratio [HR; 95% confidence interval (CI)]: 1.69 [1.07–2.68], $p = 0.03$). After adjusting for all covariates and major depressive episode, anhedonia remained a significant predictor (HR [95% CI]: 1.45 [1.03–2.05], $p = 0.04$). A similar result was observed after adjusting for covariates and severity of depression (HR [95% CI]: 1.52 [1.09–2.11], $p = 0.01$) (Davidson, et al. 2010a).

In primary care cohorts, somatic symptoms were predictive of coronary artery disease (CAD) events, independent of cardiovascular risk factors and other depressive symptoms (Hawkins, et al. 2014). A lack of

positive affect also mediated the relationship between depressive symptom severity and CAD events, although to a lesser effect (Hawkins, et al. 2014). However, in adults aged ≥ 65 years, there was a significant inverse association between positive affect and incidence of stroke (Ostir, et al. 2001). Mortality in patients with cardiac conditions was reported by 10 studies (Fig. 3A), five of which demonstrated independent associations of negative emotional states with significantly increased risk of mortality, with HRs ranging from 1.02 to 2.18 (Damen, et al. 2013; Davidson, et al. 2010a; Leroy, et al. 2010; Meyer, et al. 2015; Tully, et al. 2015), while two studies reported that high positive affect was associated with decreased risks of clinical events (odds ratio [OR; 95% CI]: 0.33 [0.15–0.72], $p = 0.005$) (Denollet, et al. 2008) and repeat diagnostic cardiac testing to determine the presence of coronary ischemia or coronary occlusions (Bekendam, et al. 2018; Denollet, et al. 2008). In a general cohort, three studies reported that negative emotional states were significantly associated with increased risk of mortality and/or cardiac events, with HRs from 1.06 to 1.38 (Fig. 3B) (Lawrence, et al. 2015; Nabi, et al. 2008; Petrie, et al. 2018).

Quality assessment of included studies

The included studies were assessed by the CEBM tool for prognostic studies (Table S1) (Centre for Reviews and Dissemination, 2008). While 19/37 studies met the criteria for high quality, 14/37 were classified as low quality, of which most were cross-sectional ($n = 9/14$). This was due to lack of clear reporting of the timepoint in the course of disease at which patients were recruited, the duration of follow-up and the objectivity or blinding of outcome criteria. Most studies recruited patients at a common point in the course of their disease, had an adequate follow-up period and adjusted for important prognostic factors and confounders in their analysis.

Discussion

To our knowledge, this is the first exploratory literature review investigating the specific relationship between anhedonia and a broad range of physical health and somatic diseases. Here, we provide new insights into the clinical significance of anhedonia. The findings may help to direct the attention of physicians to the wide-reaching relevance of this topic to clinical practice and to raise general awareness regarding adequate treatment of anhedonia across diagnostic (somatic or psychiatric) boundaries. This exploratory review identified 40 unique studies reporting a variety of outcomes related to the association of anhedonia and low positive affect with physical health, somatic diseases and mortality. A total of 14 studies reported at least one psychiatric diagnosis, with the most common being depression. This highlights how psychiatric conditions, often characterised by symptoms such as anhedonia and low positive affect, can influence and exacerbate physical conditions and emphasises the importance of considering the management of both mental and physical health to ensure comprehensive patient care.

In patients with cardiac, gastrointestinal and mental health conditions, and the adults aged ≥ 65 years cohort, low positive affect or anhedonia were associated with increased functional impairment and lower HRQoL, whilst higher positive affect significantly reduced the risk of functional decline. The fact that these effects were observed across a broad range of populations suggests that anhedonia may have clinical relevance regardless of whether patients have pre-existing physical conditions or psychiatric disorders. Furthermore, in cohorts of patients with gastrointestinal and cardiac disorders, greater anhedonia and higher negative affect predicted pain symptoms, indicating the extent to which emotional and physical symptoms are interconnected. Anhedonia, as a symptom of depression, was also linked to an increased likelihood of having T2D. Whereas positive affect was associated with less inflammation and positive emotional states were significantly associated with lower blood pressure. Inflammation has been associated

Table 3
Baseline characteristics of patients of relevance in included studies.

