

The longitudinal association between weight change and health-related quality of life in adults and children: a systematic review

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Abstract

This systematic review examined longitudinal associations between weight change (weight gain and loss) and both physical and mental aspects of health-related quality of life (HRQOL) compared with stable weight in adults and children of the general population. MEDLINE, EMBASE, PsycINFO, and PubMed databases were searched. Longitudinal observational studies measuring HRQOL with six predefined instruments were synthesised according to type of association: weight change and change in HRQOL (change-on-change association); and weight change and HRQOL at follow-up (predictive association). Twenty studies of adults (n = 15) or children (n = 5) were included. 15 studies used the SF-12 or SF-36. Results of nine studies in adults examining the change-on-change association were combined through a tallying of 606 analyses. Weight gain was most often associated with reduced physical, but not mental HRQOL, across all baseline body mass index categories and in both males and females. Weight loss may be associated with improved physical, but not mental HRQOL, among adults with overweight and obesity. Weight gain was more strongly associated with HRQOL than weight loss, implicating a greater need for preventative strategies to tackle obesity. Results in children and for the predictive association generally reflected these findings, but require further research.

Introduction

Since 1980, the prevalence of overweight and obesity has increased worldwide by 28% among adults and 47% among children.¹ This global epidemic is a major public health priority, with universal concern regarding the health risks and associated costs and lost productivity.²

Overweight and obesity are associated with elevated morbidity and mortality risks across the lifespan^{3,4}, in addition to reduced health-related quality of life (HRQOL).⁵ HRQOL is a multidimensional concept that focuses on the impact of a disease or health state on an individual's physical, mental, and social wellbeing.⁶ Low HRQOL has been shown to predict premature mortality, some morbidities, and health service utilisation.⁷⁻⁹

Systematic reviews and meta-analyses of cross-sectional studies show that a higher than normal body mass index (BMI) in adults (defined as $>25\text{kg/m}^2$) and children (defined in individual studies by age and sex specific centile cut-offs) is associated with lower physical HRQOL, with strong evidence of a dose-responsive relationship.¹⁰⁻¹⁴ Associations with mental HRQOL tended to be weaker or less consistent.¹⁰⁻¹⁴ These results, however, are unable to demonstrate any longitudinal relationship between weight changes and HRQOL. It is reasonable to hypothesise

that weight gain over the lifespan would lower physical HRQOL, while weight loss would improve physical HRQOL.

In a systematic review and meta-analysis of randomised controlled trials for weight loss, Warkentin et al¹⁵ showed intentional weight loss is associated with improved physical, but not with overall or mental HRQOL. A systematic review of weight loss interventions by Kroes et al¹⁶ further found a direct dose-responsive relationship, with greater degrees of weight loss correlating with greater improvements in physical HRQOL. The review found only one study reporting a significant correlation between weight loss and improved mental HRQOL after surgery, with the other studies showing no correlation.¹⁶ Exposure to the weight loss intervention, rather than to weight loss itself, may partly mediate these HRQOL improvements.¹⁷⁻²⁰ Moreover, the results of weight loss studies are not transferable to the general population with or without obesity, as people with obesity seeking weight loss treatment have lower HRQOL than the general population with obesity.²¹

Longitudinal observational studies offer the potential to examine the relationship between weight changes and HRQOL in the general population without confounding effects from interventions. The primary objective of this systematic review of published observational studies was to determine if exposure to weight changes (weight gain or loss) in adults and children with and without obesity is longitudinally associated with HRQOL outcomes, compared with stable weight.

Methods

We conducted a systematic review registered with PROSPERO, the International Prospective Register for Systematic Reviews (<http://www.crd.york.ac.uk/prospero/>, registration number CRD42016027434).

Search strategy

We searched the following databases on 28th January 2016: MEDLINE (Ovid)(1946–2016), EMBASE (Ovid)(1947–2016), PsycINFO (Ovid)(1806–2016) and PubMed (1809–2016), with an updated search conducted on 28th July 2016. The MEDLINE search strategy is displayed in Table 1 and translated strategies for other databases are available in the Supplementary Material Table S1. To minimise duplication, we utilised EMBASE and PubMed search options to exclude studies already indexed in MEDLINE. Full citations were exported into the referencing software EndNote X7 for storage, management and removal of duplicates. One author (MJH) sought further relevant studies by hand searching references and contacting authors of included studies. He additionally applied PubMed 'cited by' and 'similar articles' tools to all included studies. All records identified by the former were retrieved, while for the latter the first 10 records by relevance were retrieved.

Study selection

All titles and abstracts from the initial electronic search were screened by the primary reviewer (MJH) for inclusion. Full texts of included studies and references of included systematic reviews were then screened against eligibility criteria. To increase the quality of the review by ensuring the accuracy of the primary reviewer, a second

reviewer (KJH) independently screened half of the titles and abstracts for inclusion and subsequently performed full text screening. Reviewers were blinded to studies' authors during the initial screen of titles and abstracts. Inter-rater agreement was assessed by Cohen's kappa co-efficient calculated using Stata version 13.0 (Stata Corporation, College Station, TX).²² Discrepancies between reviewers were resolved through discussion with a third reviewer (RM).

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Table 1 Search strategy for MEDLINE via Ovid

Nr.	Search Term
1	exp "Quality of Life"/
2	((life adj2 qualit\$) or QOL\$ or HRQL or HRQOL or SF12 or SF-12 or short form 12 or SF-36 or SF36 or short form 36 or Euroqol or EQ-5D or EQ5D or (Pediatric Quality adj Life Inventory) or PedsQL or KIDSCREEN or Child Health Questionnaire or CHQ).tw.
3	1 or 2
4	exp Body Composition/ or exp Overweight/ or Body Weight/ or "Body Weights and Measures"/ or Thinness/ or Body Mass Index/ or Body Size/ or Waist Circumference/ or Waist-Hip Ratio/ or Waist-Height ratio/ or Weight Gain/ or Weight Loss/ or Skinfold Thickness/ or Pediatric Obesity/ or Growth Charts/ or Adipose Tissue/
5	(body weight or body mass or body size or body fat or body composition or abdominal fat or obesity or obese or overweight or thinness or underweight or fatty tissue or adipos\$ or body measure\$ or bmi or waist circumference or waist hip ratio or weight height ratio or height weight ratio or waist height ratio or skinfold thickness or weight gain or weight increase or weight change or weight loss or weight reduction or weight decrease or growth chart\$ or weight centile or weight percentile).tw.
6	4 or 5
7	exp Cohort Studies or Case-control Studies/ or Epidemiologic Studies/
8	(prospective or retrospective or longitudinal or observational or follow up or cohort or case control).tw.
9	7 or 8
10	3 and 6 and 9
11	10 and (exp animals/ or exp veterinary medicine/ or exp animal experimentation/)
12	10 and humans/
13	11 not 12
14	10 not 13
15	14 not (case reports or editorial or in vitro).pt.
16	limit 15 to (english or french or german or spanish)

