

# The longitudinal association between weight change and health-related quality of life: the KORA S4/F4 cohort study

Michael Laxy · Rolf Holle · Angela Döring ·  
Annette Peters · Matthias Hunger

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## Abstract

**Objectives** Despite the increasing importance of patient-centered perspectives, the impact of weight change on the health-related quality of life (HRQL) has remained unclear. This work aims to investigate this longitudinal relationship. **Methods** Data was collected from a population-based cohort study of 3,080 Germans. Anthropometrics and HRQL were assessed at baseline and after a 7-year follow-up period. Using linear regression the average change in HRQL scores was calculated among 5 mutually exclusive weight change groups. Multilevel growth modeling was conducted to differentiate between interpersonal (cross-sectional) and intrapersonal (longitudinal) associations between body mass index (BMI)/BMI change and HRQL.

**Results** Heavy weight gain ( $\geq 10\%$  body weight) was associated with impairments in physical health among women ( $-2.82$  points, CI:  $-4.29, -1.34$ ) and obese men ( $-4.33$  points, CI:  $-7.62, -1.04$ ) and with improvements in mental health among women ( $+3.20$  points, CI:  $+1.37, +5.02$ ). Results from the multilevel models were consistent, showing negative associations between BMI change and physical health, positive associations between BMI change and mental health and a high degree of similarity between interpersonal and intrapersonal associations. **Conclusions** Weight gain leads to clinically relevant impairments in physical health. More research is needed to clarify the antipodal effects of weight change on physical and mental health components.

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M. Laxy (✉) · R. Holle · M. Hunger  
Helmholtz Zentrum München, German Research Center for  
Environmental Health, Institute of Health Economics  
and Health Care Management, Neuherberg, Germany  
e-mail: michael.laxy@helmholtz-muenchen.de

R. Holle  
e-mail: holle@helmholtz-muenchen.de

M. Hunger  
e-mail: matthias.hunger@helmholtz-muenchen.de

A. Döring · A. Peters  
Helmholtz Zentrum München, German Research Center for  
Environmental Health, Institute of Epidemiology II,  
Neuherberg, Germany  
e-mail: doering@helmholtz-muenchen.de

A. Peters  
e-mail: peters@helmholtz-muenchen.de

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## Introduction

Previous research has extensively addressed the impact of excess body weight on a variety of medical conditions (Calle and Thun 2004; Flegal et al. 2005; Guh et al. 2009; Hubert et al. 1983; Redon 2001; Sullivan et al. 2008). However, there is less evidence available regarding the role of weight change on the individuals' functional capacity over time. In recent years, it has become clear that the patients' perspective is crucial for developing clinical pathways and national legislation bodies have started to consider these principles in decision-making and allocation of national health care resources (Dolan 2000; Rawlins and Culyer 2004). Within this process, research has gradually shifted towards patient-centered approaches and has incorporated generic or disease-specific instruments to

assess health-related quality of life (HRQL). HRQL is a multidimensional construct including physical, emotional and social components which measures self-evaluated health. Generic measurements like the SF-12 (Jenkinson and Layte 1997; Ware et al. 1995, 1996) are well-established psychometric instruments that measure different domains of mental and physical health over a broad range of clinical and non-clinical conditions. However, due to the focus on cross-sectional designs (Hopman et al. 2007; Huang et al. 2006; Hunger et al. 2011; Jia and Lubetkin 2005; Soltoft et al. 2009), or randomized clinical trials with surgery- or lifestyle-centered approaches in selected populations (Ackermann et al. 2009; Engel et al. 2003; Kaukua et al. 2002; Kolotkin et al. 2012; Maciejewski et al. 2005), there is only weak evidence about the longitudinal association between weight change and HRQL on population level (Fontaine and Barofsky 2001). Preceding cross-sectional studies showed somehow consistent findings with impaired physical health among underweight, overweight and obese individuals compared to normal weight peers and indicated an inverse U-shaped relationship between BMI and HRQL (Hopman et al. 2007; Huang et al. 2006; Jia and Lubetkin 2005). Comparable outcomes have been found in other large representative samples (Hunger et al. 2011; Larsson et al. 2002). To the best of our knowledge, only three population-based studies had a longitudinal design (Fine et al. 1999; Leon-Munoz et al. 2005; Verkleij et al. 2012). Fine et al. (1999) who investigated changes of HRQL dimensions in women found that heavy weight gain was associated with impairments in physical and mental health domains. A similar outcome has been reported for the elderly Spanish population (Leon-Munoz et al. 2005). In contrast, a recent study showed that weight gain led not only to a general reduction in physical health but also to improvements in mental health among women. The high prevalence of obesity which finally evolves from weight gain over time and the inconsistent evidence from previous studies highlights the need for further research.

The objective of this study was to examine the impact of weight change on HRQL over a 7-year follow-up period on the basis of a large population-based cohort. By analyzing this longitudinal association, the study is intended to extend previous research and to bridge the gap in the understanding of potential causal mechanisms between weight change and HRQL.

