

REVIEW

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# Quality of life in patients with acromegaly: a scoping review

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## Abstract

**Purpose** To evaluate the available evidence regarding the quality of life (QoL) in patients with acromegaly, by synthesizing the psychosocial factors of QoL, QoL measures, and complementary interventions targeting QoL.

**Methods** A scoping review was conducted using the PRISMA-ScR guideline. We searched six English databases (PubMed, Embase, CINAHL, Scopus, Web of Science, and the Cochrane Library) from the inception to August 21, 2023. We included observational studies involving psychosocial factors and complementary interventions targeting QoL (concept) in patients with acromegaly (population) in any setting (context). The design characteristics, psychosocial factors, measures, details of interventions, and outcomes of included studies were described in detail.

**Results** Twenty-one studies were identified, including sixteen cross-sectional studies and five interventional studies. Ten categories of psychosocial factors that are associated with QoL in acromegaly. Depression and anxiety were the most frequent psychosocial factors. Seven different validated QoL measures were used. AcroQoL was the most common measure. Two categories of complementary interventions targeting QoL were identified including psychological and exercise interventions.

**Conclusions** Our scoping review provides a reasonably clear picture of the current research status of QoL in acromegaly. However, this review also highlights the need to deepen understanding of QoL and psychosocial factors in the future, as well as conduct longitudinal research and qualitative research to clarify the changing trends of psychosocial factors and specific experiences of patients. Further, more potential clinical complementary interventions are needed to improve QoL for patients with acromegaly.

**Keywords** Acromegaly, Quality of life, Psychosocial factors, Scoping review

## Introduction

Acromegaly is a rare and insidious hormonal disorder, characterized by excessive secretion of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) [1]. The prevalence is between 28 and 137 cases per million and the incidence lies between 2 and 11 cases per million per

year [2]. As a result of the excessive secretion of GH and IGF-1, patients with acromegaly may experience changes in facial appearance and enlargement of the hands and feet, as well as other multiple system disorders, including cardiovascular disorders, endocrine and metabolic disorders, musculoskeletal disorders, neuropsychological diseases, and malignant neoplasm [3]. A multimodal therapeutic approach can be achieved including surgery, radiation, and medication therapy in clinical practice, which effectively improves the morbidity and mortality of patients [4]. Traditional clinical treatment goals for acromegaly include biochemical control, tumor size

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reduction, and signs/symptoms improvement [5]. While there is an inconsistency between the biochemical control and the result of quality of life (QoL) [6, 7]. Wolters et al. [6] published a prospective study about the QoL before and during the first 2.5 years of acromegaly treatment. They found all patients had achieved disease control through surgery and/or medication treatment, but QoL remained impaired and was still lower than the general population during the study period. In the other prospective study, Kyriakakis et al. [7] stated that impaired QoL primarily consisted of physical function and psychosocial well-being.

In addition, the diagnosis of acromegaly is often delayed, and some irreversible acromegaly-associated comorbidities may develop during the delay [8]. This means that a significant portion of patients are still affected by the irreversible long-term effects of acromegaly, resulting in impaired QoL [9]. QoL as an important parameter in clinical practice can help healthcare professionals better understand patients' subjective feelings about the impact of their diseases. The World Health Organization (WHO) defines QoL as "an individual's perception of their position in life, in the context of culture and value system in their life and relation to their goals, expectations, standards, and concerns" [10]. The goals of health outcomes include reduction of mortality, morbidity and improvement of QoL [11]. However, studies of the impact on the QoL of patients with acromegaly typically focus on biological elements, such as biochemical control and therapeutic approach [12–14]. Comparatively fewer studies explore the psychosocial aspects of QoL, which could provide key information about the impact on QoL of patients with acromegaly.

Psychosocial factors are defined as any exposure that may affect physical health outcomes through psychological mechanisms, including individual cognition, emotion, personality, social interaction, and so on [15], which are candidate modifiable factors to QoL for patients with acromegaly. Acromegaly has been reported to be associated with psychological comorbidities such as depression [16] and anxiety [17]. A recent study showed the superiority of psychopathology (depression and anxiety) over biochemical control and other variables in predicting QoL [18]. Further, acromegaly is associated with progressive morphometric changes. It has been reported that negative perception of body image is related to impaired social relationships QoL domain in other pituitary tumor patients [19]. Thus, the assessment and therapy of psychosocial factors for patients with acromegaly need to be considered.

It is necessary to raise again that biochemical control does not mean an improvement of QoL. So the complementary interventions targeting QoL beyond conventional therapy (surgery, radiation, and medication

therapy) become of paramount importance. Yet, the existing literature on interventions targeting QoL is heterogeneous and inconclusive. In 2017, Geraedts et al. [20] conducted a systematic review of predictors of QoL in patients with acromegaly. They found depressive symptoms and BMI were significant predictors of QoL in acromegaly, and only interventions with lanreotide autogel and pegvisomant were shown to consistently improve QoL. Broersen et al. [21] reported QoL improved during acromegaly treatment in a systematic review, most of the studies they included identified medication as the main treatment.

Therefore, in this review, using the framework of Arksey and O'Malley [22], we aimed to comprehensively review psychosocial factors of QoL, QoL measures, and complementary interventions target QoL, with the specific aims of describing the designs and the defining features of included studies. The specific research questions that guided this scoping review were as follows: (1) What psychosocial factors affect the QoL in patients with acromegaly? (2) What types of complementary interventions target QoL beyond conventional therapy (surgery, radiation, and medication therapy) in patients with acromegaly? (3) What are measures for QoL in patients with acromegaly?

## Methods

This scoping review is conducted following the framework of Arksey and O'Malley and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [23]. PRISMA-ScR checklist is presented in Appendix 1. This scoping review was not registered.

## Search strategy

Our research team consulted 2 information specialists and reviewed previous relevant studies to develop search strategies. We performed a comprehensive literature search using six electronic databases, including PubMed, Embase, CINAHL, Scopus, Web of Science, and the Cochrane Library. All databases were searched from the inception to August 21, 2023. The reference lists in the included studies were traced back to identify additional studies. The search strategy combined terms for (1) acromegaly, and (2) QoL, and has been included as Appendix 2.

