REVIEW ARTICLE

The Morbidity and Mortality Associated With Overweight and Obesity in Adulthood

A Systematic Review

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SUMMARY

Background: Overweight and obesity are generally thought to elevate morbidity and mortality. New data call this supposed association into question.

Methods: The Cochrane, Pubmed, and other databases were systematically searched for a combination of relevant terms and subject headings. Meta-analyses and cohort studies based on the German population were evaluated for possible associations between overweight/obesity and adult morbidity and mortality. Case-control and cross-sectional studies were excluded.

Results: A total of 27 meta-analyses and 15 cohort studies were evaluated. The overall mortality of overweight persons (body mass index [BMI] 25–29.9 kg/m^2) is no higher than that of persons of normal weight (BMI 18.5–24.9 kg/m^2), but their mortality from individual diseases is elevated, diminished or unchanged, depending on the particular disease. The overall morbidity is unknown. Both obesity (BMI >30 kg/m^2) and overweight are associated with increased disease-specific morbidity for some diseases, but decreased or unchanged for others. In general, obesity confers a higher risk than overweight. Morbidity and mortality are markedly influenced by the patient's age, sex, ethnic origin, and social status. The external validity of the comparative predictive performance (c-statistic) of BMI, waist circumference, and ratio of waist to hip circumference cannot be determined from the available analyses.

Conclusion: The prevailing notion that overweight increases morbidity and mortality, as compared to so-called normal weight, is in need of further specification. Obesity, however, is indeed associated with an elevated risk for most of the diseases studied.

Key words: overweight, morbidity, mortality, body mass index, obesity

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The majority of Germans are at the very least overweight (Body Mass Index [BMI] ≥25 to 29.9 kg/m^2), and about 20% are obese (BMI ≥30 kg/m^2)—with sex-related and age-related differences (1e). The risk factors for overweight and obesity include family situation, low socioeconomic status (SES), stress, eating disorders, endocrine diseases, medications, lack of exercise, and faulty nutrition. It is especially the significance of the factor SES that is being discussed controversially in scientific circles (1–4).

Overweight, obesity, and patterns of abdominal fat distribution are classified as risk factors for a series of diseases. In 2008 the German Federal Center for Health Education authorized the authors to perform a systematic analysis of these relationships which would be transferrable to the German adult population. The present systematic review analyzes morbidity and mortality risks that are associated with overweight/obesity on the basis of international meta-analyses and German population-related cohort studies. Effects related to sex, age, smoking, ethnic origin, and SES are considered.

Methods

A systematic review of the literature (December 2008) on morbidity and mortality risks in overweight/obesity and on the effect of confounding factors such as smoking or SES was performed in the following databases and institutions: Cochrane, PubMed, Institute for Quality and Efficiency in Health Care, Robert Koch Institute, German Agency for High Technology Assessment (HTA), International Network of Agencies for HTA.

Search terms and key words were used in combination, for example: "overweight", "obesity", "bodyweight", "body mass index", "mortality", "morbidity", "complication", "meta-analysis" (complete search strategy can be found in the Appendix as an *eSupplement*).

The included meta-analyses focused exclusively on prospective cohort studies. German population-related cohort studies were also included, because these are frequently excluded from international meta-analyses and are relevant for the German population.