## Methods

### Data source

Data used for this analysis were taken from the KORA (Cooperative Health Research in the Region of Augsburg)

S4/F4-cohort study. The study sample was drawn from non-institutionalized inhabitants of the Augsburg region in Southern Germany ( $n = 6,640$ ). From this sample 4,261 participants (participation rate = 64 %) aged 25–74 years completed the baseline S4 examination between 1999 and 2001. 3,080 (72 %) of those participants also took part in the follow-up examination F4 between 2006 and 2008. Reduction of sample size from S4 to F4 occurred due to deaths ( $n = 176$ ), demands for the deletion of data ( $n = 12$ ), or because participants were completely lost to the follow-up (206), could not be contacted ( $n = 174$ ), were unable to come ( $n = 218$ ) or refused to participate ( $n = 395$ ). The S4- and F4-surveys contained a physical examination and a standardized interview collecting data about socioeconomic characteristics, risk factors and the medical history. Study design, sampling method and data collection have been described in detail elsewhere (Rathmann et al. 2003). The KORA S4/F4 studies were approved by the Ethics Committee of the Bavarian Medical Association.

### Measures

#### *SF-12 physical and mental component summary*

HRQL was assessed with the SF-12 Health Survey Version 1 through a face-to-face interview at baseline and through a self-administered questionnaire at the follow-up. The SF-12 is a well-established compacted version of the SF-36. Its validity and reliability has been proven extensively in previous research (Gandek et al. 1998; Jenkinson and Layte 1997; Jenkinson et al. 1997; Ware et al. 1995, 1996). It contains 6 physical- and 6 mental health-related questions across 8 empirically distinct health domains. Based on principal component analysis and regression modeling, scores for the physical and mental component summary (PCS, MCS) have been derived (Ware et al. 1995, 1996). The PCS and MCS are standardized scores with a mean of 50 points and a standard deviation of 10 points. Higher scores represent a better health.

#### *Body mass index*

Height and weight were measured in light clothes and without shoes by trained investigators to the nearest of 0.1 kg, respectively, to the nearest of 0.5 cm using steel-yards (SECA 709) with integrated scales (SECA 221). The BMI was calculated by dividing weight in kilogram by square height in meters. Based on their baseline BMI, participants were classified as underweight (BMI <18.5), normal weight (BMI  $\geq 18.5$  to <25), overweight (BMI  $\geq 25$  to <30) and obese (BMI  $\geq 30$ ) (WHO 2000).

### Weight change groups

In order to examine potential dose–response relationships between the magnitude of weight change and HRQL, study subjects were categorized into five mutually exclusive groups of weight change according to their relative change in bodyweight over the 7-year follow-up period. For this categorization commonly used thresholds which are assumed to be manageable and clinically relevant were applied (CDC 2011). ‘Heavy weight loss’ was defined as a decline of more than 10 % of the initial weight and ‘moderate weight loss’ as a decline in the range between 5 and 10 %. Stable weight, the reference group, was set as a maximum deviation of 5 % from the initial level. ‘Moderate weight gain’ was categorized as an increase in body weight of 5 to 10 % and ‘heavy weight gain’ as an increase in more than 10 %.

### Covariates

Self-reported information about clinical conditions was collected at baseline and the follow-up. The history of cancer, diabetes mellitus, and cardiovascular events, namely the occurrence of stroke or myocardial infarction was assessed. Based on this information three binary variables were coded for the disease status at baseline and for the occurrence/new-occurrence of these diseases during the follow-up period. The status of weight satisfaction was assessed at baseline as a rough proxy for the voluntariness of weight change. As the relationship between age and HRQL was non-linear, age was included as a categorical variable.

### Statistical analysis

Descriptive statistics of the samples’ baseline characteristics were reported separately for men and women. Differences between weight change groups were tested through analysis of variance and Chi-square tests. To examine the association between weight change and change in HRQL, we fitted several regression models. All models were stratified by sex, adjusted for age, education and status of baseline disease and provided estimates for PCS and MCS scores.

First, ordinary least squares linear regression models were fitted, where change scores for HRQL were regressed on weight change groups and other covariates. As we assumed that the effects of weight change are crucially mediated by the initial weight status, we additionally added the baseline BMI category and an interaction term composed of the weight change category and the baseline BMI category into the model. From these models, adjusted mean change scores were calculated for each weight change

category. As a certain magnitude of the observed HRQL change is simply attributable to the factor time, statistical significance of HRQL change in the different weight change categories was tested against the category ‘stable weight’ (reference category). To identify items which contributed the most to the PCS- and MCS-score changes, additional explorative single-item analyses were performed in which the mean point change in each of the respective 6 items that loaded highest on the PCS and MCS were calculated.