Author(s), Year	Patient cohort	Sample size	Age, years, mean (SD; unless otherwise specified)	Sex, n (%)	Race, n (%)	Comorbidities, n (%; unless otherwise specified)	Medication use, n (%)
Bekendam et al. 2018	Cardiac disorders	547	61 (9)	Male: 263 (48)	-	Chronic lung conditions: 79 (14) Gastrointestinal conditions: 67 (12) TIA or stroke: 24 (4) Thyroid disorder: 34 (6) Inflammatory condition: 44 (8) Musculoskeletal condition: 49 (9)	ACEi/ARBs: 154 (28) Beta-blockers: 246 (45) Calcium antagonists: 91 (17) Platelet inhibitors: 333 (61) Statins: 329 (60) Nitro-glycerine use: 82 (15)
Brouwers et al. 2013	Cardiac disorders	210	66.7 (8.7)	Male: 166 (79)	-	Chronic obstructive pulmonary disease: 44 (21) Hypercholesterolemia: 142 (68) Diabetes: 61 (29) Kidney failure: 65 (32)	Beta blockers: 139 (66) Nitrates: 106 (51) ACEi: 121 (58) ARBs: 70 (33) Statins: 146 (70) Diuretics: 131 (62) Psychotropic medication: 36 (17) Aspirin: 75 (36)
Byrne et al. 2018	Cardiac disorders	324	66.8 (14.4)	Male: 222 (68.5)	-	Hypertension: 143 (44.1) Atrial fibrillation: 91 (28.1) T1D or T2D: 85 (26.2) Previous MI: 14 (4.3) Ventricular tachycardia: 4 (1.2) Chronic pulmonary obstructive disease: 1 (0.3)	ACEi or ARB: 281 (86.7) Beta blocker: 234 (72.2) Diuretic: 208 (64.2) Aldosterone antagonist: 106 (32.7) Antidepressant: 30 (9.3)
Carpinelli et al. 2019	Gastrointestinal disorders	IBD/IBS patients: 120	40.8 (14.5)	Female: - (57)	-	-	IBD patients (n = 64): Oral mesalazine: 26 Biologics: 16 Immunomodulators: 8 Steroids (e.g., budesonide): 8
Cooper et al. 2002	Adults aged ≥65 years	141,589	73.7 (6.1)	Female: 81,153 (58) Male: 58,900 (-)	Asian: 2122 (-) Black: 7915 (-)	Hypertension: 72,555 (-) Emphysema COPD: 16,897 (-) Resting chest pain: 248 (-) Diabetes: 21,280 (-) Stroke: 8995 (-) Heart attack: 13,680 (-) HF: 8302 (-) Crohn's, ulcerative colitis or IBD: 7139 (-) Back pain: 16,706 (-) Prostate cancer: 3428 (-) Lung cancer: 677 (-) Colon cancer: 1328 (-) Breast cancer: 2349 (-) Short of breath: 27,540 (-)	-
Damen et al. 2013	Cardiac disorders	With anhedonia: 286	63.6 (11.3)	Male: 186 (65.0)	-	Cardiac history: 182 (65.2) Stable angina/silent ischaemia: 152 (53.3) Unstable angina: 103 (36.1) MI: 30 (10.5) Hypertension: 132 (46.2)	Aspirin: 268 (94.0) ACEi: 84 (29.5) Beta-blockers: 180 (63.2) Calcium antagonists: 144 (50.5) Diuretics: 45 (15.8)

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Table 3 (continued)

Author(s), Year	Patient cohort	Sample size	Age, years, mean (SD; unless otherwise specified)	Sex, n (%)	Race, n (%)	Comorbidities, n (%; unless otherwise specified)	Medication use, n (%)
Davidson et al. 2010a	Cardiac disorders	With anhedonia: 77	55 (11.6)	Female: 42 (55.5)	-	Hypercholesterolaemia: 227 (79.4) Diabetes: 57 (19.9) Mean (SD): Prior MI: 0.47 (0.8) Prior congestive HF: 8 (11.0) PCI during hospitalisation: 41 (55.4)	Oral nitrates: 54 (18.9) Statins: 180 (63.2) SSRI: 27 (35) Non-SSRI: 10 (13)
Davidson et al. 2010b	General	1739	46.2 (18.0)	Male: 862 (49.6)	-	-	-
Denollet et al. 2008	Cardiac disorders	874	62.2 (10.9)	Male: 629 (72)	-	MI: 327 (37) Hypercholesterolaemia: 709 (81) Hypertension: 339 (39) Renal impairment: 265 (30) Diabetes: 127 (15)	Beta blockers: 856 (-) Aspirin: 840 (-) Clopidogrel: 830 (-) Statins: - (67) Calcium antagonists: - (47) ACEi: - (26)
Doyle et al. 2012	Cardiac disorders	598	-	-	-	-	-
Ehrmann et al. 2017	Diabetes	986 (T1D: 604, T2D: 382)	T1D: 43.8 (14.2) T2D: 60.7 (9.4)	Female: T1D: - (44) T2D: - (39)	-	-	T1D: Insulin therapy: 604 (100) Insulin pump therapy: - (18) T2D: Insulin therapy: - (65) Insulin pump therapy: 0
Hawkins et al. 2014	Primary care	Depressed: 386	66.1 (-)	Female: - (76.7)	African American: - (52.1)	Diabetes: - (23.8) Hypertension: - (56.0) Hyperlipidemia: - (51.6) Excess body weight (highest quartile): - (23.3)	-
Hu and Gruber (2008)	Mixed	153	74 (8.64)	Female: - (75)	Black: - (56)	-	-
Lawrence et al. 2015	General	N = 31,481 (not happy: ^a 11.6%)	%: 18–44 (not happy): 11.2 45–64 (not happy): 12.2 65+ (not happy): 11.9 67.8 (13.4)	Male (not happy): - (11.1) Female (not happy): - (12.0)	White (not happy): - (10.0) Black (not happy): - (20.1) Other (not happy): - (14.7)	-	-
Leroy et al. 2010	Cardiac disorders	291	67.8 (13.4)	Male: 232 (-) Female: 61 (-)	-	-	-
Leveille et al. 1992	Women aged ≥65 years	1337	Sustained high function physical function: 71.9 (-) Worsened physical function: 73.7 (-)	Female: 1337 (100)	White: - (95)	-	-
Lin et al. 2018	Primary care	1055	42.5 (12.3)	Male: 355 (33.7) Female: 699 (66.3)	African-American: 972 (92.1) Hispanic: 6 (0.6) Asian: 2 (0.2) Caucasian: 45 (4.3) Mixed: 15 (1.4) Other: 12 (1.1)	Depressive symptom severity (BDI): 15.7 (12.5)	-
Luong et al. 2016	General	365	44.14 (20.27)	Female: - (55)	-	-	-

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Table 3 (continued)