## Eligibility criteria

The eligibility criteria were developed according to the PCC (Participants /Concept /Context) structure [24]. Participants were diagnosed with acromegaly by any available diagnostic criteria. The concept of this scoping review was observational studies involving psychosocial factors (e.g. cross-sectional studies or cohort studies) and

interventions targeting QoL in patients with acromegaly. And in our scoping review, there were no limits to the context.

We excluded interventions that target QoL through medical therapy (e.g. pegvisomant, lanreotide, somatostatin), and the interventions compared different treatment methods (e.g. surgery vs. medicine). QoL measures that have not been validated (e.g. Patient Assessed Acromegaly Symptom Questionnaire, PASQ) and didn't focus on overall QoL were also excluded. In addition, newspaper articles, comments, and conference abstracts were not included.

### Study selection

EndNote X9 was used to manage all the retrieved studies. The study selection was conducted in two steps. In the first step, two investigators independently reviewed the titles and abstracts against the inclusion and exclusion criteria. The full text of potentially relevant studies was screened against the eligibility criteria in the second step. Any disagreements were resolved by consensus with a third review investigator.

### Data extraction and charting

A standardized data extraction table was developed by our research team. The relevant data on psychosocial factors were extracted, including author, year of publication, country, study design, sample, disease duration, psychosocial measure, and QoL measure. The relevant data of interventions target QoL in patients with acromegaly were extracted, including author, year of publication, country, study design, sample, type of intervention, content of intervention, and does. Two investigators independently extracted data according to the eligibility criteria. In case of disagreements, a third investigator was involved.

## Results

### Overview of selected papers

The six electronic databases and references screening yielded 2419 studies. We removed 1511 duplicates, leaving 908 studies. Of these studies, 748 were excluded through the title and abstract screening process, and 160 studies were subsequently full-text reviewed. 139 studies were excluded with reasons: surgery and/or medication interventions ( $n=71$ ); not psychosocial factors ( $n=30$ ); non-validated QoL measure and aspects of QoL ( $n=12$ ); conference papers ( $n=26$ ). We ultimately included 21 studies [18, 25–44] in our review, including sixteen cross-sectional studies [18, 25–39], and five intervention studies [40–44]. A flow chart of the study selection is presented in Fig. 1.

### Design characteristics

Sixteen cross-sectional studies were published between 2004 and 2022 [18, 25–39], and the sample size ranged from 40 [32] to 291 [36] patients. Four studies were conducted in the Netherlands [30, 34, 35, 38], three in Italy [25, 28, 39], two in China [33, 37] and Turkey [26, 27] respectively, and a single study in Belgium [36], Germany [18], Greece [32], Mexico [29] and Poland [31] respectively.

Five intervention studies were published between 2014 and 2023 [40–44], including one randomized controlled trial [40], two non-randomized clinical trials [42, 44], and two self-comparison before and after trials [41, 43]. The sample size ranged from 7 [41] to 45 [40] patients. Two studies were conducted in Brazil [42, 43] and Turkey [41, 44] respectively, and one multicenter study [40] in Spain and Italy. Tables 1 and 2 show an overview of the studies included.

### Psychosocial factors of QoL in patients with acromegaly

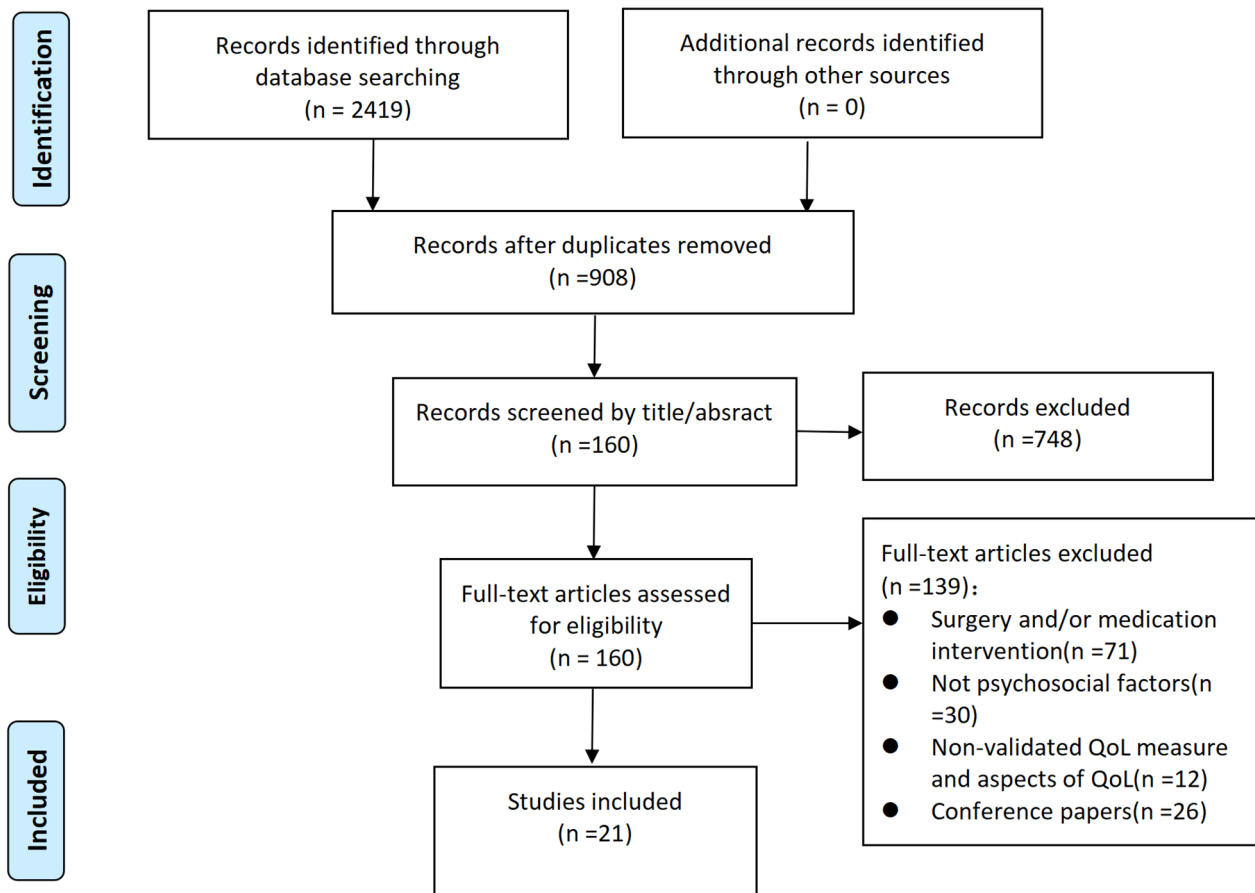
The eligible studies reported on ten categories of psychosocial factors of QoL. The most prevalent psychosocial factors in the included studies were depression ( $n=7$ ) [18, 25–30], and anxiety ( $n=4$ ) [18, 28–30]. Two studies assessed psychiatric distress [31, 32], body image [33, 34] and illness perceptions [35, 36] respectively. There were single studies for acceptance of illness [31], stigma [37], and medicine beliefs [38] and sleep quality [39].