TABLE 1

Included meta-analyses

Meta-analysis	Target parameter	Exposure parameter	Review period	Included studies[*1]	Study cohorts[*1]
Ni Mhurchu et al. (e8)	Stroke, coronary heart disease	BMI	Not specified	n = 4	M, F (Australia/New Zealand)
Bergström et al. (e12)	Renal cell carcinoma	BMI	1966–1998	n = 6	M, F*2
Berrington de Gonzalez et al. (e28)	Pancreatic cancer	BMI	1966–2003	n = 8	M, F (EU, USA)
Beuther et al. (e32)	Asthma	BMI	1966–2006	n = 7	M, F (EU, USA, Canada)
Bogers et al. (e6)	Coronary heart disease	BMI	1996–2005	n = 14	M, F (EU, USA, Canada)
Connolly et al. (e13)	Breast cancer	WHR	1966–2002	n = 5	F (EU, USA)
Dai et al. (e14)	Colon cancer, rectal cancer	BMI, WC, WHR	Until Dec 2006	n = 15	M, F (EU, USA, Canada, Australia, Asia)
de Laet et al. (e11)	Bone fractures	BMI	Not specified	n = 12	M, F (EU, Canada, Asia)
Hartemink et al. (e9)	Type 2 diabetes	BMI	1980–2004	n = 31	M, F (EU, USA)
Harvie et al. (e15)	Breast cancer	WHR	1966–2002	n = 5	F (EU, USA)
Janssen et al. (e4)	All cause mortality	BMI	Not specified	n = 32	M, F (EU, USA, Asia) Age >65 years
de Koning et al. (e5)	Cardiovascular events	WC, WHR	1966–2006	n = 15	M, F*[2]
Larsson et al. (e19)	Non-Hodgkin's lymphoma	BMI	1966–2007	n = 10	M, F (EU, USA, Australia, Asia)
Larsson et al. (e17)	Multiple myeloma	BMI	1966–2007	n = 11	M, F (EU, USA, Australia, Asia)
Larsson et al. (e22)	Hepatic cell carcinoma	BMI	1966–2007	n = 11	M, F (EU, USA, Asia)
Larsson et al.(e20)	Gallbladder cancer	BMI	1966–2007	n = 8	M, F (EU, USA, Asia)
Larsson et al. (e16)	Pancreatic cancer	BMI	1966–2006	n = 21	M, F (EU, USA, Asia)
Larsson et al. (e21)	Leukemia	BMI	1966–2007	n = 9	M, F (EU, USA, Australia, Asia)
Larsson et al. (e18)	Colon cancer, rectal cancer	BMI, WC, WHR	1966–2007	n = 31	M, F (EU, USA, Canada, Australia, Asia)
MacInnes et al. (e24)	Prostate cancer	BMI, WC	1966–2004	n = 23	M (EU, USA)
McGee (6)	All cause mortality, overall cancer mortality, coronary heart disease, cardiovascular events	BMI	Not specified	n = 26	M, F*[2]
Moghaddam et al. (e23)	Colorectal cancer	BMI, WC	Until April 2007	n = 23	M, F (EU, USA, Canada, Australia, Asia)
Olsen etal. (e25)	Epithelial ovarian cancer	BMI	Until April 2006	n = 11	F*[2]
Renehan et al. (e26)	Total cancers	BMI	Until Nov 2007	n = 67	M, F (EU, USA, Australia, Asia)
Ursin et al. (e27)	Breast cancer	BMI	1966–1992	n = 4	F (EU)
Wanahita et al. (e7)	Atrial fibrillation	BMI	1966–2007	n = 5	M, F (EU, USA)
Wang et al. (e29)	Renal cell carcinoma	BMI	1980–2006	n = 16	M, F (EU, USA, Asia)

EU, European population; F, females; M, males

[*1] Only meta-analyses of prospective population-related cohort studies are listed

[*2] No information is available on the origin of the included cohorts

TABLE 2

Included cohort analyses

Study	Reference	Target parameter	Exposure parameter	Study cohort	Observation period (median)
EPIC*[1]	(e31)	Breast cancer	BMI, WC, WHR	F (n = 176 886)	4.7 years
EPIC*[1]	(e30)	Colorectal cancer	BMI, WC, WHR	F (n = 238 546) M (n = 129 731)	6.1 years
EPIC*[2]	(e53)	Renal cell carcinoma	BMI, WC, WHR	F (n = 218 819) M (n = 129 731)	6 years
EPIC*[2]	(e54)	Prostate cancer	BMI, WC, WHR	M (n = 129 502)	8.5 years
EPIC*[3]	(5)	All cause mortality	BMI, WC, WHR	F (n = 235 035) M (n = 124 352)	9.7 years
EPIC-Potsdam	(e55)	Type 2 diabetes	BMI	F (n = 10 371) M (n = 7720)	7 years
DOMS	(8, e56)	All cause mortality	BMI	F (n = 4601) M (n = 1591)	14.8 years
	(7)	Cardiovascular, cancer-related and diabetes-specific mortality	BMI	F (n = 4601) M (n = 1591)	14.8 years
GRIPS	(e57)	Myocardial infarction	BMI	M (n = 5639)	10 years
Heidelberg cohort study of the elderly	(e33)	Asthma	BMI	F+M (n = 3624)*[4]	8.5 years
MONICA/KORA	(e58)	Myocardial infarction or sudden cardiac death	BMI	F (n = 3001) M (n = 3238)	7.8 years
	(e10)	Type 2 diabetes	BMI, WC, WHR	F (n = 2957) M (n = 3 055)	9.2 years
ProGERD*[5]	(e34)	Gastroesophageal reflux disease	BMI	F+M (n = 6215; part M = 53%)	5 years
PROCAM	(e59)	Type 2 diabetes	BMI	M (n = 3537)	6.3 years
	(e60)	Non-fatal myocardial infarction or coronary death	BMI	F (n = 7328) M (n = 16 288)	8 years