Author(s), Year	Patient cohort	Sample size	Age, years, mean (SD; unless otherwise specified)	Sex, n (%)	Race, n (%)	Comorbidities, n (%; unless otherwise specified)	Medication use, n (%)
Meyer et al. 2015	Cardiac disorders	564	62.50 (11.49)	Male: - (79.7)	-	Diabetes: - (12.7) Hypercholesterolemia: - (66.1) Hypertension: - (61.8)	Aspirin: 86.6 Beta blockers: 83.2 Statins: 85.2 Diuretics: 19.1 ACEi: 64.3 Clopidogrel: 58.5
Nabi et al. 2008	General	8918	n: 39–45: 2469 45–50: 2340 50–55: 1827 55–64: 2282	Male: 6093 (-) Female: 2825 (-)	White: 8134 (-) Other: 784 (-)	Hypertension: 1645 (-) Diabetes: 81 (-)	-
Nefs et al. 2016	Diabetes	1465	67 (10)	Female: 743 (51)	Non-Western: 32 (2)	CVD: 478 (33) MI: 160 (11) Bypass/angioplasty: 190 (13) Stroke: 97 (7) Arterial disease: 306 (21) Microvascular disease: 358 (33) Retinopathy: 54 (5) Other chronic conditions: 699 (48) Kidney disease: 49 (3) Asthma/COPD: 177 (12) Cancer: 133 (9) Arthrosis: 466 (32) Rheumatoid arthritis: 102 (7) Heart attack: 301 (14) Diabetes: 429 (17)	-
Ostir et al. 2001	Adults aged ≥65 years	2478	n (%): 65–74: 1632 (66) 75–84: 730 (29) ≥85: 116 (5)	Male: 722 (-) Female: 1706 (-)	White: 1129 (46) Black: 1349 (54)	Heart attack: 301 (14) Diabetes: 429 (17)	-
Ostir et al. 2006	Adults aged ≥65 years	2564 (taking BP medication: 841, not taking BP medication: 1723)	Taking BP medication: 72.7 (6.2) Not taking BP medication: 72.4 (6.3)	Male: Taking BP medication: 280 (32.3) Not taking BP medication: 829 (46.4) Female: Non-type D low positive affect: 29 (28.2) Type D: 22 (18.2)	Hispanic: 2564 (100)	Taking BP medication: Diabetes: 287 (33.1) Not taking BP medication: Diabetes: 311 (17.4)	-
Pelle et al. 2009	Cardiac disorders	276 (non-type D low positive affect: 103, type D: 56)	Non-type D low positive affect: 66.5 (9.0) Type D: 68.0 (8.8)	Female: Non-type D low positive affect: 29 (28.2) Type D: 22 (18.2)	-	Non-type D low positive affect: Cardiac history (CABG, MI, or PCI): 69 (67.0) Stroke/TIA: 21 (20.4) Diabetes: 25 (24.3) Hypercholesterolaemia: 54 (52.4) Hypertension: 35 (34.0) Renal disease: 12 (11.7) COPD: 10 (9.7) PAD: 13 (12.6) Type D: Cardiac history (CABG, MI, or PCI): 34 (60.7) Stroke/TIA: 3 (5.4) Diabetes: 15 (26.8) Hypercholesterolaemia: 32 (57.1) Hypertension: 19 (33.9) Renal disease: 8 (14.3)	Non-type D low positive affect: Beta-blockers: 64 (62.1) ACEi: 76 (73.8) Calcium antagonists: 10 (9.7) ARB: 18 (17.5) Spironolactone: 19 (18.4) Nitrates: 28 (27.2) Statins: 50 (48.5) Aspirin: 40 (38.8) Diuretics: 76 (73.8) Type D: Beta-blockers: 39 (69.6) ACEi: 42 (75.0) Calcium antagonists: 13 (23.2) ARB: 11 (19.6) Spironolactone: 11 (19.6)

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Table 3 (continued)

Author(s), Year	Patient cohort	Sample size	Age, years, mean (SD; unless otherwise specified)	Sex, n (%)	Race, n (%)	Comorbidities, n (%; unless otherwise specified)	Medication use, n (%)
						COPD: 6 (10.7) PAD: 10 (17.9)	Nitrates: 21 (37.5) Statins: 33 (58.9) Aspirin: 24 (42.9) Diuretics: 49 (87.5) ACEi: 47 (63.5) Calcium antagonists: 5 (6.8) Nitrates: 15 (20.3) Statins: 62 (83.8) Aspirin: 57 (77.0) Diuretics: 10 (13.5) Anti-depressants: 10 (13.5) Anxiolytics: 12 (16.2)
Pelle et al. 2011	Cardiac disorders	With anhedonia: 74	57.7 (10.1)	Male: 58 (78.4)	-	Diabetes: 13 (17.6) Dyslipidaemia: 42 (56.8) Hypertension: 27 (36.5) COPD: 6 (8.1)	-
Petrie et al. 2018	General	5554 (PANAS: positive affect lower tertile: 1629, middle tertile: 1915, PANAS: negative affect middle tertile: 2137, upper tertile: 1836)	%: PANAS: positive affect Lower tertile: 47–49: 40.5 71–74: 59.5 Middle tertile: 47–49: 54.8 71–74: 45.2 PANAS: negative affect Middle tertile: 47–49: 55.3 71–74: 44.7 Upper tertile: 47–49: 52.2 71–74: 47.8	PANAS: positive affect Lower tertile, male: - (45.4) Female: - (54.6) Middle tertile, male: - (46.8) Female: - (53.2) PANAS: negative affect Middle tertile, male: - (46.7) Female: - (53.3) Upper tertile, male: - (40.0) Female: - (60.0)	-	PANAS: positive affect Lower tertile: MI: - (6.3) Angina: - (8.4) Stroke: - (3.6) Diabetes: - (4.5) Middle tertile: MI: - (4.8) Angina: - (6.4) Stroke: - (1.7) Diabetes: - (3.3) PANAS: negative affect Middle tertile: MI: - (5.1) Angina: - (5.9) Stroke: - (1.6) Diabetes: - (3.3) Upper tertile: MI: - (5.0) Angina: - (7.5) Stroke: - (2.7) Diabetes: - (3.4)	-
Rathbun et al. 2020	Other	474	61.87 (9.81)	Female: 283 (59.7)	White: 122 (25.7)	History of knee injury: 133 (28.4)	Analgesic use: 196 (41.4)
Richman et al. 2005	Mixed	1041	Level of hope: Low: 61.8 (-) Medium: 61.7 (-) Level of curiosity: Low: 62.0 (-) Medium: 61.9 (-)	Male: Level of hope: Low: - (46) Medium: - (45) Level of curiosity: Low: - (44) Medium: - (44)	-	-	
Sanchez et al. 2023	Cardiac disorders	Anhedonia depression: 95	60.5 (11.3)	Male: 35 (36.9)	Hispanic: 42 (44.2) Black: 25 (26.0)	Hypertension: 80 (83.9) Dyslipidaemia: 59 (62.5)	Aspirin: 94 (98.5) Clopidogrel: 74 (78.1) Statin/lipid lowering: 88 (92.7) Beta blocker: 81 (85.5)
Spindler et al. 2009	Cardiac disorders	502	65 (10.2)	Male: 309 (78)	-	Diabetes: 76 (15) Hypertension: 99 (20) Hypercholesterolaemia: 278 (56) Angina: 371 (88)	-