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Eligibility criteria

Longitudinal observational studies reporting an association between weight change and HRQOL outcomes and of at least one year follow-up were included, as we considered this the minimum duration for meaningful changes in weight or HRQOL. To reduce publication bias, we sought studies published in all languages known to the authors (English, French, German and Spanish). Cross-sectional studies, case reports, editorials, conference proceedings and abstracts, and primary intervention studies for weight loss were excluded, as they either provide no longitudinal data; are of low evidence level; or, in the case of the latter, introduce the potential for confounding by the intervention. Secondary analyses of intervention studies were considered if the analyses were presented for the control group separately or if exposure to the intervention was shown not to, or could not impact independently on weight and HRQOL.

Studies were included if they reported subscales, component summary scores or overall HRQOL using the Short Form-36²³ (SF-36), Short Form-12²⁴ (SF-12), or Euroqol 5D²⁵ (EQ-5D) in adults or the Pediatric Quality of Life Inventory²⁶ (PedsQL), Child Health Questionnaire²⁷, or KIDSCREEN²⁸ in children. These instruments were selected for inclusion because of their frequent use and demonstrated validity.^{29, 30} To ensure data completeness, studies reporting fewer than half of an instrument's subscales were excluded. We included studies with participants of all weight categories, including underweight (BMI < 18.5kg/m²).

Studies were excluded if they analysed only hospitalised or pregnant participants or participants all having a disease or condition (other than overweight or obesity), or receiving a specific treatment, as these variables may confound the relationship between weight change and HRQOL. For studies analysing the same sample and conducting the same analysis but at different follow-up times, only the most recent or complete study was included to avoid data duplication. Studies analysing the same participants answering different research questions were included as separate studies.

Data extraction

Data of included studies was extracted by one reviewer (MJH). Extracted data included: study details (authors, year of publication, location); participant characteristics (age range and/or mean and standard deviation, sex distribution, population source); primary aim of the study; methods (design, assessment of body weight and HRQOL, statistical methods applied); results for analyses between weight change and HRQOL; and sources of funding. For analyses treating weight change as a categorical variable, we extracted results for two categories: dichotomised as weight gain and weight loss, each compared with weight stable. Weight stable groups were those with no or minimal weight change, as defined in respective studies. If weight change was a continuous variable, it was not possible to distinguish between weight gain and weight loss and we extracted the linear measure of association. For studies providing separate analysis for participants with specific diseases or exposed to an intervention impacting independently on weight or HRQOL, only data on

participants without the disease or intervention were extracted. If required, first and/or last study authors study were contacted to retrieve any missing data or unreported information. Significance of all associations was inferred from statistical tests or confidence intervals, with $p < 0.05$ considered significant unless otherwise stated.

Synthesis of results

Variable treatment of weight change data precluded a meta-analysis. Instead we performed a narrative synthesis of study results, focused on the direction of association of weight changes with HRQOL, rather than effect sizes. Results were summarised in a table, stratified by both age group (adults: baseline age ≥ 18 years, children: baseline age < 18 years) and type of longitudinal association. Two types of longitudinal associations were examined: the longitudinal relationship between weight change and change in HRQOL between baseline and follow-up (change-on-change association); and the longitudinal relationship between weight change and HRQOL at follow-up without adjustment for baseline HRQOL (predictive association). Studies associating weight change and HRQOL at follow-up with adjustment for baseline HRQOL were interpreted as belonging to the change-on-change association.

Where HRQOL was measured by SF-36, SF-12 or PedsQL, results for physical and mental/psychosocial component summary scores, or for instrument subscales were included. For SF-36 and SF-12, subscales of physical functioning, physical role limitation, bodily pain, and general health relate to physical HRQOL, while subscales of social functioning, emotional role limitation, vitality, and mental health relate to

mental HRQOL.^{23, 24} For other HRQOL instruments, results for either the overall scores or subscales were included.

Tallying synthesis

A subset of studies treating weight change as a categorical variable produced many results, which could not be easily summarised through narrative synthesis. To summarise these results, we tallied the number of analyses from these studies according to the direction of weight change experienced (gain or loss) and the resulting change in HRQOL subscales or component summary scores. All categorical change-on-change results in adults were combinable through a tallying synthesis, as all studies used the SF-36 or SF-12. Tallied analyses were presented graphically in vertical bar charts categorised by direction (reduced, improved, or neither reduced nor improved) and statistical significance (significant or non-significant) of associations. Analysed, but non-reported results were combined with the non-significant associations. We also presented the tallied analyses stratified by sex (male and female) and baseline BMI category (normal weight, BMI < 25kg/m²; overweight BMI = 25 – 29.9kg/m²; and obese, BMI > 30kg/m²).

Quality and risk-of-bias assessment

Two reviewers (MJH and JKH) independently assessed the quality of included studies as poor, fair or good using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (QATOCSS).³¹ Discrepancies between reviewers were resolved through discussion with a third reviewer (RM).