### The QoL measures

A total of 7 validated QoL measures were used in our scoping review, including the Acromegaly Quality of Life Questionnaire (AcroQoL), Short Form 36-item Health Survey (SF-36), EuroQol Five Dimensions Questionnaire (EuroQoL-5D), WHO Quality of Life Scale-BREF (WHOQoL-BREF), Nottingham Health Profile (NHP), RAND-36 and Physical Symptoms Checklist. SF-36 and RAND-36 include the same items, but the recommended scoring algorithm is somewhat different. Two studies used three QoL measures as an outcome [30, 35], and five studies used two QoL measures [18, 29, 31, 34, 38]. The AcroQoL was the most frequently used QoL measure in 15 studies [18, 25–32, 34–39]. SF-36 was used to assess in 4 studies [18, 29, 30, 33], and EuroQoL-5D in 2 studies [35, 38].

### The influence of the psychosocial factors of QoL in patients with acromegaly

In the studies we included involving depression, the general conclusion was that depression was significantly negatively correlated with QoL [18, 25–29]. Studies involving anxiety found that a high level of anxiety was associated with a worse QoL [18, 28, 29]. Two studies found that psychiatric distress was associated with a lower QoL [31,



**Fig. 1** Flow chart of study selection process

32]. Two studies that investigated body image found that higher scores of body image were associated with a lower QoL [33, 34]. Illness perceptions were found to be associated with QoL negatively in 2 studies [35, 36]. One study found that greater acceptance of illness was more likely to have a higher QoL [31]. Higher stigma was significantly associated with a lower QoL [37]. One study that investigated medicine beliefs found that stronger beliefs about specific necessity to stay healthy are related to a worse QoL [38]. A poorer sleep quality was reported that associated with a worse QoL [39].

**Interventions target QoL in patients with acromegaly**

Two categories of interventions targeting QoL were identified including psychological (n=3) [40–42] and exercise (n=2) [43, 44] interventions. Psychological interventions included mindfulness therapy, psychological focus group therapy, and cognitive-behavioral therapy. Exercise interventions included therapist-oriented home rehabilitation and exercise.

Santos et al. [40] conducted an 8-week mindfulness therapy in patients with acromegaly that evaluated the effect on quality of life. However, there was no change

in QoL. Halilolu et al. [41] designed a self-comparison before and after trial using psychological focus group therapy and found it was a useful intervention positively affecting QoL and depression. Kunzler et al. [42] developed a cognitive-behavioral therapy technique “Think Healthy”, showing an effective improvement in the quality of life.

Lima et al. [43] designed a 2-month therapist-oriented home rehabilitation therapy and found the QoL was improved during the intervention period, while the gain was lost after 1 month of washout. Hatipoglu et al. [44] used a non-randomized clinical trial to explore the impact of exercise programs on QoL in patients with acromegaly. After 3 months, the score of AcroQoL was not changed.

**Discussion**

This scoping review highlights psychosocial factors of QoL and measures used to assess the QoL in patients with acromegaly, as well as nonpharmacological and/or surgical interventions targeting QoL. 21 studies were synthesized across 10 countries from 2004 to 2023, of which the details were described in our review.

**Table 1** Psychosocial factors of QoL in patients with acromegaly.

Author (year)	Country	Design	Sample	Age(years)	Sex(M/F)	Disease duration (years)	Therapy	Psycho-social measure	Quality of Life measure
<b>Depression</b>									
Cangiano (2022)	Italy	cross-sectional	n = 171	20–85	76/95	-	Surgery(n = 90) MEDICATION (n = 157) Radiotherapy (n = 26)	Depression AIMS	AcroQoL
Geraedts (2015)	Germany	cross-sectional	n = 80	54.7 ± 12.3	37/43	10.8 ± 10.0	-	BDI	AcroQoL and SF-36
Kepicoglu (2014)	Turkey	cross-sectional	n = 133	47 ± 11.5	52/81	8.1 ± 6.9	Surgery(n = 114) MEDICATION (n = 133) Radiotherapy (n = 38)	BDI	AcroQoL
Celik(2013)	Turkey	cross-sectional	n = 57	-	0/57	4(2.25,13)	Surgery(n = 45) MEDICATION (n = 40) Radiotherapy (n = 15)	BDI	AcroQoL
Pivonello (2022)	Italy	cross-sectional	n = 223	56(48,64.5)	94/129	5(2,10)	-	BDI-II	AcroQoL
Ballesteros (2021)	Mexico	cross-sectional	n = 85	38.0 ± 13.6	38/47	-	-	BDI	AcroQoL and SF-36
<b>Anxiety</b>									
Geraedts (2015)	Germany	cross-sectional	n = 80	54.7 ± 12.3	37/43	10.8 ± 10.0	-	STAI	AcroQoL and SF-36
Pivonello (2022)	Italy	cross-sectional	n = 223	56(48,64.5)	94/129	5(2,10)	-	STAI Form Y 1 and 2	AcroQoL
Ballesteros (2021)	Mexico	cross-sectional	n = 85	38.0 ± 13.6	38/47	-	-	BAI	AcroQoL and SF-36
<b>Depression and anxiety</b>									
Biermasz (2004)	the Netherlands	cross-sectional	n = 118	58.6 ± 12.9	61/57	-	-	HADS	AcroQoL, SF-36 and NHP
<b>Psychiatric distress</b>									
Jawiarczyk (2020)	Poland	cross-sectional	n = 50	51.7 ± 14.5	19/31	8.4 ± 8.8	-	GHQ	AcroQoL and WHOQoL-BREF
Anagnostis (2014)	Greece	cross-sectional	n = 40	60 ± 2.0	15/25	-	Surgery(n = 31) MEDICATION (n = 23) Radiotherapy (n = 13)	POMS	AcroQoL
<b>Body image</b>									
Zhang (2022)	China	cross-sectional	n = 68	46.4 ± 12.5	31/37	-	-	BICI	SF-36
Roerink (2015)	the Netherlands	cross-sectional	n = 73	59.4 ± 10.5	40/33	-	Surgery(n = 64) MEDICATION (n = 39) Radiotherapy (n = 14)	DAS59	AcroQoL and RAND-36
<b>Illness perceptions</b>									
Tiemensma (2011)	the Netherlands	cross-sectional	n = 81	60 ± 12	47/34	-	-	IPQ-R	AcroQoL, EuroQoL-5D and Physical Symptoms Checklist