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Table 3 (continued)

Author(s), Year	Patient cohort	Sample size	Age, years, mean (SD; unless otherwise specified)	Sex, n (%)	Race, n (%)	Comorbidities, n (%; unless otherwise specified)	Medication use, n (%)
Stebenne et al. 2017	Cardiac disorders	246	59.9 (10.6)	Male: - (65)	White: - (95)	MI: - (24) Hypertension: - (61) Diabetes: - (14)	-
Sullivan et al. 2001	Cardiac disorders	111	62.0 (9.1)	Male: - (8)	-	-	-
Tully et al. 2015	Cardiac disorders	158	64.7 (10.6)	Female: 33 (20.9)	Aboriginal: 6 (3.8)	Hypertension: 102 (64.6) Hypercholesterolaemia: 118 (74.7) T1D: 2 (1.3) T2D: 48 (30.4) Chronic lung disease: 33 (20.9) Renal disease: 11 (7.0) HF: 40 (25.3) Peripheral vascular disease: 18 (11.4) Cerebrovascular disease: 16 (10.1) Previous MI <30 days: 51 (32.3)	SSRI: 6 (3.8) Tricyclic: 3 (1.9) Aspirin: 122 (77.2)
Van Oudenhove et al. 2011	Gastrointestinal disorders	259	39.5 (12.9)	Female: 195 (75)	-	-	-
Versteeg et al. 2009	Cardiac disorders	562 (GMS negative affect high: 242; GMS positive affect low: 259)	GMS negative affect High: 62.9 (11.8) GMS positive affect Low: 63.2 (11.0)	Female: GMS negative affect High: 87 (36.0) GMS positive affect Low: 77 (29.7)	-	GMS negative affect High: MI: 81 (33.5) Multi-vessel disease: 106 (43.8) Hypertension: 104 (43.0) Hypercholesterolaemia: 210 (86.8) Diabetes: 42 (17.4) GMS positive affect Low: MI: 83 (32.0) Multi-vessel disease: 117 (45.2) Hypertension: 114 (44.0) Hypercholesterolaemia: 220 (84.9) Diabetes: 43 (16.6)	GMS negative affect High: Aspirin: 223 (92.1) Calcium antagonists: 10 (4.1) Beta-blockers: 153 (63.2) ACEi: 99 (40.9) Statins: 175 (72.3) Diuretics: 27 (11.2) GMS positive affect Low: Aspirin: 239 (92.3) Calcium antagonists: 9 (3.5) Beta-blockers: 165 (63.7) ACEi: 95 (36.7) Statins: 192 (74.1) Diuretics: 22 (8.5) 32 (40)
Whitton et al. 2023	Mental health disorders	Mood disorder: 80	28.7 (9.7)	Female: 54 (67.5)	White: 59 (73.8) Hispanic: 8 (10.0)	Unipolar mood disorder (MDD/dysthymia or MDD in partial remission): 58 (72.5) Bipolar mood disorder (I/II, depressed, mixed or hypomanic): 22 (27.5) Untreated hypertension: 153 (47.4) Controlled hypertension: 95 (29.4) Uncontrolled hypertension: 75 (23.2) Complicated hypertension: 70 (21.6) Dyslipidaemia: 185 (57.3) Cardiovascular comorbidities: 62 (19.2) T2D: 61 (18.9)	
Willame et al. 2022	Cardiac disorders	323	n (%): <50: 134 (41.5) ≥50 and <65: 150 (46.4) ≥65: 39 (12.1)	Male: 206 (63.8) Female: 117 (36.2)	-		Benzodiazepine receptor agonists: 45 (13.9) Antidepressant therapy: 67 (20.7) Other psychotropic treatments: 23 (7.1)

^a Patients who responded 'not happy' in response to the question "Taken all together, how would you say things are these days—would you say that you are very happy, pretty happy, or not too happy?" ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor antagonist; BDI: Beck Depression Inventory; BP: blood pressure; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; GMS: Global Mood Scale; HF: heart failure; IBD: inflammatory bowel disease; IBS: irritable bowel syndrome; MDD: major depressive disorder; MI: myocardial infarction; PAD: peripheral arterial disease; PANAS: Positive and Negative Affect Schedule; PCI: percutaneous coronary intervention; SD: standard deviation; SSRI: selective serotonin re-uptake inhibitor; T1D: type 1 diabetes; T2D: type 2 diabetes; TIA: transient ischemic attack.

with decreased dopamine availability and release (Bekhhbat, et al. 2022). Dopamine signalling underpins reward processing pathways implicated in anhedonia; hence, inflammation-related metabolic changes may contribute to the somatic health risks observed in individuals with anhedonia (Bekhhbat, et al. 2022).