F, females; M, males, BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio;
DOMS, Duesseldorf Obesity Mortality Study; EPIC, European Prospective Investigation into Cancer and Nutrition;
GRIPS, Goettingen Risk, Incidence and Prevalence Study;
MONICA/KORA, Monitoring Trends and Determinants in Cardiovascular Disease Study/Cooperative Health Research in the Augsburg Region;
ProGERD, Progression of Gastroesophageal Reflux Disease; PROCAM, Prospective Cardiovascular Muenster Study;
*1 Multicenter study: 9 European countries including Germany; *2 Multicenter study: 8 European countries including Germany
*3 Multicenter study: 10 European countries including Germany; *4 No information on sex distribution;
*5 Multicenter study: Germany, Austria, and Switzerland

The titles and abstracts of identified publications were independently evaluated by two scientists (Lenz, Richter); the reference lists in the evaluated reviews were checked for additional publications. The following were excluded:

- Case control studies, because of their susceptibility to control group distortion (selection bias)
- Cross-sectional studies, because these do not permit any risk assessments to be made
- Meta-analyses that include cross-sectional or case control studies
- Studies that use cohorts consisting of children, adolescents, or exclusively high risk groups such as dialysis patients or patients with heart failure
- Examinations that merely evaluate surrogate parameters such as blood pressure or left-ventricular hypertrophy.

The quality of the included studies was documented using Cochrane criteria (2e) (*eSupplement*).

Where available, adjusted body mass index-associated risk data were extracted from the evaluated publications. The relationship between exposure and outcome parameters was analyzed in the light of factors such as age, sex, socioeconomic status, and ethnic origin.

The presentation of the results is descriptive. Meta-meta-analyses or meta-analyses of all the included cohort studies were not performed. Such analyses would require that individual data for all cohort participants from the individual studies be available, because the exposure and reference parameters reported in the publications cannot be directly compared for most of the target parameters.

TABLE 3

Overweight-associated mortality risk

Target parameter	Exposure	Reference	Risk (95% CI)		Source
			Women	Men	
All cause mortality	BMI >25 to <30	BMI ≥18.5 to 25	RR = 0.97 (0.93 to 0.99)	RR = 0.97 (0.92 to 1.01)	Meta-analysis (6)
	BMI 25.0 to <26.5	BMI 23.5 to 25	RR = 1.01 (0.92 to 1.11)	RR = 0.91 (0.84 to 0.99)	Cohort study (5)
	BMI 26.5 to <28.0	BMI 23.5 to 25	RR = 1.07 (0.97 to 1.18)	RR = 0.96 (0.88 to 1.04)	Cohort study (5)
	BMI 28.0 to <30.0	BMI 23.5 to 25	RR = 1.11 (1.00 to 1.22)	RR = 1.08 (1.00 to 1.17)	Cohort study (5)
Overall cancer mortality	BMI >25 to <30	BMI ≥18.5 to 25	RR = 0.99 (0.92 to 1.05)	RR = 0.93 (0.89 to 0.97)	Meta-analysis (6)
CVD mortality	BMI >25 to <30	BMI ≥18.5 to 25	RR = 1.03 (0.95 to 1.12)	RR = 1.10 (1.03 to 1.16)	Meta-analysis (6)
CHD mortality	BMI >25 to <30	BMI ≥18.5 to 25	RR = 1.10 (1.00 to 1.20)	RR = 1.16 (1.09 to 1.24)	Meta-analysis (6)

BMI, body mass index (in kg/m^2); CI, confidence interval; CVD, cardiovascular disease; CHD, coronary heart disease; RR, relative risk

Results

A total of 2384 potentially relevant publications were identified (selection procedure see *eSupplement*). 27 meta-analyses (*Table 1*) and 15 publications on cohort studies (*Table 2*) were analyzed.