Previous cross-sectional studies have mainly described the association between HRQL and BMI across different subjects, whereas longitudinal studies mainly have examined the effect of weight change in kilogram. This methodological dissimilarity has been a barrier for comparing interpersonal associations of individuals at various BMI levels with intrapersonal associations related to BMI change over time. In order to close this gap and to differentiate between these two perspectives, we further fitted a two-level growth model with time (level 1) being nested within individuals (level 2) with BMI as independent and HRQL as dependent variable. The BMI was split into the individual’s mean over time ( $\overline{\text{BMI}}_i$ ) and into the individual’s deviation from the mean ( $\text{BMI}_{ij} - \overline{\text{BMI}}_i$ ), which was introduced as a time-varying covariate into the model (Hedeker 2004). This technique enables to examine pure time effects and to distinguish between ‘within-subject’ and ‘between-subject’ associations of BMI and HRQL. The used model is characterized through the following equations:

Level 1 (within-subject model):

$$\text{HRQL}_{ij} = \pi_{0i} + \pi_{1i}(\text{Time})_{ij} + \pi_{2i}(\text{BMI}_{ij} - \overline{\text{BMI}}_i) + \varepsilon_{ij}$$

Level 2 (between-subject model):

$$\begin{aligned} \pi_{0i} &= \beta_0 + \beta_{\text{BS}}(\overline{\text{BMI}}_i) + v_{0i}; & \pi_{1i} &= \beta_{\text{time}}; \\ \pi_{2i} &= \beta_{\text{WS}}; \end{aligned}$$

wherein  $\beta_0$  is the global intercept,  $\beta_{\text{time}}$  the average change over time (‘pure time effect’),  $\beta_{\text{BS}}$  the effect of  $\overline{\text{BMI}}_i$  (‘cross-sectional association’), and  $\beta_{\text{WS}}$  is the effect of  $\text{BMI}_{ij} - \overline{\text{BMI}}_i$  (‘longitudinal association’).  $v_{0i}$  represents the random individual-specific deviation from the global intercept with zero mean and variance  $\sigma_v^2$ , and  $\varepsilon_{ij}$  the error term which is assumed to be normally and conditionally independently distributed from  $v_{0i}$  with zero mean and common variance  $\sigma^2$  (Hedeker 2004). In addition, multi-level models were stratified according to the subjects’ baseline weight category.

All underweight participants ( $n = 15$ ) and subjects with missing anthropometric or HRQL data ( $n = 183$ ) were omitted. To limit the potential biasing effect of new severe diseases, all subjects with cardiovascular events and cases

of cancer during the follow-up period were excluded from the main analysis ( $n = 210$ ). As these comorbidities are presumed channels through which weight gain affects quality of life, we additionally build up less restrictive models including incident cases of cancer and CVD events in our sensitivity analyses. To control for voluntariness of weight change an additional model including the variable ‘weight satisfaction’ was tested. Data analyses were carried out using SAS 9.2 (SAS Institute, Cary, North Carolina, USA).

## Results

### Study population and pattern of weight change

Characteristics of the cohort at baseline are presented in Table 1. Mean age was 49.0 years (std = 13.3) and around half of the sample at least had gained a secondary education degree. Only one-third of the cohort was classified as normal weight. The proportion of underweight people was very small, whereas 45 % of the individuals were overweight and more than 22 % obese.

Table 1 further shows the pattern of weight change and the characteristics of subjects across the weight change categories. 58 % of the cohort maintained a stable body weight within a deviation of 5 % of their initial level, 31 % experienced weight gain and only 11 % lost weight. The pattern of weight change among men and woman was comparable with a slightly higher proportion of weight losers among women. At baseline, future weight losers were older, had a higher initial BMI, were less likely satisfied with their initial weight status and had a lower prevalence of CVD and diabetes. Further, participants with heavy weight loss between baseline and the follow-up also reported more frequently having been diagnosed with diabetes within this time period.

### Change-score analysis

Absolute adjusted mean change scores for PCS and MCS are depicted in Fig. 1. The exact numbers of participants in each baseline weight and weight change category on which the models are based on are presented in Table 2. Asterisks denote statistical significance of differences between the weight change categories and the reference category ‘stable weight’. The following estimates and confidence intervals also refer to the change score differences between these groups. The inclusion of the interaction between baseline weight category and weight change category improved the model fit in men (PCS,  $p = 0.03$ ; MCS,  $p = 0.02$ ) but not in women (PCS,  $p = 0.45$ ; MCS,  $p = 0.28$ ).

### PCS

Among women, heavy weight gain led to general impairments (estimate =  $-2.82$ , CI:  $-4.29$  to  $-1.34$ ) and weight loss to non-significant improvements in PCS. The size of score impairments between weight maintainers and heavy weight gainers was almost irrespective of the initial BMI category (normal weight: est =  $-2.89$ ; overweight: est =  $-2.63$ ; obesity: est =  $-2.73$ ).