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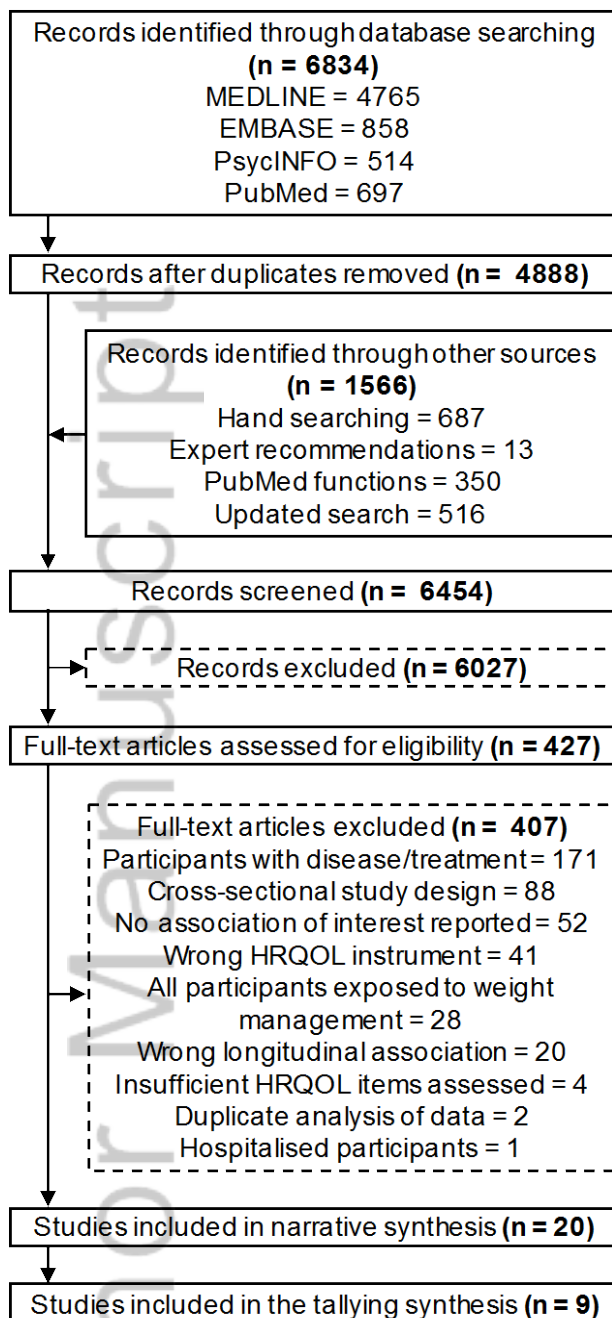


Figure 1 Results of search and screening process from the identification to the inclusion of studies, based on PRISMA flow diagram³²

Table 2 Characteristics of included studies separately for adults and children, according to the longitudinal association analysed

Age group	Association type	Reference	Follow-up (years)	Country	Sample size	Sex (% F)	Age range or mean (SD)	Weight change exposure (categories) ^a	Weight stable comparator (categories)	HRQOL outcome (items analysed)
Adults	Change-on-change	Batsis ³³ 2015	6	USA	664	F&M (61.1)	67.9 (5.3)	WG (≥5%) WL (≥5%)	ΔW < ±5%	ΔSF-12 (PCS/MCS)
		Cameron ³⁴ 2012	5	Australia	5,985	F&M (54.7)	51.3 (4.5)	WG (>0 kg/m ²)	ΔW ≤ 0 kg/m ²	ΔSF-36 (PCS/MCS)
		de Hollander ³⁵ 2013	15	the Netherlands	3408	F&M (56.5)	24–66	WG (NW→OW; NW/OW→O)	WS (NW→NW)	ΔSF-36 ^b (8 subscales)
		Fine ³⁶ 1999	4	USA	40,098	F (100)	46–71	WG ^c (2.25–9kg; ≥9kg) WL ^c (2.25–9kg; ≥9kg)	ΔW ^c < ±2.25kg	ΔSF-36 (7 subscales)
		Herpetz ³⁷ 2015	9	Germany Austria	83	F&M (71.9)	42.5 (11.8)	ΔBMI (continuous)	NA	ΔSF-36 (PCS/MCS)
		Laxy ³⁸ 2014	7	Germany	3080	F&M (51.8)	25–74	1. WG (5–10%; >10%) 1. WL (5–10%; >10%) 2. ΔBMI (continuous)	1. ΔW < ±5%	ΔSF-12 (PCS/MCS)
		León-Muñoz ³⁹ 2015	2	Spain	2364	F&M (56.4)	60–93	WG ^c WL ^c	2. NA ΔW ^c = no	ΔSF-36 (8 subscales)
		Milder ⁴⁰ 2014	5	the Netherlands	4,135	F&M (51.5)	26–70	WG (2.1–4kg; 4.1–6kg; >6kg) WL(>2kg)	ΔW < ±2kg	ΔSF-36 ^b (8 subscales)
		Pan ⁴¹ 2014	4	USA	105,269	F (100)	29–71	WG ^{c, d} (2.25–6.74kg; ≥6.75kg) WL ^{c, d} (2.25–6.74kg; ≥6.75kg)	ΔW ^c < ±2.25kg	ΔSF-36 (PCS/MCS)
	Williams ⁴² 2006	2	Australia	7270	F (100)	45–50	WG ^c (2.25-4.4kg; ≥4.5kg) WL (≥2.25kg)	ΔW ^c < ±2.25kg	ΔSF-36 (PCS/MCS)	
	Predictive	Burns ⁴³ 2001	5	the Netherlands	1113	F&M (52.0)	26–59	WG (5–10%; >10%) WL (5–10%; >10%)	ΔW < ±5%	SF-36 ^b (8 subscales)
		Connor ⁴⁴ 2016	~14.5	USA	270	F (100)	30–74	ΔBMI ^c (continuous)	NA	SF-12 (PCS/MCS)
		Döring ⁴⁵ 2015	8	Sweden	16,666	F&M	18–84	WG ^c (5.1–9.9%; ≥10%)	ΔW ^c ≤ ±5%	EQ-5D

Kozak ⁴⁶ 2011	20	USA	3014	(56.6) F&M (55.0)	18–30	WL ^c (5.1–9.9%; ≥10%) 1. WG (NW→OW; NW→O) 2. WG (OW→O)	1. WS (NW→NW) 2. WS (OW→OW)	SF-12 (PCS/MCS)
Strandberg ⁴⁷ 2003	26	Finland	1147	M (0.0)	39–56 (47)	WG ^{c, e+} (0.1–4.0kg; 4.1–9.0kg; 9.1–14.9kg; ≥15kg)	ΔW ^c ≤ 0kg	SF-36 ^b (8 subscales)

Table 2 Continued.