**Table 1** (continued)

Author (year)	Country	Design	Sample	Age(years)	Sex(M/F)	Disease duration (years)	Therapy	Psycho-social measure	Quality of Life measure
T'Sjoen (2007)	Belgium	cross-sectional	n=291	54.8±13.5	149/142	-	-	SSS	AcroQoL
<b>Acceptance of illness</b>									
Jawiarczyk (2020)	Poland	cross-sectional	n=50	51.7±14.5	19/31	8.4±8.8	-	AIS	AcroQoL and WHOQoL-BREF
<b>Stigma</b>									
Li(2022)	China	cross-sectional	n=102	45.3±13.5	42/60	-	Surgery(n=89) MEDICATION (n=13)	SSCI	AcroQoL
<b>Medicine beliefs</b>									
Andela (2015)	the Netherlands	cross-sectional	n=73	60.1±11.6	40/33	16.1±10.0	Surgery(n=62) MEDICATION (n=28) Radiotherapy (n=17)	BMQ	AcroQoL and EuroQoL-5D
<b>Sleep quality</b>									
Wennberg (2019)	Italy	cross-sectional	n=67	56(48,64.5)	26/41	30 (11, 42.5)	MEDICATION (n=57) Radiotherapy (n=6)	PSQI	AcroQoL

As stated by the WHO, there are three patient-related health outcomes in chronic disease management: reducing mortality, reducing morbidity, and improving QoL [45]. As the life expectancy of patients with acromegaly increases, more and more researchers believe that QoL should be managed as an independent treatment goal in acromegaly [46]. This is the first scoping review of QoL in patients with acromegaly, which provides a clear mapping for the development of QoL in patients with acromegaly.

Successful surgery or medication can improve the quality of life of patients, but it is rarely completely normalized and not always associated with biochemical markers.

We only included 5 interventions targeting QoL. In the preliminary screening, we found that there were a large number of surgery, medication, and radiation intervention studies whose outcomes included QoL, which was the challenge we encountered whether such studies should be included. For patients with well-defined acromegaly, surgery, medication, and radiation therapy were common methods in clinical practice. Successful surgery or medical treatment could improve the patient's QoL, but it is rarely completely normalized and not always associated with biochemical markers [47]. Medical treatment, could lower GH and IGF-1, and improve both comorbidities of acromegaly and QoL. However, the long-term need for monthly injections of somatostatin analogs to control the disease may hurt AcroQoL scores [48]. In recent decades, the life expectancy of patients with acromegaly has also significantly

increased, requiring new complementary methods that can alleviate physical and emotional consequences and the long-term disease burden on the health system [49]. So we only included interventions targeting QoL beyond these conventional methods. In our review, only psychological focus group therapy and cognitive-behavioral therapy showed potential in QoL by Halilolu et al. [41] and Kunzler et al. [42], and Kunzler et al. [50] conducted a 9-month follow-up at the end of the cognitive-behavioral intervention, they found the effects of intervention were maintained. However, the intervention benefits of therapist-oriented home rehabilitation carried out by Lima et al. [43] disappeared after one month of wash-out, so the long-term effect of intervention is an aspect that researchers need to consider when designing. While the findings are not conclusive as only a small number of interventions were included, it provides a new perspective on designing interventions to improve QoL. There are all small sample sizes in the included interventions, which is an unavoidable difficulty in rare diseases such as acromegaly. Further work with large randomized controlled trials and strong experimental designs are needed to replicate these benefits and more potential clinical complementary interventions are needed to improve QoL for patients with acromegaly.

Ten categories of psychosocial factors that are associated with QoL in acromegaly include depression, anxiety, psychiatric distress, body image, illness perceptions, acceptance of illness, cognitive function, stigma, medicine beliefs, and sleep quality. Most psychosocial