Similar effects were reported in a study of 10,815 participants with newly diagnosed cardiovascular diseases in the UK Biobank, whereby the lowest psychological wellbeing score had the highest risk for cardiovascular disease (Sun, et al. 2022). The opposing outcomes for negative and positive affect emphasise the significant impact of emotional state on physical health, particularly with respect to the protective effects of positive emotions. Additionally, significant positive associations between anhedonia/negative emotional states, and mortality were reported in 10 studies, including patients with cardiac and diabetic conditions and the general population. This demonstrates the extent to which anhedonia may affect a patient's prognosis (Davidson et al., 2010a). In one study, only anhedonia predicted the risk of MACE and ACM beyond the power of all covariates and other depression indices, suggesting a clear connection between anhedonia and its role in physical disease and mortality.

Most studies included patients with cardiac conditions, which may be reflective of psychocardiology as an interdisciplinary field being one of the first to focus on the reciprocal, bidirectional relationship between heart disease and mental health. These findings are consistent with the documented relationship between aspects of anhedonia (notably reward processing) and obesity, both on its own and with comorbid MDD (Mansur, et al. 2019). Individuals with obesity and MDD may exert less effort in tasks compared with those of with lower body mass indexes (Mansur, et al. 2019). These individuals are also more likely to achieve poorer outcomes in weight loss programmes as they can find it harder to implement and adhere to changes in diet (Komulainen, et al. 2011). These disturbances in reward processing, which are also implicated in anhedonia, require further clinical support to ensure long-lasting chronic disease management and effective counselling (Gill, et al. 2023). The aforementioned studies align with multiple lines of

evidence indicating a robust association between disparate dimensions of anhedonia and obesity (Hajje, et al. 2026). Recently, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide receptor agonists (GIP RAs) have been used to treat diabetes and obesity, and there is evidence of potential preventative effects against cognitive dysfunction and depressive symptoms in patients with mental health disorders (McIntyre, et al. 2025b). This suggests they could be beneficial in patients with anhedonia. In addition, anhedonia has been implicated as a risk factor for suicidality and suicidal ideation (Gillissie, et al. 2023; Serretti 2023). Data are mixed as to the association between GLP-1 RA use and suicidality, however, the most comprehensive literature indicates that there is no causal relationship (Hurtado, et al. 2024; McIntyre, et al. 2025a; et al. 2025b; Ueda, et al. 2024; Wang, et al. 2024). Understanding the connections between the pathways underpinning somatic diseases and anhedonia may inform the development of novel interventions.

The findings regarding positive affect are equally important, as anhedonia and lack of positive affect are both dimensions of PMH. Many studies reported a link between greater positive psychological wellbeing and improved physical health outcomes. For example, beneficial effects have been noted in patients with coronary heart disease, where increases by an SD (8.8-point) in positive affect score were associated with a 16% decreased risk of all-cause mortality (Hoen, et al. 2013). Similarly, in a review based on cardiovascular disease, positive affect was protective against 10-year incident coronary heart disease and associated with decreased risk of death and myocardial infarction for 2 years following stent implantation (Sin 2016). These findings are crucial for understanding how a deficiency in positive affect, such as in the case of anhedonia, may impact physical health. A prospective cohort study in Japan found that higher life satisfaction was significantly associated with a reduced risk of atherosclerotic cardiovascular disease, independent of traditional risk factors and stress (Arafa, et al. 2023). Similarly, in a survey of 12,998 participants in the University of Michigan's Health and Retirement Study, higher life satisfaction was associated with lower risk of pain and mortality and improved physical functioning (Kim, et al.

Table 4
HRQoL and patient-reported outcomes.

Study name	Definition of anhedonia	Outcome	Outcome measurement method	Follow-up	Relative effect measure	Value (95% CI)	p-value
Cohort of patients with cardiac disorders Spindler et al. 2009	Negative affect	Physical component summary	SF-36	N/A	Coefficient	NR	NR
Spindler et al. 2009	Positive x negative affect	Physical component summary	SF-36	N/A	Coefficient	−0.36 (NR–NR)	0.005
Spindler et al. 2009	Positive affect	Physical component summary	SF-36	N/A	Coefficient	0.21 (NR–NR)	0.03
Pelle et al. 2009	Low positive affect (non-Type D)	Physical component summary	SF-21	1 year	Coefficient	−0.11 (NR–NR)	0.07
Versteeg et al. 2009	Negative affect (high)	Mobility Self-care Usual activities Pain/discomfort	EQ-5D	1 year	Odds ratio ^a	2.63 5.33 2.80 2.43	<0.001 0.04 <0.001 <0.001
Versteeg et al. 2009	Positive affect (low)	Mobility Self-care Usual activities Pain/discomfort	EQ-5D	1 year	Odds ratio ^a	0.97 8.14 1.87 1.24	0.89 0.006 0.009 0.33
Cohort of patients with gastrointestinal disorders Van Oudenhove et al. 2011	Positive affect (lack of)	Physical composite summary	SF-36	N/A	Coefficient	0.03 (NR–NR)	<0.0001
Adults aged ≥65 years Leveille et al. 1992	Positive outlook and mood	Physical function	Unspecified scale	1 year	Hazard ratio	0.61 (0.43–0.84)	NR
Cohort of patients with mental health disorders Whitton et al. 2023	Anhedonia (severe)	Physical component summary	SF-36	3 months and 6 months	Coefficient	−3.65 (−5.28 – −2.03)	<0.001

^a The OR for high negative affect was calculated relative to low negative affect, while the OR for low positive affect was compared to high positive affect. Only the most comprehensively adjusted multivariable analyses are presented. Follow-up duration is marked as N/A for cross-sectional studies. Bold text indicates statistical significance. CI: confidence interval; EQ-5D: EuroQol-5 dimensions; N/A: not applicable; NR: not reported; SF-21/36: 21/36-Item Short Form Survey.