Age group	Association type	Reference	Follow-up (years)	Country	Sample size	Sex (% F)	Age range or mean (SD)	Weight change exposure (categories)	Weight stable comparator (categories)	HRQOL outcome (items analysed)
Children	Change-on-change	Sawyer ⁴⁸ 2011	4	Australia	3363	F&M (49.0)	4–5	ΔBMI z-score (continuous)	NA	PedsQL (PCS/MCS, subscales)
	Predictive	Gopinath ⁴⁹ 2013	5	Australia	1025	F&M (52.6)	12–13	WL (OW/O→NO)	WS (O→O)	PedsQL (PCS/MCS, subscales)
		Herman ⁵⁰ 2010	22	Canada	310	F&M (50.6)	7–18	WG ^c (NW→OW/O)	WS ^c (NW→NW)	SF-36 (subscales)
		Parkinson ⁵¹ 2015	2–5	UK	331 – 445	F&M (51.0)	6–8	ΔFMI (continuous) ΔWC (continuous)	NA	KIDSCREEN-27 subscales
		Wake ⁵² 2010	8	Australia	932	F&M (49.4)	5–10.7	WG (NW→OW/O)	(NW→NW)	PedsQL (PCS/MCS)

Abbreviations: Δ, change; BMI, body mass index; CD, cannot determine; EQ-5D, Euroqol 5D; FMI, fat mass index; F, female; HRQOL, health-related quality of life; M, male; MCS, mental/psychosocial component summary score; NA, not applicable; NR, not reported; NW, normal weight; O, obese; OW, overweight; PCS, physical component summary score; PedsQL, Pediatric Quality of Life Inventory; SF-12, Short Form 12; SF-36, Short Form 36; WC, waist circumference; WG, weight gain; WL, weight loss; WS, weight stable; ΔW, weight change

^aThe symbol → represents transition from one weight category to another.

^bSF-36 scores calculated using the RAND-36 calculation methodology.⁵³

^c Measured by self-report

^d Measurement converted from pounds, based on the authors provided conversion ratio (1lb = 0.45kg)

^e Baseline weight measurement was retrospective (recalled weight at age at 25 years)

Table 3 Main results from included studies on the association between direction of weight change and HRQOL outcomes and the number of analysis contributing the tallied synthesis.

Age group	Association type	Reference	Weight gain		Weight loss		Weight change ^a	
			Physical	Mental	Physical	Mental	Physical	Mental
Adults	Change-on-change	Batsis ³³ 2015	1	1	1	1	Significant, direction not reported	Non-significant
		Cameron ³⁴ 2012	6	6				
		de Hollander ³⁵ 2013	16	16				
		Fine ³⁶ 1999	48	64	48	64		
		Herpetz ³⁷ 2015						
		Laxy ³⁸ 2014	12	12	12	12		
	Predictive	León-Muñoz ³⁹ 2005	16	16	16	16	Non-significant	Non-significant
		Milder ⁴⁰ 2014	72	72	24	24		
		Pan ⁴¹ 2014	6	6	6	6		
		Williams ⁴² 2006	2	2	1	1		
		Burns ⁴³ 2001	Lower physical functioning and general health subscales	Lower vitality subscale	Non-significant	Non-significant		
		Connor ⁴⁴ 2016 Döring ⁴⁵ 2015	Lower overall EQ-5D in all BMI categories	Lower overall EQ-5D in all BMI categories	Lower overall EQ-5D in normal weight and overweight ^b	Lower overall EQ-5D in normal weight and overweight ^b		
Kozak ⁴⁶ 2011 Strandberg ⁴⁷ 2003	Lower PCS Lower on all physical subscales	Non-significant Lower mental subscales, except mental health						

Children Change-on-change	Sawyer ⁴⁸ 2011								Inverse association with PCS	Inverse association with social subscale
Predictive	Gopinath ⁴⁹ 2013				Higher PCS in obese	Non-significant				
	Herman ⁵⁰ 2010	Lower general health subscale	Non-significant							
	Parkinson ⁵¹ 2015								Non-significant ^b	Non-significant ^b
	Wake ⁵² 2010	Lower PCS	Lower MCS							

EQ-5D, Euroqol 5D; MCS, mental/psychosocial component summary score; PCS, physical component summary score; TS, tallied synthesis

^a Weight change as a continuous variable

^b Significance was set at the $p < 0.01$ level

Results

Figure 1 shows the study selection process. One reviewer screened titles and abstracts of 4888 articles identified from the electronic search and 1566 from other sources. From these, 427 were selected for full text screening, which identified 20 studies meeting the eligibility criteria for inclusion in our review. To increase the quality of the review, a second reviewer additionally screened a sample of 2444 articles independently. The Cohen's kappa coefficient for was 0.799, representing very substantial agreement between the two reviewers.⁵⁴

Characteristics of included studies are summarised in Table 2. All studies were cohort studies, with follow-up times ranging from two to 26 years. Fifteen studies were in adults and five in children. Eleven studies analysed the change-on-change association, while nine analysed the predictive association. Fifteen studies analysed weight change exclusively as a categorical variable; four studies exclusively as a continuous variable; and one study as both. Anthropometric data was measured by self-report in eight studies and by physical examination in twelve. In adults, ten studies used SF-36; four studies used SF-12; and one study used EQ-5D. In children, three studies used PedsQL; one study used SF-36; and one study used KIDSCREEN-27.

Further study characteristics, including data source, statistical methods, quality and risk of bias assessment results are summarised in Supplementary Material Table S2. Of note, two studies sourced data from the Nurses Health Study^{36, 41} and a further

two studies from the Doetinchem Cohort Study.^{35, 40} Two studies included underweight participants within the normal weight category, the remaining studies excluded underweight participants.^{36, 40} According to the QATOCCs quality assessment instrument, two of the included studies were rated as good^{35, 40}; 17 as fair^{33, 34, 36-39, 41-43, 45-52}; and one as poor quality.⁴⁴

Of the studies treating weight change as a categorical variable, nine studies in adults examining the change-on-change association contributed to the tallying synthesis.³³⁻⁴² These nine studies provided 606 analyses of the association between weight change and change in HRQOL, with Table 3 summarising the number of analyses contributed by each study.³³⁻⁴²

Weight gain

Adults

Results for weight gain in adults via the change-on-change association are summaries in Figure 2A. Overall, from nine studies there were 374 analyses of the association between weight gain and change in HRQOL.³³⁻⁴² Of these, 30.5% (n = 114) were significant. Five studies analysed component summary scores.^{33, 34, 38, 41, 42} Physical component summary scores were reduced with weight gain in 22 of 27 analyses, 12 of which were significant. There were no analyses in which weight gain was associated with significantly improved physical component summary score. Mental component summary scores improved with weight gain in 14 of 27 analyses, 6 of which were significant. There were no analyses in which weight gain was associated with significantly reduced mental component summary score. Four

studies analysed subscale scores.^{35, 36, 39, 40} Physical subscales were predominantly reduced with weight gain. Mental subscales were mixed in their direction of association, except for vitality, which was predominantly reduced.