Continued Table 1

Author (year)	Results
<b>Depression</b>	
Cangiano(2022)	Depression was significantly negatively correlated with AcroQoL.
Geraedts (2015)	Depression can be significantly predictive of QoL measured by AcroQoL and SF-36.
Kepicoglu(2014)	Depression was significantly negatively correlated with AcroQoL.
Celik(2013)	A strong negative correlation was found between AcroQoL total score and BDI score.
Pivonello(2022)	BDI-II total score was the best predictor of AcroQoL physical domain score.
Ballesteros(2021)	The higher scores of BDI correlated with lower QoL as assessed by global, and all subdomain scores in AcroQoL.
<b>Anxiety</b>	
Geraedts (2015)	Anxiety can be significantly predictive of QoL measured by AcroQoL and SF-36.
Pivonello(2022)	STAI Y 1 and 2 score correlated with AcroQoL total score.
Ballesteros(2021)	The higher scores of BAI correlated with lower QoL as assessed by global, and all subdomain scores in AcroQoL.
<b>Depression and anxiety</b>	
Biermasz(2004)	HADS were significantly negatively correlated with AcroQoL, SF-36 and NHP.
<b>Psychiatric distress</b>	
Jawiarczyk(2020)	No association between the scores of GHQ-28 and QoL.
Anagnostis(2014)	AcroQoL scores were negatively associated with POMS.
<b>Body image</b>	
Zhang(2022)	The BICI score was negatively correlated with SF-36.
Roerink(2015)	DAS59 scores were significantly negatively correlated with AcroQoL.
<b>Illness perceptions</b>	
Tiemensma(2011)	Illness perceptions was significantly negatively correlated with AcroQoL, EQ-5D, and Physical Symptoms Checklist.
T'Sjoen(2007)	SSS was significantly negatively correlated with AcroQoL.
<b>Acceptance of illness</b>	
Jawiarczyk(2020)	The level of acceptance of illness was significantly positively correlated with AcroQoL and WHOQoL-BREF.
<b>Stigma</b>	
Li(2022)	Total stigma was significantly positively correlated with the AcroQoL.
<b>Medicine beliefs</b>	
Andela(2015)	BMQ subscale Specific-Necessity SA was negatively associated with AcroQoL subscales psychological-appearance and psychological-personal relations and the total score on the AcroQoL.
<b>Sleep quality</b>	
Wennberg(2019)	Sleep quality was associated with poorer overall AcroQoL, physical AcroQoL, psychological AcroQoL, and social AcroQoL.

factors are modifiable and might provide valuable targets for future interventions. Depression and anxiety are the most frequent psychosocial factors investigated. A cross-sectional survey shows that the prevalence of psychiatric comorbidity in patients with acromegaly ranges from 40 to 50% [17]. Due to the disruption of body image, patients with acromegaly are more likely to exhibit anxiety-related personality traits [51]. Arthropathy is associated with poor mood and QoL [52, 53]. Cangiano et al. reported that 28% of patients with acromegaly displayed depression. The proportion was significantly higher than those reported in subjects with primary osteoarthritis of the hand and in patients without osteoarthritis [25]. Arthropathy is a common and disabling complication of acromegaly, and it does not seem to entirely regress after hormonal normalization, so therapies are often unable to restore joint function to its previous state. Almost three out of four patients complain of articular pain, stiffness, or limitations during both active and biochemically

controlled disease [53]. Moreover, Tseng et al. reported that presence of comorbidities might affect QoL of patients with acromegaly, and patients with diabetes mellitus (DM) had lower psychological score and psychological scores than those without DM [54]. A recent study emphasizes that the significant decrease in the QoL of patients with acromegaly is mainly driven by psychopathology rather than biochemical control of the disease. It is recommended to conduct systematic psychopathological screening and specific psychological treatment for acromegaly to improve the QoL of patients [18]. In our review, the included studies were cross-sectional designs that evaluated the impact of psychosocial factors on QoL at the current time point. We cannot know how psychosocial factors affect QoL over time. The cross-sectional design excludes some possible influencing factors in modulating QoL in patients affected with acromegaly. In addition, the lack of qualitative research also makes it difficult for us to understand the true thoughts of patients

**Table 2** Characteristics of included intervention studies.

Author (year)	Country	Design	Sample	Type of intervention	Content of intervention	Dose
<b>Psychological interventions</b>						
Santos (2023)	Spain and Italy	Multicentre randomized controlled trial	n=45	Mindfulness therapy	Centre 1: Mindfulness-Based Stress Reduction Centre 2: Compassion and Mindfulness Based Daily Life Therapy	Meditate 6 days per week, In Centre 1 formal meditation 45 minutes per day, informal meditation was no specific time request. In Centre 2, both formal and informal meditation 20 minutes per day, and also had other tasks related to daily life activities.
Halilolu (2020)	Turkey	Self comparison before and after	n=7	Psychological focus group therapy	Using insight-oriented and supportive psychotherapy techniques, encouraging patients to try new techniques of socialization and talk about different aspects of the illness.	Weekly group psychotherapy sessions.
Kunzler(2018)	Brazil	Non-randomized clinical trial	n=20	Cognitive-behavioral therapy (CBT)	Basic concepts of CBT; emotional regulation; increase self-esteem and self-confidence, and supply of a brain-shaped piggy bank; "Think healthy and feel the difference" technique; the technique for approaching anger, assertiveness training, and the coping card; the technique for approaching fear; the technique adapted for shame about one's physical appearance in acromegaly; clarifications on acromegaly; a summary of the topics covered in the sessions.	Nine weekly 90-min "Think healthy" group therapy sessions.
<b>Exercise interventions</b>						
Lima (2019)	Brazil	Self comparison before and after	n=17	Therapist-oriented home rehabilitation	5 min of warm-up exercises, 20 min of muscle strengthening and resistance exercises for the upper and lower limbs, 10 min of balance training, 20 min of aerobic training, 5 min of global stretching and relaxation exercises.	Before starting the protocol, the patients were instructed by how to perform the physical exercises, and followed an exercise programme from a booklet with instructions for each exercise prescribed for 3 times a week, for a total of 24 sessions.
Hatipoglu (2014)	Turkey	Non-randomized clinical trial	n=20	Exercise	Each session consisted of warming up, cardio, strength, balance and stretching. At the end of each month, the difficulty of the exercises was increased.	Exercised 3 days a week for three consecutive months. And each exercise session, which lasted 75 min, was supervised.

with acromegaly. Further work with longitudinal research and qualitative research should be conducted to clarify the changing trends of psychosocial factors and specific experiences of patients.

There were 7 different QoL measures utilized across the 16 studies. Most studies use specific QoL measures of acromegaly, the Acromegaly Quality of Life Questionnaire (AcroQoL). AcroQoL is the most widely used tool for measuring the QoL in acromegaly currently, the effectiveness and clinical applicability have been validated in a 6-month prospective study [55]. Standardized measures can increase comparability between different studies.