Table 5
Physical health outcomes.

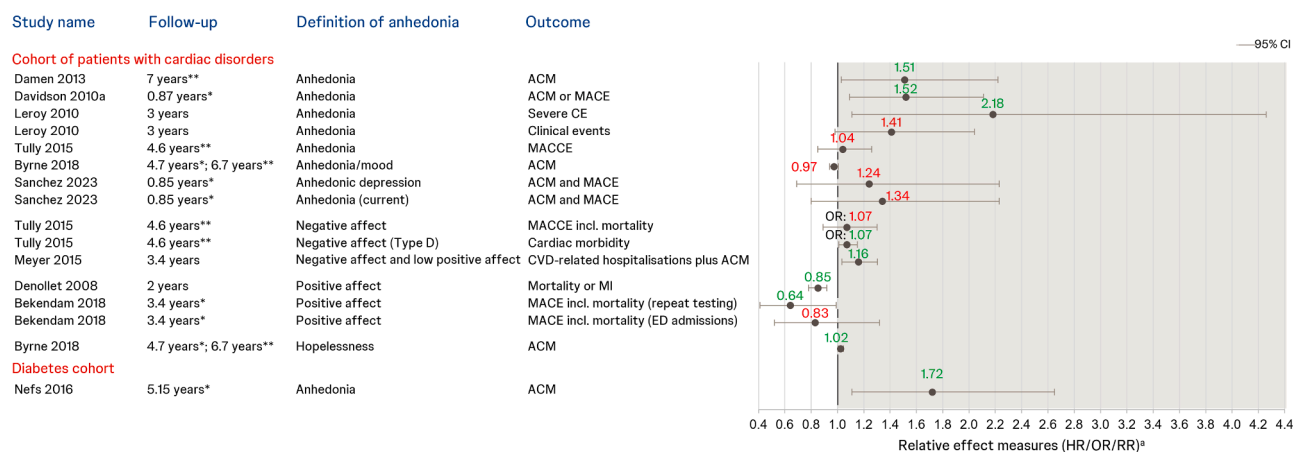
Study name	Definition of anhedonia	Outcome	Outcome measurement method	Follow-up	Relative effect measure	Value (95% CI)	p-value
Cohort of patients with cardiac disorders Stebenne et al. 2017	Negative affect	Chest pain	10-point rating scale	N/A	Odds ratio	1.02 (1.01–1.02)	<0.001
Brouwers et al. 2013	Positive affect	sTNFr2	Blood sampling	1 and 1.5 years	Coefficient	3.78 (NR–NR)	0.053
Stebenne et al. 2017	Positive affect	Chest pain	10-point rating scale	N/A	Odds ratio	1.01 (1.00–1.02)	0.038
Cohort of patients with gastrointestinal disorders Carpinelli et al. 2019	Anhedonia	Abdominal pain	VAS	N/A	Coefficient	0.007 (0.001–0.14)	0.03
Patients aged ≥65 years Ostir et al. 2006	Positive emotion	Blood pressure	Sphygmomanometer	NR	Odds ratio	0.97 (0.93–1.00)	NR

Only the most comprehensively adjusted multivariable analyses are presented. Follow-up duration is marked as N/A for cross-sectional studies. Bold text indicates statistical significance. CI: confidence interval; N/A: not applicable; NR: not reported; sTNFr2: soluble tumour necrosis factor receptor 2; TNF-α: tumour necrosis factor-α; VAS: visual analogue scale.

Table 6
Somatic disease/chronic illness outcomes.

Study name	Definition of anhedonia	Outcome	Outcome measurement method	Follow-up	Relative effect measure	Value (95% CI)	p-value
Cohort of patients with cardiac disorders Willame et al. 2022	Anhedonic depression	T2D	T2D diagnosis criteria	NR	Odds ratio	2.62 (1.21–5.66)	<0.05
Willame et al. 2022	Non-anhedonic depression	T2D	T2D diagnosis criteria	NR	Odds ratio	0.92 (0.36–2.37)	<0.05
Pelle et al. 2009	Non-type D and low positive affect	Cardiac symptoms	HCS	1 year	Coefficient	0.04 (NR–NR)	0.43
Pelle et al. 2009	Non-type D and low positive affect	Feelings of disability	HCS	1 year	Coefficient	0.1 (NR–NR)	0.04
Mixed cohort Richman et al. 2005	Hope (highest scores)	Hypertension incidence	Patient records	1 year	Odds ratio	0.52 (0.27–0.99)	<0.05
Richman et al. 2005	Curiosity (highest scores)	Hypertension incidence	Patient records	1 year	Odds ratio	0.36 (0.18–0.71)	<0.01
Richman et al. 2005	Hope (highest scores)	Diabetes mellitus prevalence	Patient records	1 year	Odds ratio	0.52 (0.28–0.96)	<0.05
Richman et al. 2005	Curiosity (highest scores)	Diabetes mellitus prevalence	Patient records	1 year	Odds ratio	0.56 (0.32–0.97)	<0.05
Richman et al. 2005	Hope	RTIs	Patient records	1 year	Coefficient	–0.16 (NR–NR)	0.14

Only the most comprehensively adjusted multivariable analyses are presented. Bold text indicates statistical significance. These are not head-to-head studies and therefore all data should be interpreted with caution. CI: confidence interval; RTIs: respiratory tract infections; HCS: health complaints scale; NR: not reported; T2D: type 2 diabetes.