Results for weight gain via the predictive association are summarised in Table 3. Weight gain predicted lower physical component summary scores or physical subscales in three studies.^{43, 46, 47} Weight gain predicted lower mental subscales in two studies^{43, 47} and was non-significantly associated with mental component summary scores in one study.⁴⁶

Results for dose-responsivity are summarised in Supplementary Material Table S3. Of the ten studies examining categories representing greater and lesser degrees of weight gain, all showed physical HRQOL outcomes reduced in a dose-responsive manner with weight gain, particularly among women.^{35, 36, 38, 40-43, 45-47} Dose-responsivity of mental HRQOL outcomes with weight gain was inconsistent.

Subgroup analyses stratified by baseline BMI category showed results for weight gain were similar among adults with normal weight, overweight and obesity (Supplementary Material Figure S1). Döring et al⁴⁵ found weight gain predicted lower overall EQ-5D score for all BMI categories (Table 3). Stratification by sex showed reduced physical HRQOL with weight gain was similar for males and females (Supplementary Material Figure S3). Improved mental component summary scores with weight gain was only seen in females, however, there were fewer analyses for men.

Children

Results for weight gain in children are summaries in Table 3. None of the identified studies examined weight gain via the change-on-change association in children. For the predictive association, weight gain predicted lower physical component summary scores or physical subscales in two studies.^{50, 52} Weight gain predicted lower mental component summary scores in one study⁵² and was non-significantly associated with mental subscales in the other.⁵⁰

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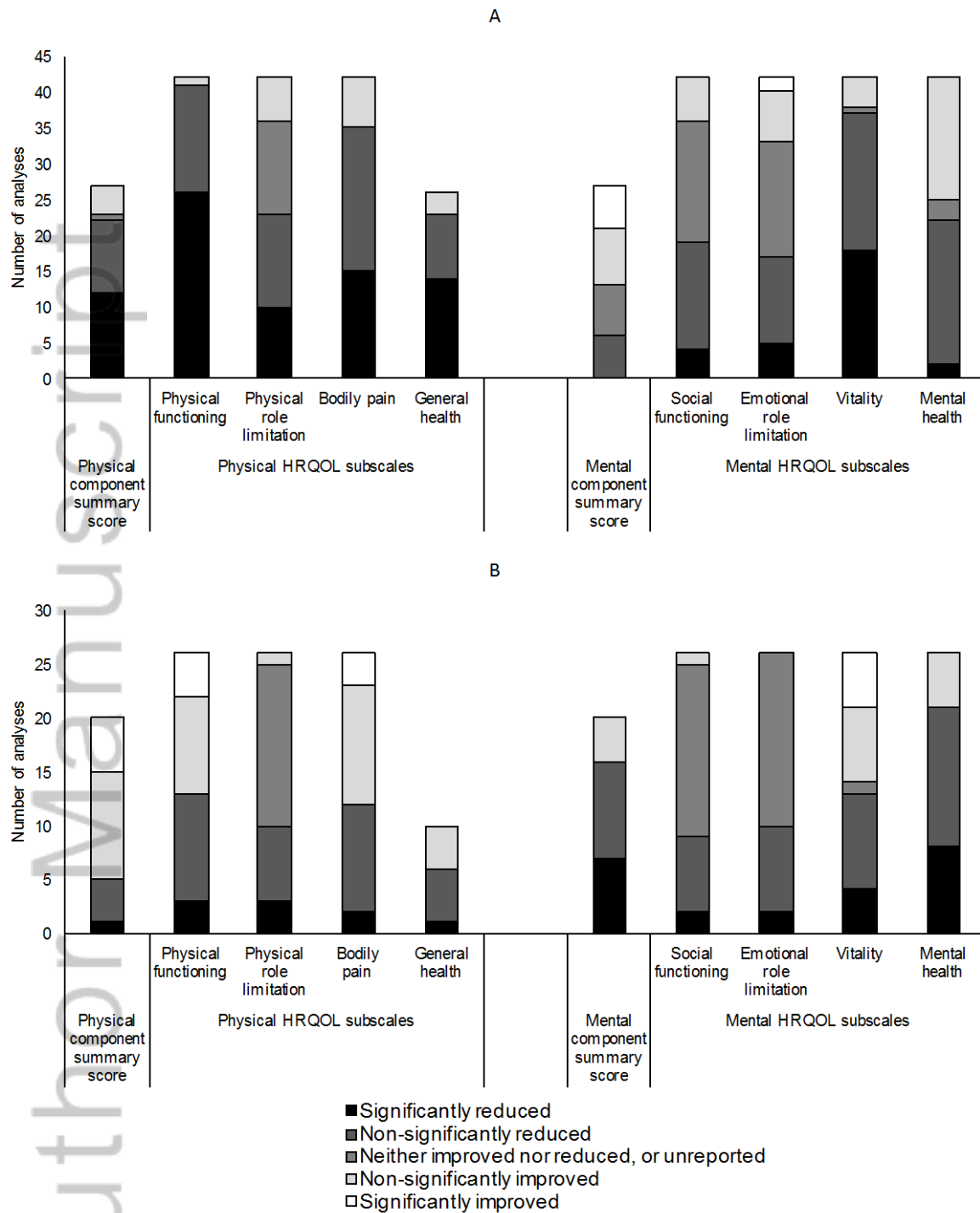


Figure 2 Tallied synthesis of 606 analyses for the association between weight gain (A) (n = 374) and weight loss (B) (n = 232) and changes in physical and mental component summary scores and subscales

Weight loss

Adults

Results for weight loss in adults via the change-on-change association are summarised in Figure 2B. Overall, from seven studies there were 232 analyses of the association between weight loss and change in HRQOL.^{33, 36, 38-42} Of these, 21.6% (n = 50) were significant. Four studies analysed component summary scores.^{33, 38, 41, 42} There were significant reductions and improvements in physical component summary scores with weight loss. Mental component summary scores were most often reduced. Three studies analysed subscale scores.^{36, 39, 40} There were significant reductions and improvements in physical subscales and the mental subscale of vitality with weight loss. Other mental subscales were most often reduced.