However, there is a discrepancy in cultural background and medical level among different countries, so researchers should test or develop QoL measures based on the treatment and psychosocial characteristics of patients with acromegaly in their own country. In addition, we also call on researchers to use the COSMIN risk of bias checklist [56] as a guide to comprehensively and objectively evaluate the performance of the developed tool.

#### Limitations

Though we proposed a strict screening and search strategy among the six major databases to determine a



Continued Table 2

Author (year)	Providers	Control	Duration	Outcomes	Improvement of QoL
Santos (2023)	Mindfulness teacher and research staff	Normal clinical routine	8 weeks	Quality of life, mood, pain, sleep, self-compassion, life satisfaction, blood pressure and heart rate	THERE WAS NO CHANGE IN QoL.
Halilolu (2020)	Psychoanalyst and clinical psychologist	-	12 months	Quality of life and depression	There was an effective improvement on QoL.
Kunzler (2018)	-	-	3 months	Quality of life and depression	There was an effective improvement on QoL.
Lima (2019)	Physiotherapist	-	2 months	Quality of life, fatigue, body composition, handgrip strength, lower extremity functionality, body balance and functional capacity	QoL was improved during the intervention period, while the gain was lost after 1 month of wash-out.
Hatipoglu (2014)	-	-	3 months	Quality of life, BMI, hormone levels, depression and body image.	THERE WAS NO CHANGE IN QoL.

widespread belief in results, there were still some limitations that need to be addressed. First, the lack of qualitative and mixed methods of research endangers a deeper understanding of the characteristics that affect QoL,

as trends, specific experiences, and insights can only be captured through these methods. Second, in our scoping review, we only included studies that focus on overall QoL and QoL measurement tools must be validated, which may result in missing relevant studies. Third, considering the breadth of the definition of 'psychosocial factors', there may also be a range of other factors that have not yet been reported. Finally, we only searched the English database, which may lead to publication bias due to the omission of other language literature.

## Conclusions

Our scoping review identified ten categories of psychosocial factors for QoL in acromegaly, seven validated QoL measures, and two categories of interventions targeting QoL, which provide a reasonably clear picture of the current research status of QoL in acromegaly. However, this review also highlights the need to deepen understanding of QoL and psychosocial factors in the future, as well as conduct longitudinal research and qualitative research to clarify the changing trends of psychosocial factors and specific experiences of patients. Further, more potential clinical complementary interventions are needed to improve QoL for patients with acromegaly.

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## Author contributions

Wei Wang: Conceptualization, Methodology, Literature retrieval, Literature screening, Data extraction, Visualization, Writing—original draft preparation. Ting Yang: Conceptualization, Methodology, Supervision, Validation, Writing—reviewing and editing. Qinghua Huang: Literature retrieval, Literature screening, Data extraction, Visualization.

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## Data availability

All data generated or analysed during this stage are included in this published article [and its Additional files].

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

All authors agree to publish the manuscript in *Orphanet Journal of Rare Diseases*.

### Competing interests

The authors have no conflict of interest to declare.