Among men, a similar effect was observed for the obese subgroup only (est =  $-4.33$ , CI:  $-7.62$  to  $-1.04$ ). Although based on a very low number of cases, heavy weight loss among normal weight men ( $n = 3$ ) and women ( $n = 13$ ) was associated with increased physical health (women:  $+4.83$ ; men:  $+6.97$ ).

### MCS

The association between weight change and MCS scores among women was in the opposite direction: compared to stable weight peers, moderate and heavy female weight gainers experienced improvements in mental health (est =  $+2.62$ , CI:  $1.05$ – $4.18$ ; est =  $+3.20$ , CI:  $1.37$ – $5.02$ ). This effect was dominated by great MCS score increases among overweight heavy (est =  $+5.33$ ) and obese moderate weight gainers (est =  $+5.12$ ). A similar but weaker and not significant pattern was observed among men.

### Explorative single-item analysis

The explorative single-item analysis showed that from the six items that load highest on the PCS score the ‘general health’ item, as well as the items ‘moderate activities’ (physical functioning) and ‘climb several flights’ (physical functioning) were high inversely associated with weight change in both sexes. From the six items that load highest on the MCS score all items (mental health, role-emotional, social-functioning) beside ‘energy’ (vitality) were positively associated with weight change, particularly among women (supplementary figure).

### Multi-level growth models

The results of the multi-level growth analysis for the association between BMI and HRQL in Table 3 depict three different effects: the ‘time’ estimate ( $\beta_{\text{time}}$ ) illustrates the pure effect of time over the 7-year follow-up period, independently from any BMI change, the ‘between-subject’ estimate ( $\beta_{\text{BS}}$ ) shows the cross-sectional association between BMI levels and HRQL and the ‘within-subject’ estimate ( $\beta_{\text{WS}}$ ) reflects the longitudinal impact of BMI change over time.

**Table 1** Characteristics of the cohort at baseline and comorbidity prevalence and incidence at baseline/during follow-up, stratified for sex and weight change categories (Germany, 1999–2008)

	Sample characteristics at baseline ( <i>n</i> = 3,080), <i>n</i> (%)			Sample characteristics among weight change categories ( <i>n</i> = 3,046*), <i>n</i> (%)					<i>p</i> value
	All	Men	Women	Heavy weight loss	Moderate weight loss	Stable weight	Moderate weight gain	Heavy weight gain	
All	3,080	1,486 (48.2 %)	1,594 (51.8 %)	108 (3.6)	234 (7.7 %)	1,763 (57.9 %)	575 (18.9 %)	366 (12.0 %)	
Men	1,486 (48.2 %)			41 (2.8 %)	108 (7.3 %)	885 (59.9 %)	285 (19.3 %)	158 (10.7 %)	0.02 <sup>#</sup>
Women	1,594 (51.8 %)			67 (4.3 %)	126 (8.0 %)	878 (56.0 %)	290 (18.5 %)	208 (13.3 %)	
Age									
Mean (std)	49.0 (13.3)	49.6 (13.4)	48.5 (13.2)	53.1 (13.6)	52.3 (14.0)	50.6 (13.0)	46.0 (12.3)	43.2 (12.4)	<0.001 <sup>‡</sup>
Body mass index									
Mean (std)	27.1 (4.6)	27.5 (3.9)	26.8 (5.1)	30.5 (5.6)	27.9 (4.8)	27.1 (4.4)	26.7 (4.4)	26.5 (4.6)	<0.001 <sup>‡</sup>
Weight status									
Underweight	15 (0.5 %)	2 (0.13 %)	13 (0.8 %)	0 (0 %)	0 (0 %)	7 (0.4 %)	4 (0.7 %)	4 (1.1 %)	<0.001 <sup>#</sup>
Normal	999 (32.6 %)	366 (24.7 %)	633 (40.1 %)	17 (15.7 %)	60 (25.6 %)	558 (31.7 %)	207 (36.0 %)	155 (42.4 %)	
Overweight	1,364 (44.6 %)	796 (53.7 %)	568 (36.0 %)	44 (40.7 %)	122 (52.1 %)	811 (46.0 %)	245 (42.6 %)	133 (36.4 %)	
Obese	683 (22.3 %)	318 (21.5 %)	365 (23.1 %)	47 (43.5 %)	52 (22.2 %)	387 (22.0 %)	119 (20.7 %)	74 (20.2 %)	
Education									
Primary	1,589 (51.7 %)	773 (52.1 %)	816 (51.3 %)	69 (63.9 %)	128 (54.7 %)	929 (52.8 %)	272 (47.3 %)	180 (49.3 %)	0.02 <sup>#</sup>
Secondary	757 (24.6 %)	293 (19.8 %)	464 (29.2 %)	21 (19.4 %)	54 (23.1 %)	404 (23.0 %)	170 (29.6 %)	97 (26.6 %)	
Tertiary	729 (23.7 %)	417 (28.1 %)	312 (19.6 %)	18 (16.7 %)	52 (22.2 %)	426 (24.2 %)	133 (23.1 %)	88 (24.1 %)	
Satisfied with weight status	1,761 (58.2 %)	959 (65.9 %)	802 (51.1 %)	40 (37.0 %)	124 (53.9 %)	1,043 (60.0 %)	321 (57.2 %)	214 (59.9 %)	<0.001 <sup>#</sup>
Comorbidity prevalence (baseline, S4)									
CVD	84 (2.7 %)	62 (4.2 %)	22 (1.4 %)	8 (7.4 %)	4 (1.7 %)	44 (2.5 %)	11 (1.9 %)	12 (3.3 %)	0.01 <sup>#</sup>
Diabetes	92 (3.0 %)	48 (3.2 %)	44 (2.8 %)	7 (6.5 %)	12 (5.1 %)	42 (2.4 %)	14 (2.4 %)	14 (3.8 %)	0.02 <sup>#</sup>
Cancer	128 (4.2 %)	52 (3.5 %)	76 (4.8 %)	6 (5.6 %)	10 (4.3 %)	79 (4.5 %)	19 (3.3 %)	12 (3.3 %)	0.61 <sup>#</sup>
Comorbidity incidence (follow-up time, S4–F4)									
CVD	87 (2.8 %)	56 (3.8 %)	31 (1.9 %)	5 (4.6 %)	5 (2.1 %)	51 (2.9 %)	11 (1.9 %)	12 (3.3 %)	0.43 <sup>#</sup>
Diabetes	125 (4.1 %)	74 (5.0 %)	51 (3.2 %)	16 (14.8 %)	10 (4.3 %)	71 (4.0 %)	17 (3.0 %)	8 (2.2 %)	<0.001 <sup>#</sup>
Cancer	128 (4.2 %)	70 (4.7 %)	58 (3.6 %)	7 (6.5 %)	11 (4.7 %)	78 (4.4 %)	17 (3.0 %)	13 (3.6 %)	0.36 <sup>#</sup>