Results for weight loss via the predictive association are summarised in Table 3. In one study weight loss was not significantly associated with either physical or mental HRQOL at follow-up.⁴³

Results for dose-responsivity are summarised in Supplementary Material Table S4. From the five studies examining categories representing greater and lesser degrees of weight loss, there was inconsistency in the dose-responsivity of both physical and mental HRQOL outcomes with weight loss.^{36, 38, 41, 43, 45}

Subgroup analyses stratified by baseline BMI category indicated that in adults with overweight and obesity, weight loss was most often associated with improvements in physical HRQOL and vitality (Supplementary Material Figure S2). In adults with normal

weight, weight loss was most often associated with reductions in physical and mental HRQOL (Supplementary Material Figure S2). Döring et al⁴⁵ found weight loss among adults with overweight and obesity predicted lower overall ED-5Q score at follow-up (Table 3). Sex differences in HRQOL outcomes with weight loss were not reliably discernible because there were too few analyses in men (Supplementary Material Figure S4).

Children

Results for weight loss in children are summarised in Table 3. None of the identified studies examined weight loss via the change-on-change association in children. For the predictive association, one study found weight loss in children with obesity predicts higher physical component summary scores at follow-up, but was not significantly associated with mental component summary scores.⁴⁹

Weight change

Adults

Results in adults for weight change as continuous variable are summarised in Table 3. For the change-on-change association, weight change was significantly associated with changes in physical component summary scores in two studies.^{37, 38} Only one study reported the direction of association as inverse.³⁸ Weight change was directly associated with changes in mental component summary scores in one study³⁸ and non-significantly associated in the other.³⁷ For the predictive association, weight change was not significantly associated with either physical or mental HRQOL at follow up in one study.⁴⁴

Children

Results in children for weight change as continuous variable are summarised in Table 3.

For the change-on-change association, weight change was inversely associated changes in both physical component summary scores and one mental subscale in one study.⁴⁸ For the predictive association, weight change was not significantly associated with physical and mental HRQOL at follow-up in one study.⁵¹

Discussion

In this systematic review we included 20 studies examining the longitudinal association between weight change and HRQOL in adults and children. For the change-on-change association in adults, we made four key findings:

- 1) Weight gain was consistently associated with a reduction in both physical HRQOL and the mental HRQOL subscale of vitality across all BMI categories and in both males and females, with demonstrated dose-responsivity.
- 2) Weight gain was inconsistently associated with changes in other mental HRQOL subscales, with associations comparatively less consistent in their direction; less often significant; and less often demonstrating dose-responsivity.
- 3) Weight loss among adults with overweight and obesity seemed to be associated with improved physical HRQOL and vitality, yet changes in other mental HRQOL subscales were inconsistent.

4) Weight loss among adults of normal weight seemed to be associated with reductions in both physical and mental HRQOL.

Results for children; for the predictive association; and for weight change as a continuous variable were generally consistent with these findings.

Comparison with existing research and interpretation

Previous systematic reviews and meta-analyses of cross-sectional studies have similarly demonstrated a strong dose-responsive inverse relationship between weight and physical HRQOL in both adults and children.^{10, 11, 13, 14, 55} Secondary analyses of longitudinal intervention studies further show weight gain is associated with reduced physical HRQOL.^{56, 57} The mechanism of this association is unknown. The physical burden of carrying additional weight may directly impede physical aspects of life, thereby reducing HRQOL. It may also result from the development of obesity-related co-morbidities, such as cardiovascular disease and osteoarthritis, and their subsequent negative HRQOL impacts, particularly in adults.⁵⁸ Most included studies adjusted for baseline co-morbidities, however, only five adjusted for incident co-morbidities and it is possible not all co-morbidities were accounted for.^{34, 38-41} Furthermore, convincing evidence exists for a positive, dose-responsive association between physical activity, physical fitness and HRQOL.⁵⁹⁻⁶¹ While several included studies adjusted for baseline levels, only Pan et al⁴¹ adjusted for changes in physical activity. While our key findings echo those of Pan et al⁴¹, it remains possible that changes in weight and physical HRQOL were partly mediated through changes in physical activity and fitness. This mechanism may be more prominent

in children, as obesity-related co-morbidities, while possible in children, are more common in adulthood.³

As with our findings, existing literature on weight and mental HRQOL outcomes is inconsistent. One review in adults found mental HRQOL was significantly lower only with BMI $\geq 40\text{kg/m}^2$ and was significantly higher in the overweight category.⁵⁵ In children, one review¹⁴ showed an inverse relationship between weight and overall mental HRQOL, while three reviews found only one PedsQL mental subscale was consistently lower at higher weights.^{10, 11, 13} Longitudinal intervention studies found weight gain to be variably associated with improved^{56, 57} and reduced⁶² mental HRQOL. It is possible that weight and mental HRQOL are unrelated or only weakly related, with mental HRQOL only affected at extremes of weight change. Furthermore, generic HRQOL instruments used in these studies and in our review are less sensitive to weight than obesity-specific instruments, and may not detect subtle mental HRQOL changes with weight changes.^{21, 62} Throughout most of human history increased weight has been considered a sign of health and prosperity.⁶³ This is still true in many cultures today, which may further dilute negative impacts of weight gain on mental HRQOL or even account for observed improvements in mental HRQOL with weight gain.⁶³

Previous reviews of weight loss interventions have similarly found improved physical HRQOL outcomes with weight loss among adults with overweight and obesity.^{15, 16} It is possible those who experienced improved HRQOL with weight loss in our included studies were intentionally seeking treatment. People seeking treatment for obesity have lower HRQOL than the general population with obesity, and therefore stand to gain the most

from weight loss treatment, limiting the generalisability of results from treatment-seeking populations.²¹ In these populations, it may also be exposure to the intervention itself which causes improved HRQOL independent of actual weight loss.¹⁷⁻²⁰

The finding of reduced physical and mental HRQOL outcomes with weight loss among adults with normal may relate to underweight. Two studies combined participants with underweight and normal weight in one category.^{36, 40} Adults with underweight have lower HRQOL than adults with normal weight.⁶⁴ If adults of normal weight or underweight lose further weight, a reduced HRQOL should logically follow. The reduced HRQOL and weight loss may also be result from the development of a disease, such as cancer.⁶⁵ While we excluded studies, which included only participants with diagnosed illnesses, we were unable to differentiate between intentional weight loss from lifestyle modification or medical intervention and unintentional weight loss.