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## References

- Colao A, Grasso LFS, Giustina A, Melmed S, Chanson P, Pereira AM, Pivonello R. Acromegaly. *Nature reviews. Disease Primers*. 2019;5(1):20.
- Lavrentaki A, Paluzzi A, Wass JA, Karavitaki N. Epidemiology of acromegaly: review of population studies. *Pituitary*. 2017;20(1):4–9.
- Gadelha MR, Kasuki L, Lim DST, Fleseriu M. Systemic complications of Acromegaly and the impact of the Current Treatment Landscape: an update. *Endocr Rev*. 2019;40(1):268–332.
- Giustina A, Barkan A, Beckers A, Biermasz N, Biller BMK, Boguszewski C, Bolanowski M, Bonert V, Bronstein MD, Casanueva FF, Clemmons D, Colao A, Ferone D, Fleseriu M, Frara S, Gadelha MR, Ghigo E, Gurnell M, Heaney AP, Ho K, Melmed S. A Consensus on the diagnosis and treatment of Acromegaly comorbidities: an update. *J Clin Endocrinol Metab*. 2020;105(4):dgz096.
- Katznelson L, Laws ER Jr, Melmed S, Molitch ME, Murad MH, Utz A, Wass JA. & Acromegaly Society (2014). Acromegaly: an endocrine society clinical practice guideline. *The Journal of clinical endocrinology and metabolism*, 99(11), 3933–3951.
- Wolters TLC, Roerink SHPP, Sterenborg RBTM, Wagenmakers MAEM, Husson O, Smit JWA, Hermus AR, M. M., Netea-Maier RT. The effect of treatment on quality of life in patients with acromegaly: a prospective study. *Eur J Endocrinol*. 2020;182(3):319–31.
- Kyriakakis N, Lynch J, Gilbey SG, Webb SM, Murray RD. Impaired quality of life in patients with treated acromegaly despite long-term biochemically stable disease: results from a 5-years prospective study. *Clin Endocrinol*. 2017;86(6):806–15.
- Sibeoni J, Manolios E, Verneuil L, Chanson P, Revah-Levy A. Patients' perspectives on acromegaly diagnostic delay: a qualitative study. *Eur J Endocrinol*. 2019;180(6):339–52.
- Liu S, Adelman DT, Xu Y, Sisco J, Begelman SM, Webb SM, Badia X, Thethi TK, Fonseca V, Shi L. Patient-centered assessment on disease burden, quality of life, and treatment satisfaction associated with acromegaly. *J Invest Medicine: Official Publication Am Federation Clin Res*. 2018;66(3):653–60.
- WHO Quality of Life Assessment Group. *What quality of life?* Geneva, Switzerland: World Health Forum; 1996.
- Guilbert JJ. The world health report 2. *Educ Health (Abingdon)*. 2003;16(2):230.
- Shimatsu A, Nagashima M, Hashigaki S, Ohki N, Chihara K. Efficacy and safety of monotherapy by pegvisomant, a growth hormone receptor antagonist, in Japanese patients with acromegaly. *Endocr J*. 2016;63(4):337–47.
- Fujio S, Arimura H, Hirano H, Habu M, Bohara M, Moinuddin FM, Kinoshita Y, Arita K. Changes in quality of life in patients with acromegaly after surgical remission - A prospective study using SF-36 questionnaire. *Endocr J*. 2017;64(1):27–38.
- van der Klaauw AA, Biermasz NR, Hoftijzer HC, Pereira AM, Romijn JA. Previous radiotherapy negatively influences quality of life during 4 years of follow-up in patients cured from acromegaly. *Clin Endocrinol*. 2008;69(1):123–8.
- Singh-Manoux A. Psychosocial factors and public health. *J Epidemiol Commun Health*. 2003;57(8):553–5.
- Moon S, Hong S, Han K, Park CY. Risk of depression in patients with acromegaly in Korea (2006–2016): a nationwide population-based study. *Eur J Endocrinol*. 2023;189(3):363–71.
- Sievers C, Dimopoulou C, Pfister H, Lieb R, Steffin B, Roemmler J, Schopohl J, Mueller M, Schneider HJ, Ising M, Wittchen HU, Stalla GK. Prevalence of mental disorders in acromegaly: a cross-sectional study in 81 acromegalic patients. *Clin Endocrinol*. 2009;71(5):691–701.
- Geraedts VJ, Dimopoulou C, Auer M, Schopohl J, Stalla GK, Sievers C. Health outcomes in Acromegaly: depression and anxiety are promising targets for improving reduced quality of life. *Front Endocrinol*. 2015;5:229.
- Vermalle M, Alessandrini M, Grailton T, Paladino NC, Baumstarck K, Sebarg F, Dufour H, Brue T, Castinetti F. Lack of functional remission in Cushing's syndrome. *Endocrine*. 2018;61(3):518–25.
- Geraedts VJ, Andela CD, Stalla GK, Pereira AM, van Furth WR, Sievers C, Biermasz NR. Predictors of quality of life in Acromegaly: no Consensus on biochemical parameters. *Front Endocrinol*. 2017;8:40.
- Broersen LHA, Zamanipoor Najafabadi AH, Pereira AM, Dekkers OM, van Furth WR, Biermasz NR. Improvement in symptoms and Health-Related Quality of Life in Acromegaly patients: a systematic review and Meta-analysis. *J Clin Endocrinol Metab*. 2021;106(2):577–87.
- Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol*. 2005;8(1):19–32.
- Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, Peters MDJ, Horsley T, Weeks L, Hempel S, Akl EA, Chang C, McGowan J, Stewart L, Hartling L, Aldcroft A, Wilson MG, Garrity C, Lewin S, Straus SE. PRISMA Extension for scoping reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med*. 2018;169(7):467–73.
- Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, McInerney P, Godfrey CM, Khalil H. Updated methodological guidance for the conduct of scoping reviews. *JBI Evid Implement*. 2021;19(1):3–10.
- Cangiano B, Giusti E, Premoli C, Soranna D, Vitale G, Grottole S, Cambria V, Mantovani G, Mungari R, Maffei P, Dassiè F, Giampietro A, Chiloiro S, Tanda M, L., Ippolito S, Cannavò S, Ragonese M, Zambon A, Persani L, Fatti L, M., ... PRO-ACRO study group on Motor Disability in Acromegaly, of the Italian Society of Endocrinology (SIE) (2022). Psychological complications in patients with acromegaly: relationships with sex, arthropathy, and quality of life. *Endocrine*, 77(3), 510–518.
- Kepicoglu H, Hatipoglu E, Bulut I, Darici E, Hizli N, Kadioglu P. Impact of treatment satisfaction on quality of life of patients with acromegaly. *Pituitary*. 2014;17(6):557–63.
- Celik O, Kadioglu P. Quality of life in female patients with acromegaly. *J Endocrinol Investig*. 2013;36(6):412–6.
- Pivonello R, Auremma RS, Veneri D, Dassiè A, Lorusso F, Ragonese R, Liotta M, Sala M, Zarino E, Lai B, Urbani E, Bogazzi C, Mantovani F, Cannavò G, Maffei S, Chiodini P, P., Colao A. Global psychological assessment with the evaluation of life and sleep quality and sexual and cognitive function in a large number of patients with acromegaly: a cross-sectional study. *Eur J Endocrinol*. 2022;187(6):823–45.
- Ballesteros-Herrera D, Briseño-Hernández P, Pérez-Esparza R, Portocarrero-Ortiz LA. (2021). Differences in quality of life between genders in acromegaly. *Endocrinol Diabetes Metabolism*, 4(2), e00229.
- Biermasz NR, van Thiel SW, Pereira AM, Hoftijzer HC, van Hemert AM, Smit JW, Romijn JA, Roelfsema F. Decreased quality of life in patients with acromegaly despite long-term cure of growth hormone excess. *J Clin Endocrinol Metab*. 2004;89(11):5369–76.
- Jawarczyk-Przybyłowska A, Szcześniak D, Ciułkiewicz M, Bolanowski M, Rymaszewska J. Importance of Illness Acceptance among other factors affecting quality of life in Acromegaly. *Front Endocrinol*. 2020;10:899.
- Anagnostis P, Efstathiadou ZA, Charizopoulou M, Selaimatzidou D, Karathanasi E, Poulasouchidou M, Kita M. Psychological profile and quality of life in patients with acromegaly in Greece. Is there any difference with other chronic diseases? *Endocrine*. 2014;47(2):564–71.
- Zhang X, Li Y, Zhong Y, Wang Z. Variables Associated with body image concerns in Acromegaly patients: a cross-sectional study. *Front Psychol*. 2022;13:733864.
- Roerink SH, Wagenmakers MA, Wessels JF, Sterenborg RB, Smit JW, Hermus AR, Netea-Maier RT. Persistent self-consciousness about facial appearance, measured with the Derriford appearance scale 59, in patients after long-term biochemical remission of acromegaly. *Pituitary*. 2015;18(3):366–75.
- Tiemensma J, Kaptein AA, Pereira AM, Smit JW, Romijn JA, Biermasz NR. Affected illness perceptions and the association with impaired quality of life in patients with long-term remission of acromegaly. *J Clin Endocrinol Metab*. 2011;96(11):3550–8.
- T'Sjoen G, Bex M, Maiter D, Velkeniers B, Abs R. Health-related quality of life in acromegalic subjects: data from AcroBel, the Belgian registry on acromegaly. *Eur J Endocrinol*. 2007;157(4):411–7.
- Li Y, Zhang X, Zhang J, Zhang D, Wang Y, Zhu Y, Xu X. Stigma and unhealthy psychological characteristics in patients with acromegaly: a cross-sectional study and identification of the associated factors. *Acta Neurochir*. 2022;164(8):2069–81.
- Andela CD, Biermasz NR, Kaptein AA, Pereira AM, Tiemensma J. More concerns and stronger beliefs about the necessity of medication in patients with acromegaly are associated with negative illness perceptions and impairment in quality of life. *Growth hormone & IGF research. Official J Growth Hormone Res Soc Int IGF Res Soc*. 2015;25(5):219–26.
- Wennberg A, Lorusso R, Dassiè F, Benavides-Varela S, Parolin M, De Carlo E, Fallo F, Mioni R, Vettor R, Semenza C, Maffei P. Sleep disorders and cognitive dysfunction in acromegaly. *Endocrine*. 2019;66(3):634–41.
- Santos A, Nalin C, Bortolotti G, Dominguez-Clave E, Daniela G, Cortesi L, Pagani M, Momblan MAM, Gich I, Webb SM, Trevisan R, Resmini E. The effect of mindfulness therapy in acromegaly: a pilot study. *Clin Endocrinol*. 2023;98(3):363–74.
- Hailolu Z, Szer S, Korkmaz ZP, Ahin S, Durcan E, Oral G et al. (2020). The effects of psychological focus group therapy on the quality of life of female patients with acromegaly. *Turkish J Endocrinol Metabolism*(4).