S4 baseline examination 1999–2001, F4 follow-up examination 2006–2008, CVD cardiovascular disease (myocardial infarction, stroke), mean arithmetic mean, std standard deviation

\* 34 subjects with missing anthropometric data; statistical tests for differences across weight change categories

# Chi-square test

‡ ANOVA

**PCS**

Among women, the overall decrease in PCS due to the effect of time was small ( $\beta_{time} = -0.17$ ), but appeared to be strong in the obese subgroup ( $\beta_{time} = -1.14$ , CI:  $-2.24$  to  $-0.04$ ). The ‘between-subject’ estimate indicated that high BMI levels were associated with low physical health ( $\beta_{BS} = -0.22$ , CI:  $-0.29$  to  $-0.14$ ). The ‘within-subject’ estimates illustrated that an increase of one BMI point was associated with a PCS decrement of 0.46 points (CI<sub>WS</sub> =  $-0.69$  to  $-0.23$ ). This negative longitudinal association was strongest among initially normal weight ( $\beta_{WS} = -0.84$ ) and overweight women ( $\beta_{WS} = -0.63$ ).

Men also experienced great declines in physical health over time ( $\beta_{time} = -0.64$ , CI:  $-1.14$  to  $-0.15$ ), and similar as for women, this negative effect of time appeared strongest for obese individuals ( $\beta_{time} = -1.70$ , CI:  $-2.97$  to  $-0.43$ ). BMI levels were adversely associated with physical health ( $\beta_{BS} = -0.21$ , CI:  $-0.30$  to  $-0.11$ ). This

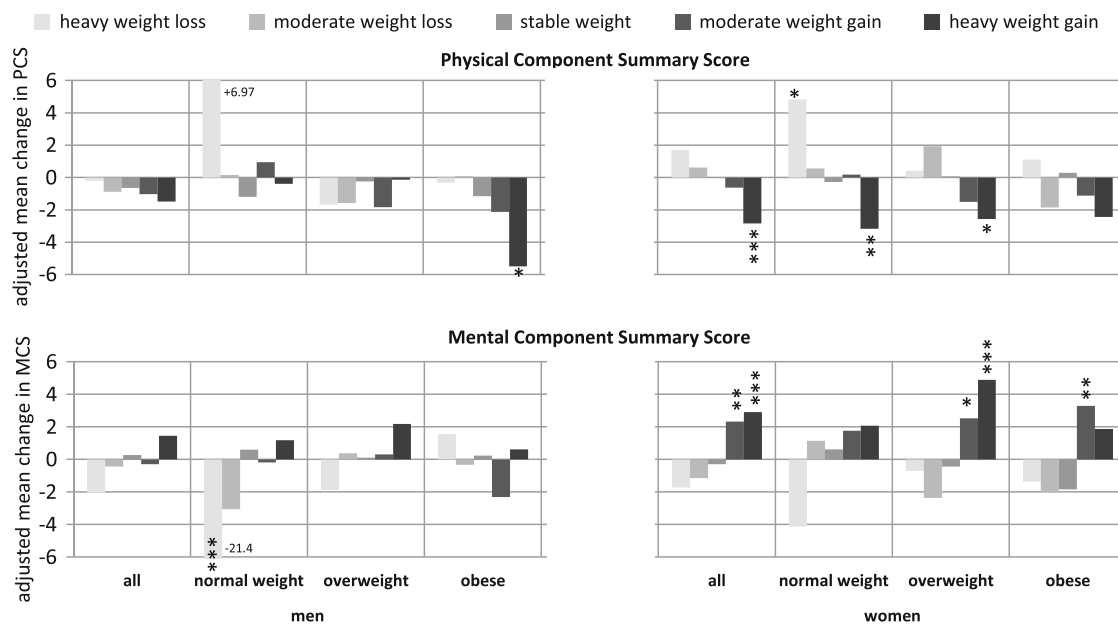
negative relationship in the cross-sectional perspective appeared non-linear and was greatest in the obese subsample ( $\beta_{BS} = -0.52$ , CI:  $-0.77$  to  $-0.27$ ). In contrast to women, BMI change and PCS scores were only inversely associated among obese participants ( $\beta_{WS} = -0.64$ , CI:  $-1.12$  to  $-0.16$ ), but not among normal weight or overweight peers.