Public health implications

Our findings strengthen evidence for a causal association between weight and physical HRQOL. Reduced physical HRQOL with weight gain was consistent across studies and demonstrated dose-responsivity. However, given changes in weight and HRQOL occurred concurrently, we were unable to demonstrate temporality. Studies investigating bidirectional associations found associations with BMI as the predictor of HRQOL outcomes showed stronger dose-responsivity than reverse associations with HRQOL as the predictor of weight outcomes.^{34, 66} This suggests weight as a causal factor for physical HRQOL outcomes. Further research involving multiple measurement intervals is needed to clarify the temporal relationship.

Reduced physical HRQOL with weight gain may also be clinically important. Five point differences in SF-36 subscale scores and two to three point differences in summary scores are considered clinically important.^{23, 67} Several included studies using the SF-36 reported clinically important reductions in physical HRQOL outcomes with weight gain.^{34-36, 39-41, 43, 47} These studies examined population samples resembling the general population. Clinically important reductions in physical HRQOL with weight gain are of public health concern when seen at the general population level.

Furthermore, our findings suggest weight loss may be unable to reverse the negative impacts of weight gain on HRQOL. Among the studies there was a lower proportion of significant associations for weight loss compared with weight gain, suggesting HRQOL is less strongly associated with weight loss. Several included studies found that persistent overweight or obesity was associated with even lower physical HRQOL outcomes than developing overweight or obesity.^{35, 38, 46, 52} It may be difficult for weight loss to reverse the combined HRQOL effects of weight gain and the length of time spent with overweight or obesity. If this is true, public health approaches aimed at preventing weight gain are likely to have a greater positive impact on HRQOL than strategies designed to deal with obesity once it has fully developed.⁶³

As with adults, we found reduced physical HRQOL with weight gain in children. These negative physical HRQOL impacts of weight gain in childhood are compounded by the persistence of childhood obesity into adulthood.⁶⁸ This is of particular public health concern, given the rising prevalence of obesity among children. Thus our findings support the World Health Organization's position that more attention should be given to strategies

aimed at preventing weight gain and obesity at the population level, and that prevention should target both children and adults.⁶³ Prevention of weight gain from early in life may not only affect morbidity and mortality, but may also improve HRQOL in the general population.³

Strengths and limitations

To the authors' knowledge, this is the first systematic review to examine the longitudinal association between weight gain and HRQOL. Our review also adds longitudinal information absent from previous reviews of cross-sectional studies. This temporal element allowed us to examine predictive and change-on-change associations for weight changes and HRQOL outcomes. These associations were examined in both children and adults.

At the study level, we decided to include only longitudinal observational studies, which are more prone to various types of bias. Our research question could not be answered with randomised control trials, as weight loss interventions do not provide information on weight gain and exposure to interventions themselves may cause HRQOL changes independent of weight loss.¹⁷⁻²⁰ In the included studies, long follow-up times often led to considerable loss to follow-up, and the selection of healthier populations. The number of significant reductions and significant improvements in HRQOL may, therefore, be under- and overestimated, respectively. Finally, two studies assessed self-reported weight change by recall, potentially introducing recall bias.^{39, 47}

At the review level, we searched for and included only the six most prevalent HRQOL instruments to reduce heterogeneity. We did not search for HRQOL synonyms, such as well-being, health status and utility. This may have inadvertently excluded some relevant studies measuring HRQOL with other instruments. The tallying synthesis was provided to summarise the number and direction of associations between weight change and HRQOL, but neglects the magnitude of weight and HRQOL changes. This synthesis was only possible for the change-on-change association in adults, as all studies used the SF-36 or SF-12. In the synthesis, there were fewer analyses of weight loss, reducing the reliability of our findings for weight loss. The synthesis was also not weighted by sample size and its internal validity is limited by the high degree of between-study heterogeneity in design, population characteristics, and statistical methods. In particular, differences in the definitions of weight change precluded a meta-analysis. Finally, we assumed unreported results to be non-significant. This was an attempt to include all negative results, though the assumption of non-significance may have caused misclassification.

The external validity of our findings may be limited. Studies contributing many analyses were overrepresented in the tallying synthesis. The study by Fine et al³⁶ surveyed middle- and older-aged predominantly white female nurses and contributed over one third of the tallied analyses. Additionally, all studies were from developed Western nations and just five studies were in children. Several studies indicate age, ethnicity, sex, and socioeconomic status may influence the relationship between weight and HRQOL.⁶⁹⁻⁷² None of the included studies examined participants with underweight as a distinct category. Our findings may, therefore, be less generalisable to children and younger-

adults; populations of lower socioeconomic status; people of non-white ethnicities; non-Western or developing nations; people with underweight; and males. Notably, of the included studies that examined males and females separately, all reported weight change to be more strongly associated with HRQOL in females than males.^{34, 35, 38-40, 43} The fewer analyses for men prevented us from concluding this definitively.

Conclusions

This review found a consistent, dose-responsive, and inverse relationship between weight gain and physical HRQOL and vitality in adults. Associations between weight gain and mental HRQOL were less consistent. For adults with overweight and obesity, weight loss may be associated with improved physical HRQOL and vitality. However, for adults of normal weight, weight loss may be associated with decreased physical and mental HRQOL. The relationships between weight change and HRQOL in children mimicked those in adults, but require further research to replicate findings. Since weight gain was more strongly associated with HRQOL than weight loss and weight gain is seen to have a detrimental impact on physical HRQOL from childhood, this review suggests public health preventative strategies for both adults and children offer the greatest potential to reverse the negative HRQOL impacts of the obesity epidemic.