**Fig. 3A.** Mortality outcomes for metabolic conditions.

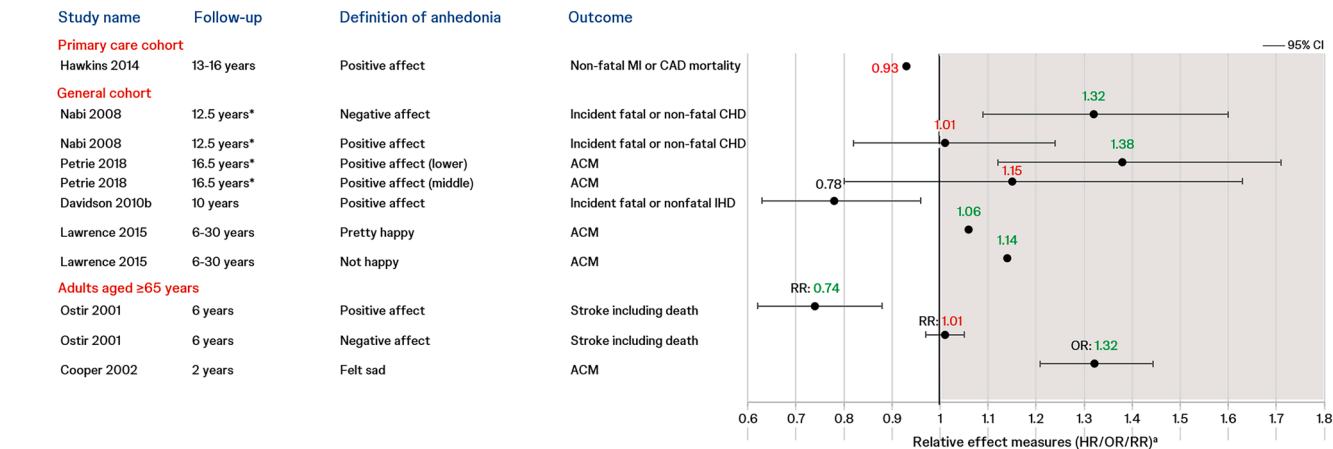


Fig. 3B. Mortality outcomes in a general cohort.

^aThe reference groups for each condition comprised individuals without the specified conditions (e.g., those without negative or positive affect). However, in Petrie et al. (2018), the reference group for the lower/middle tertile of positive affect was individuals in the higher tertile of positive affect, and in Lawrence et al. (2015), the reference group consisted of individuals who were very happy. All studies report HR except Tully et al. (2015) and Cooper et al. (2002) where OR was reported and Ostir et al. (2001) where RR was reported. *Mean, **Median follow-up. Only the most comprehensively adjusted multivariable analyses are presented. Relative effect measures are colour coded based on statistical significance (red: no statistical significance; green: statistical significance; black: not reported). ACM: all-cause mortality; CAD: coronary artery disease; CE: cardiac event; CHD: coronary heart disease; CVD: cardiovascular disease; ED: emergency department; HR: hazard ratio; IHD: ischaemic heart disease; MACCE: major adverse cardiovascular and cerebrovascular events; MACE: major adverse cardiovascular event; MI: myocardial infarction; OR: odds ratio; RR: risk ratio.

2021). These findings suggest that enhancing positive affect, as well as enhancing hedonic tone, may be important treatment targets to improve overall PMH and associated physical health outcomes (Van Agteren, et al. 2021).

Given the growing evidence of its clinical impact, there is a need for greater identification and monitoring of anhedonic symptoms across all clinical settings. This should be facilitated by the wider adoption of validated and harmonised scales for more nuanced diagnostics (e.g., the Dimensional Anhedonia Rating Scale [DARS], the Leuven Affect and Pleasure Scale [LAPS] or the Snaith-Hamilton Pleasure Scale, the latter most frequently used despite the unclear formulation of the items) and the education of healthcare professionals to raise awareness of the transdiagnostic relevance of anhedonia to somatic disciplines (Franken, et al. 2007; Pan, et al. 2025; Trøstheim, et al. 2020). Current depression scales often omit any measures of anhedonia, which is concerning given the aforementioned increased risk of suicide in patients with depressive disorders with this symptom (Gillissie, et al. 2023; Serretti 2023). Recent research has found that esketamine, a treatment approved by the Food and Drug Administration and European Medicines Agency for moderate to severe treatment resistant depression, demonstrates an anti-anhedonic effect that is independent of its broader effects on other depressive symptoms (Danon, et al. 2026). Despite this, there is still limited choice in terms of effective treatment, emphasising the need to prioritise the development of treatments that specifically target anhedonia and other residual symptoms to directly impact hedonic tone (Carney, et al. 2024; Pizzagalli 2022).

Our review did not explore the underlying mechanisms of anhedonia, for which research is currently limited, but there is evidence to suggest that anhedonia can also alter the perception of somatic symptoms in patients with depression (Pérez-Morenilla, et al. 2025). It is important to note that the temporal and causal relationships remain unclear, and these results reinforce the need for further longitudinal research to elucidate the relationships and observe how anhedonia affects the progression of somatic diseases over time. Additionally, another study reported that inflammation may induce anhedonic symptoms in animal models and human studies, suggesting a common cause of both anhedonia and somatic conditions (Swardfager, et al. 2016). Among individuals with post-COVID-19 condition, or “long covid”, higher baseline anhedonia was associated with greater

impairment of psychosocial functioning (Liao, et al. 2024). This may indicate that anhedonia serves as an index of underlying pathology, but the potential relevance of behavioural aspects imposed by anhedonia should also be considered. Our findings highlight the need for research into these pathways, as treating anhedonia could result in significant clinical benefits.