In both sexes the direction of the ‘within-subject’ and ‘between-subject’ associations tended to have the same direction, with larger estimates for the intrapersonal component.

**MCS**

For both genders, the effect of time on HRQL was smaller for mental health than for physical health. Only obese participants tended to experience MCS score decrements.

The ‘between-subject’ estimate indicated a small positive relationship between BMI levels and MCS



**Fig. 1** Adjusted mean health-related quality of life change scores of ordinary least squares regression analysis for weight change categories, stratified by sex (Germany, 1999–2008). Model adjusted for age, education, baseline diseases (CVD, cancer, diabetes), baseline BMI category and baseline BMI category\*weight change category; *p* values

are calculated for differences in change scores among weight change groups with ‘stable weight’ as reference category; *PCS* physical component summary, *MCS* mental component summary; \**p* < 0.05, \*\**p* < 0.01, \*\*\**p* < 0.001

**Table 2** Exact numbers of participants in total and per baseline weight and weight change category included in the change-score and multi-level growth analysis (Germany, 1999–2008)

Weight development from S4 to F4	<i>N</i>	Heavy weight loss	Moderate weight loss	Stable weight	Moderate weight gain	Heavy weight gain	<i>p</i> value
All	2,677*	92 (3.4 %)	200 (7.5 %)	1,549 (57.9 %)	515 (19.2 %)	321 (12.0 %)	
Men	1,292	34 (2.6 %)	91 (7.0 %)	768 (59.4 %)	258 (20.0 %)	141 (10.9 %)	
Baseline weight category							
Normal weight	336	3	19	187	81	46	<0.001#
Overweight	689	16	55	420	135	63	
Obese	267	15	17	161	42	32	
Women	1,385	58 (4.2 %)	109 (7.8 %)	781 (56.4 %)	257 (18.6 %)	180 (13.0 %)	
Baseline weight category							
Normal weight	589	13	35	328	119	94	<0.001#
Overweight	486	20	49	280	79	58	
Obese	310	25	25	173	59	28	

S4 baseline examination 1999–2001, F4 follow-up examination 2006–2008

\* Underweight subjects (*n* = 15), subjects with missing anthropometric (*n* = 34) or missing HRQL data (*n* = 164) and subjects with incident cases of CVD (*n* = 87) or cancer (*n* = 128) were excluded

# Chi-square test

scores among women ( $\beta_{BS} = 0.10$ , CI: 0.01–0.19). The change of BMI within female individuals over time was positively associated with MCS scores ( $\beta_{WS} = 0.71$ , CI: 0.43–0.99), as well. This longitudinal association was above average among normal weight ( $\beta_{WS} = 0.94$ , CI: 0.39–1.48) and overweight women ( $\beta_{WS} = 0.89$ , CI: 0.42–1.36).

In contrast to the change-score analysis, the longitudinal association between BMI change and MCS in men was significant ( $\beta_{WS} = 0.36$ , CI: 0.06–0.65).

Beside the unclear pattern of MCS among men, the direction of the cross-sectional and longitudinal associations between BMI and HRQL appeared clearly consistent in both genders.