42. Kunzler LS, Naves LA, Casulari LA. Cognitive-behavioral therapy improves the quality of life of patients with acromegaly. *Pituitary*. 2018;21(3):323–33.
43. Lima TRL, Kasuki L, Gadelha M, Lopes AJ. Physical exercise improves functional capacity and quality of life in patients with acromegaly: a 12-week follow-up study. *Endocrine*. 2019;66(2):301–9.
44. Hatipoglu E, Topsakal N, Atilgan OE, Alcalar N, Camliguney AF, Niyazoglu M, Cotuk HB, Kadioglu P. Impact of exercise on quality of life and body-self perception of patients with acromegaly. *Pituitary*. 2014;17(1):38–43.
45. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. (1995). *Social science & medicine* (1982), 41(10), 1403–1409.
46. Coopmans EC, Andela CD, Claessen KMJA, Biermasz NR. Evaluating the impact of Acromegaly on Quality of Life. *Endocrinol Metab Clin North Am*. 2022;51(4):709–25.
47. Webb SM, Badia X. Quality of life in Acromegaly. *Neuroendocrinology*. 2016;103(1):106–11.
48. Matta MP, Couture E, Cazals L, Vezzosi D, Bennet A, Caron P. Impaired quality of life of patients with acromegaly: control of GH/IGF-I excess improves psychological subscale appearance. *Eur J Endocrinol*. 2008;158(3):305–10.
49. Solomon E, Brănișteanu D, Dumbravă A, Solomon RG, Kiss L, Glod M, Preda C. Executive functioning and quality of life in acromegaly. *Psychol Res Behav Manage*. 2019;12:39–44.
50. Kunzler LS, Naves LA, Casulari LA. The effect of cognitive-behavioral therapy on Acromegalics after a 9-Month Follow-Up. *Front Endocrinol*. 2019;10:380.
51. Dimopoulou C, Leistner SM, Ising M, Schneider HJ, Schopohl J, Rutz S, Kosilek R, Frohner R, Stalla GK, Sievers C. Body image perception in acromegaly is not Associated with Objective Acromegalic Changes but depends on depressive symptoms. *Neuroendocrinology*. 2017;105(2):115–22.
52. Yamamoto N, Urai S, Fukuoka H, Yamamoto M, Yoshida K, Suzuki M, Shichi H, Fujita Y, Kanie K, Iguchi G, Takahashi Y, Ogawa W. The Effect of Aging on Quality of Life in Acromegaly patients under treatment. *Front Endocrinol*. 2022;13:819330.
53. Fatti LM, Cangiano B, Vitale G, Persani L, Mantovani G, Sala E, Arosio M, Maffei P, Dassiè F, Mormando M, Giampietro A, Tanda L, Masiello ER, Nazzari E, Ferone D, Corbetta S, Passeri E, Guaraldi F, Grottoli S, Cannavò S, Study Group on Motor Disability in Acromegaly of the Italian Society of Endocrinology. Arthropathy in acromegaly: a questionnaire-based estimation of motor disability and its relation with quality of life and work productivity. *Pituitary*. 2019;22(5):552–60.
54. Tseng FY, Chen ST, Chen JF, Huang TS, Lin JD, Wang PW, Huey-Heng Sheu W, Chang TC, Acromegaly Registry Study Group. Correlations of clinical parameters with quality of life in patients with acromegaly: Taiwan Acromegaly Registry. *J Formos Med Association = Taiwan Yi Zhi*. 2019;118(11):1488–93.
55. Webb SM, Badia X, Surinach NL, Spanish AcroQoL Study Group. Validity and clinical applicability of the acromegaly quality of life questionnaire, AcroQoL: a 6-month prospective study. *Eur J Endocrinol*. 2006;155(2):269–77.
56. Mookink LB, de Vet HCW, Prinsen CAC, Patrick DL, Alonso J, Bouter LM, Terwee CB. COSMIN Risk of Bias checklist for systematic reviews of patient-reported outcome measures. *Qual life Research: Int J Qual life Aspects Treat care Rehabilitation*. 2018;27(5):1171–9.

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