Strengths and limitations

While the literature reported here covers several population types, future research would benefit from including more diverse populations in studies, helping to identify relevant genetic and environmental factors that underpin the impact of anhedonia on physical health.

Approximately half of the included studies were rated as high quality, providing moderate confidence in the overall evidence base; however, further high-quality research is needed to strengthen confidence in these findings. Most of the cross-sectional studies in our analysis were deemed low in quality due to insufficient information on the temporality between exposure and outcome. This limitation increases the risk of selection bias, which is a known limitation of the evidence base. Additionally, there was more available evidence than initially anticipated, so a threshold of more than 100 patients was applied to prioritise more robust samples, resulting in the exclusion of 12 studies and potentially contributing to the selection bias. A variety of tools to define anhedonia and outcomes were used across the studies, limiting the direct comparability between studies and generalisability to the wider population, as well as precluding quantitative analyses. Nevertheless, this analysis included a range of evidence reporting various somatic diseases linked to anhedonia.

Furthermore, in some included studies, anhedonia overlapped with broader depressive experiences and somatic illnesses. Given that studies were eligible for inclusion if they reported anhedonia due to, or related to, mental disorders, it was not always possible to determine whether the effects of anhedonia were examined independently or as part of wider depressive experiences. Future research should seek to disentangle the specific contribution of anhedonia within these populations. This construct overlap extends to the temporal relationship between anhedonia and somatic illnesses. Although the search strategy was designed to identify studies in which anhedonia preceded somatic

illness, it cannot be ruled out that anhedonia was in some cases secondary to somatic disease processes, for example as a consequence of chronic inflammation associated with these conditions (Bekhat, et al. 2022; Goldsmith, et al. 2023).

This review was conducted in accordance with a pre-determined protocol, ensuring methodological rigour and consistency throughout the process. The broad definitions of anhedonia used in a comprehensive search strategy and citation chaining procedure allowed targeted and efficient identification of a wide evidence base. Per typical exploratory review methodology, abstracts and full texts were screened by a single reviewer, ensuring that a consistent approach was taken to enhance reliability and reduce selection bias. In addition to this, a subset of screening decisions was verified by a second reviewer, thereby reducing the risk of erroneous exclusions. Nevertheless, lack of systematic searching, time limits on the citation chaining process and inclusion of English-only publications may have resulted in some relevant studies being overlooked.

Conclusions

To our knowledge, this is the first exploratory literature review to compile data on the association between anhedonia and physical health (somatic diseases). Although evidence on causal links remains limited, this review suggests that anhedonia, whether occurring in the context of depression, another psychiatric disorder, or somatic illness, may represent an underappreciated prognostic factor in somatic medicine. We present evidence that lack of positive affect, or anhedonia, may increase functional impairment and reduce HRQoL, and is linked to pain symptoms and increased risk of developing diseases such as T2D. Meanwhile, higher positive affect acts as a protective factor, reducing risk of disease and mortality. It is also correlated with lower risk of functional decline and lower levels of inflammatory biomarkers when compared with low positive affect. Our findings underscore the importance of diagnosing, monitoring and treating anhedonia across both psychiatric and somatic clinical disciplines to improve all domains of patient health and wellbeing.

Authors' contributions

Substantial contributions to study conception and design: **KD, MA, AB, AF, PG, YK, SM, AR, JR, TWK, RSM**; substantial contributions to analysis and interpretation of the data: **KD, MA, AB, AF, PG, YK, SM, AR, JR, TWK, RSM**; drafting the article or revising it critically for important intellectual content: **KD, MA, AB, AF, PG, YK, SM, AR, JR, TWK, RSM**; final approval of the version of the article to be published: **KD, MA, AB, AF, PG, YK, SM, AR, JR, TWK, RSM**.

Disclosures

KD: Advisory board/lecturing fees for Boehringer Ingelheim, Eli Lilly and Company, Jamjoom, Johnson & Johnson, LivaNova, Lundbeck, Seaport, Sothema and Viatris.

MA: Advisory board/speaker for Johnson & Johnson.

AB: Employee of Costello Medical UK at the time of writing. Now an employee of Evidence Witch, Cambridge, UK.

AF: Consultant and/or speaker and/or received research grants from Angelini, Boehringer Ingelheim, Idorsia, Italfarmaco, Lundbeck, Janssen, Medicamenta, Mylan, Otsuka, Pfizer, Recordati, Rovi, Sunovion, Teva and Viatris.

PG: During the last 5 years, participated in meetings and advisory boards for AbbVie, Johnson & Johnson, Lundbeck, MindMed, Newron and Viatris.

YK, JR, TWK: Employees of Johnson & Johnson, hold Johnson & Johnson company stock/stock options.

SM: Participated in advisory boards for AMD, Boehringer Ingelheim, Johnson & Johnson, Lundbeck, Newbridge and Pfizer; received

speaker's honoraria for AbbVie, Biogen, Exeltis, Genpharma, Hikma, Johnson & Johnson, Labatec, Eli Lilly and Company, Lundbeck, MSD, Newbridge, Pfizer, Servier, Spimako, Takeda and Viatris.

AR: Participated in advisory boards for and/or received speaker's honoraria over the last three years from AbbVie, Boehringer Ingelheim, Compass, Cyclorion, FoMF, GH Research, Johnson & Johnson, LivaNova, Medice, MSD, Newron, SAGE/Biogen and Shire/Takeda; received research grants from Johnson & Johnson and Medice; board member of DGBS, DGPPN, ECNP and German Depression Foundation, aided in developing National Care Guidelines (NVL, S3) on ADHD, bipolar disorder, major depression and suicidal behaviour.

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Declaration of competing interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.euroneuro.2026.112902](https://doi.org/10.1016/j.euroneuro.2026.112902).

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