List of abbreviations

BMI – body mass index

EQ-5D – Euroqol 5D

HRQOL – Health-related quality of life

JKH – Johanna Katharina Hohls

MJH – Mark Joseph Hayes

PedsQL – Pediatric Quality of Life Inventory

QATOCCS - Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

RM – Rebecca Muckelbauer

SF-12 – Short Form 12

SF-36 – Short Form 36

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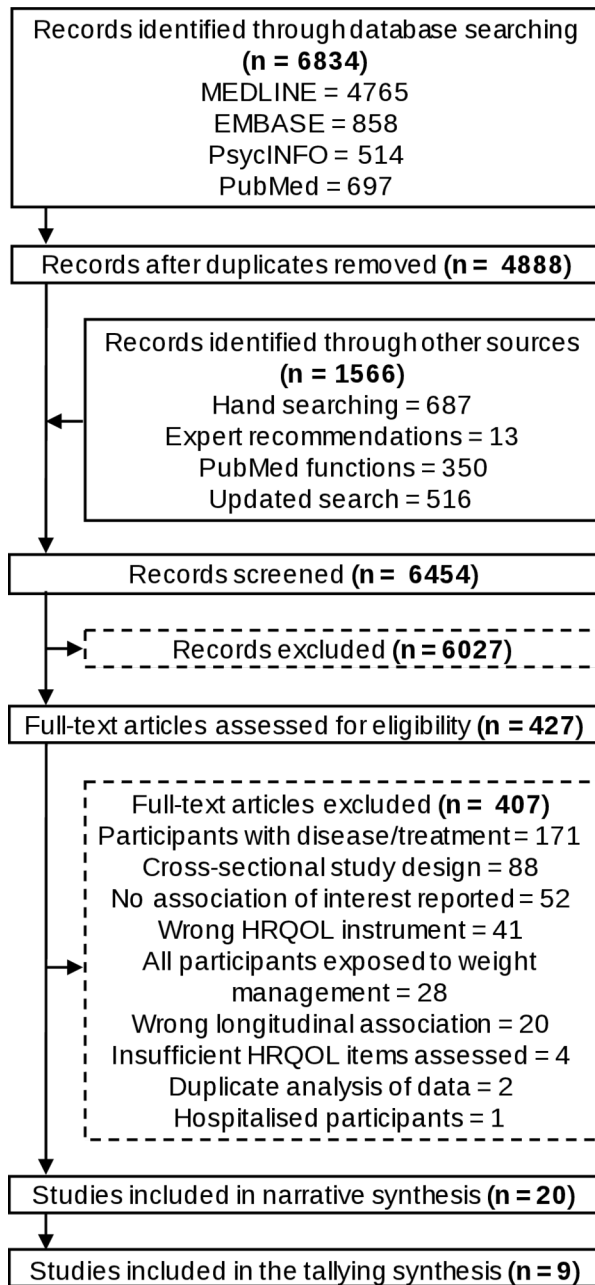
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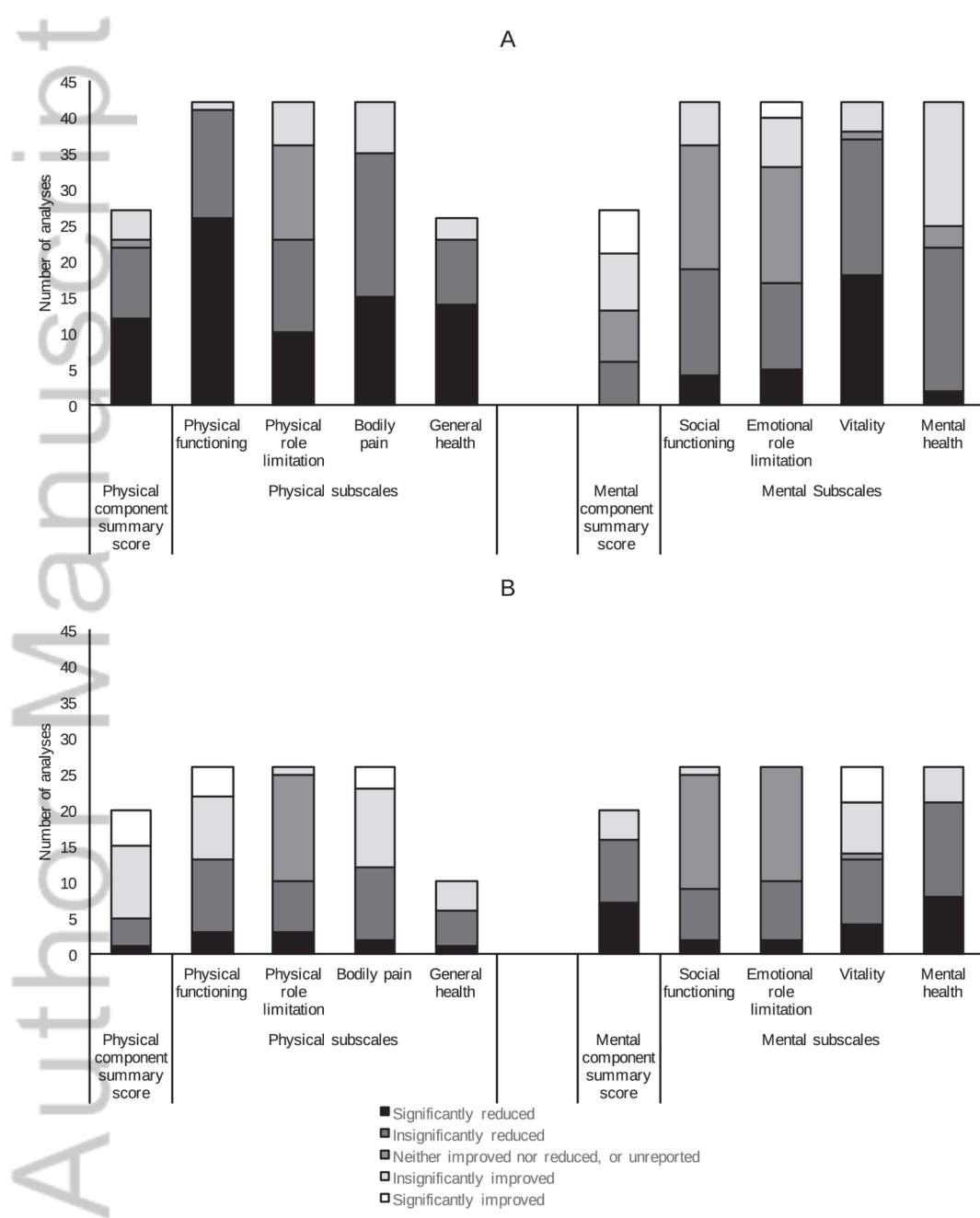
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