**Table 3** Regression coefficients for multilevel linear regression analysis of health-related quality of life scores with body mass index as time-varying covariate, stratified for sex and baseline weight category (Germany, 1999–2008)

Baseline weight category	Estimate <sup>#</sup>	Men				Women			
		PCS		MCS		PCS		MCS	
		$\beta$	95 % CI	$\beta$	95 % CI	$\beta$	95 % CI	$\beta$	95 % CI
All	Time	-0.64*	(-1.14, -0.15)	-0.07	(-0.63, 0.49)	-0.17	(-0.65, 0.32)	0.13	(-0.46, 0.72)
	BMI (between subjects)	-0.21***	(-0.3, -0.11)	-0.05	(-0.15, 0.05)	-0.22***	(-0.29, -0.14)	0.10*	(0.01, 0.19)
	BMI (within subjects)	-0.26*	(-0.52, 0.00)	0.36*	(0.06, 0.65)	-0.46***	(-0.69, -0.23)	0.71***	(0.43, 0.99)
Normal	Time	-0.15	(-1.17, 0.87)	0.02	(-1.17, 1.21)	0.64	(-0.12, 1.40)	0.36	(-0.58, 1.30)
	BMI (between subjects)	0.13	(-0.33, 0.59)	0.30	(-0.19, 0.80)	-0.19	(-0.49, 0.11)	0.14	(-0.22, 0.51)
	BMI (within subjects)	0.20	(-0.46, 0.85)	0.65	(-0.12, 1.42)	-0.84***	(-1.28, -0.40)	0.94***	(0.39, 1.48)
Overweight	Time	-0.62	(-1.25, 0.00)	0.03	(-0.71, 0.77)	-0.20	(-1.00, 0.60)	0.18	(-0.83, 1.18)
	BMI (between subjects)	-0.10	(-0.40, 0.20)	-0.20	(-0.52, 0.12)	0.00	(-0.36, 0.35)	0.39*	(0.03, 0.76)
	BMI (within subjects)	-0.06	(-0.43, 0.30)	0.35	(-0.09, 0.78)	-0.63***	(-1.01, -0.26)	0.89***	(0.42, 1.36)
Obese	Time	-1.70**	(-2.97, -0.43)	-0.64	(-1.90, 0.63)	-1.14*	(-2.24, -0.04)	-0.73	(-2.00, 0.54)
	BMI (between subjects)	-0.52***	(-0.77, -0.27)	-0.10	(-0.36, 0.16)	-0.04	(-0.26, 0.18)	0.13	(-0.11, 0.38)
	BMI (within subjects)	-0.64**	(-1.12, -0.16)	0.26	(-0.21, 0.74)	-0.13	(-0.53, 0.27)	0.34	(-0.12, 0.80)

Models adjusted for age, education and baseline diseases (CVD, cancer, diabetes)

PCS physical component summary, MCS mental component summary, BMI body mass index

<sup>#</sup>  $\beta_{\text{time}}$ : HRQL change during the follow-up period,  $\beta_{\text{BMI}}$ : HRQL change per BMI unit

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$

### Sensitivity analysis

The additional sensitivity analyses included one model with incident cases of cancer and CVD events and one model with the covariate ‘weight satisfaction’. The results of these altered change-score and multi-level models differed only negligibly from those of the original ones.

### Discussion

Cross-sectional studies provide no information about weight change related trajectories of HRQL over time. To the best of our knowledge, this study is one of the first to examine the longitudinal effect of weight change on HRQL in a population-based cohort. In our analysis, weight gain over time was inversely associated with physical health among women and obese men. However, weight gain led to improvements in mental health, particularly among women.

Our results were predominantly consistent with findings from the few previous longitudinal studies. Verkleij et al. (2012) also found a negative association between weight change and PCS scores in a large Dutch cohort, using generalized estimating equation analysis. Comparable to our outcomes, this effect was strongest in obese men and normal weight women and mainly dominated by the domains ‘general health’ among men and ‘physical

functioning’ among women. Our results and those of previous studies indicate a dose–response relationship with strongest PCS impairments for heavy weight gain (Fine et al. 1999). The negative association between weight change and physical health found in our study is also consistent with further longitudinal studies. Using the SF-36, Fine et al. (1999) revealed decreased scores for female weight gainers in the physical domains ‘physical functioning’, ‘bodily pain’ and ‘physical role limitation’ and Leon-Munoz et al. (2005) reported impairments in all 4 physical domains among obese and non-obese men and women in a cohort of elderly Spanish people based on the self-reported weight change.

With respect to mental health, Verkleij et al. (2012) revealed a positive effect of weight gain in women only. This positive association between weight change and MCS in women was confirmed by our study. However, previous research had partially reported contradictory results. In the prospective Nurses’ Health Study, the mental domain ‘vitality’ was adversely affected by weight gain and cross-sectional studies reported inconsistent associations between BMI levels and mental health (Fine et al. 1999). Our single-item analysis showed that improvements in MCS among women were mainly driven by questions referring to the domains ‘mental health’ and ‘emotional role limitation’ whereas the question referring to ‘vitality’ was slightly negative associated with weight gain. The reason for this finding remained unknown. As already suggested in

earlier studies, incorporating obesity-specific questionnaires might help to clarify the somehow surprising relationships between weight, weight change and mental health (Lopez-Garcia et al. 2003; Verkleij et al. 2012).

Most of the changes in quality of life observed in this study have to be regarded as moderate to large, implying clinical relevance (Alonso et al. 2004; Schunk et al. 2012). A change in the PCS score of 3–4 points as observed for heavy weight gainers reflects almost half a standard deviation of the PCS score and equals a decline of PCS scores between subjects aged 40–70 years in this cohort.

Although our models were fitted with different statistical methods, the outcomes from the linear regression and the multi-level growth analysis showed a very high degree of agreement concerning the associations between weight change and HRQL. Further, the symmetrical consistency in direction and size of the ‘between-subject’ and ‘within-subject’ associations illustrates a high level of similarity for interpersonal (cross-sectional) and intrapersonal (longitudinal) associations. This indicates that the BMI-related development of HRQL within a subject over time appears analogous to the difference in HRQL scores among different subjects of different baseline BMI levels. To the best of our knowledge this is a novel finding, as the relationship between the cross-sectional and longitudinal perspective has not been investigated or reported previously.

The multi-level analysis showed that in particular already obese subjects experienced a strong decline in physical health over time, independently of their change in body weight. In combination with negative cross-sectional, respectively, longitudinal associations between BMI and HRQL, one could conclude an ‘additive’ model, in which the magnitude of weight gain and the period of time suffering from excess body weight are two crucial determinants in the development of physical health over life time. This assumption is strengthened by a study of Garner et al. (2011) who revealed increasing HRQL decrements over time for severely obese women compared to normal weight peers.

We also found that weight gain tended to have a greater impact on quality of life than weight loss. This finding might have a great implication for public health policy as it supports current guidelines, to focus rather on population-based prevention approaches than on cost-intensive weight loss strategies (WHO 2000). As these results represent the valuation of weight change from a population-based subject-centered perspective, a prioritization of population-based prevention strategies should be considered in future allocation of health care resources. The high prevalence of overweight and the discrepancy in the proportion of weight gainers and weight losers furthermore illustrates the importance for preventive action.

The strengths of this study are its longitudinal design with a population-based sample, the objective measurement of anthropometrics and the methodological approach including both, linear regression of change scores, which enables comparisons with previous studies, and multi-level growth analyses. Other population-based cohort studies either incorporated interventional components (Verkleij et al. 2012), were based on self-reported weight (Leon-Munoz et al. 2005), or suffered from limited generalizability due to a mere inclusion of certain subgroups (Fine et al. 1999). Whereas cross-sectional studies only compare HRQL scores of individuals at various BMI levels, the use of multi-level growth analysis in our study splits the association of HRQL and BMI into ‘between-subject’ and ‘within-subject’ associations (Hedeker 2004). This statistical sophisticated method enables to quantify and to compare cross-sectional and longitudinal relationships. In the first model, change-score analysis was used as this method is more appropriate to answer the question of interest than analysis of covariance, which assumes equal baseline values among the groups (Fitzmaurice et al. 2004; Van Breukelen 2006). Potential bias in the estimates of change caused by effects of regression to the mean was further unlikely to have occurred in this study as firstly, standardized weight measurements are known to have a high reliability, secondly, group assignment into weight change groups was independent from the outcome variable, and thirdly, multi-level growth models which are known to be robust against regression to the mean effects confirmed the results of the change-score models.

Our study suffered also from a few limitations that should be mentioned. As already addressed in previous studies, we also had problems to differentiate between the effects of intentional, unintentional disease-related and unintentional not disease-related weight loss. Although the sensitivity analysis indicated that weight perception had no impact, it remains unclear whether this variable was an appropriate proxy for the voluntariness of weight change. Furthermore, we only controlled for certain severe diseases and did not adjust for lifestyle factors, such as physical activity. Other adverse health conditions related to excess weight or weight gain might also influence the trajectory of HRQL over time. Additional issues that need to be considered are the impact of the different HRQL-assessment methods at baseline (interviewer-administered) and follow-up (self-administered) and the uncontrolled selective or non-selective participation of subjects at the follow-up examination. As recent studies showed that the potential bias caused by different mode of questionnaire administration in longitudinal designs is rather marginal (Puhan et al. 2011), we assume that the different assessment methods in our longitudinal study possibly biased the time effect in multi-level growth model, but were unlikely to

influence the longitudinal association between weight change and HRQL. Further, the characteristics (age, BMI) of non-participants at baseline were quite comparable and there is no indication that weight change is perceived differently from this group. We therefore assume that the selective or non-selective participation of subjects at the follow-up did not impact the association between weight change and HRQL.

## Conclusion

With almost one-third of the cohort experiencing a significant gain in body weight over the 7-year period, weight gain is a highly prevalent phenomenon. Weight gain leads to clinically relevant impairments in physical health among women and obese men, but to improvements in mental health, particularly among women. Impaired physical health among obese subjects observed in cross-sectional studies is assumed to be partially attributable to the HRQL decline that had evolved in the process of weight gain over time. More research is needed to sufficiently understand the impact of weight and weight development on mental and physical components of HRQL.

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**Conflict of interest** The authors declare no conflict of interest.

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