Exposure parameters

The most commonly used anthropomorphic measure is BMI. Differing BMI categories are assigned different concomitant risks of becoming ill (e3). Measurements used to evaluate the visceral fat depot are waist circumference (WC) and the ratio of the waist-to-hip circumference ("waist-to-hip ratio", WHR). Abdominal obesity is defined as WC ≥88 cm or WHR ≥0.85 (women) and WC ≥102 cm or WHR ≥1 (men) (e3). Studies that analyze the categories overweight and obesity as exposure parameters mostly use the normal weight as a reference category. Non-categorical analyses usually define a higher BMI at about 1 or 5 kg/m^2 or a WC or WHR that is higher by some defined values as exposure parameters.

The external validity of the comparative predictive performance (c-statistic) of BMI, WC, and WHR cannot be evaluated based on the available analyses.

All cause mortality

According to the meta-analyses and German cohort studies, all cause mortality in overweight individuals is no higher than for those of normal weight (*Table 3*). The threshold for an increase in mortality risk in the EPIC study was a BMI of 28 kg/m^2 (5). In obesity, all cause mortality is increased by about 20% (*Table 4*) (6).

In Germany, women or men who are morbidly obese (BMI >36 kg/m^2) have a 1.3 to 3-fold mortality risk relative to the population of North Rhine-Westphalia (reference population) (*eSupplement, Table 2*) (7). If the BMI-associated mortality risk is mathematically eliminated (adjustment), the mortality risk for WC and WHR is increased in all quintiles when compared to the corresponding lowest quintile (except for women in the second quintile WHR; *Table 5*) (5).

With increasing age obesity plays an increasingly smaller role in the all cause mortality (*eSupplement, Table 2*) (8, e4). After age 50, there is an increased mortality risk for women with a BMI >36 kg/m^2 and for men with a BMI >40 kg/m^2 (8). After age 65, obesity is hardly (e4) or not at all associated with a shortened life expectancy (8).

Disease-specific risks

Cardiovascular risk—No meta-analyses of the association between BMI and the overall risk of developing a cardiovascular disease were identified. An association with WHR has been described in men (e5) (*eSupplement, Table 3*). The risk of developing coronary heart disease (CHD) is increased by about 20% in overweight and by about 50% in obese individuals (e6). No meta-analyses focusing on the risk of myocardial infarction were identified.

Both overweight and obesity are associated with increased risks of developing atrial fibrillation (e7). There is no association with stroke risk (e8).

The overall cardiovascular mortality in overweight is not increased for women while it is increased by about 10% in men (*Table 3*). In obesity it is increased by about 50% for both women and men (*Table 4*) (6); in morbid obesity (BMI >40 kg/m^2) the risk increases by 200% to 300% (7). The CHD mortality in overweight women is not increased while it increases by about 16% in overweight men. In obesity the CHD mortality increases by about 50% in women and by about 60% in men (6).

Type 2 diabetes—The risk of developing type 2 diabetes increases by about 20% for each 1 kg/m^2 rise in the BMI (e9). Compared to individuals of normal weight, the risk does not increase until a BMI <27.2 kg/m^2. At a BMI of 27.2 to <29.4 kg/m^2 the risk

TABLE 4

Obesity-associated mortality risk

Target parameter	Exposure	Reference	Risk (95% CI)		Source
			Women	Men	
All cause mortality	BMI >30	BMI ≥18.5 to 25	RR = 1.28 (1.18 to 1.37)	RR = 1.20 (1.12 to 1.29)	Meta-analysis (6)
	BMI 30.0 to <35.0	BMI 23.5 to 25	RR = 1.17 (1.07 to 1.29)	RR = 1.24 (1.14 to 1.35)	Cohort study (5)
	BMI ≥35.0	BMI 23.5 to 25	RR = 1.65 (1.46 to 1.85)	RR = 1.94 (1.71 to 2.20)	Cohort study (5)
Overall cancer mortality	BMI >30	BMI ≥18.5 to 25	RR = 1.10 (1.00 to 1.22)	RR = 1.06 (0.98 to 1.14)	Meta-analysis (6)
	BMI 36 to 39.9	Overall German population	SMR = 0.72 (0.5 to 1.1)	SMR = 1.16 (0.6 to 2.0)	Cohort study (7)
	BMI >40	Overall German population	SMR = 1.45 (1.1 to 1.9)	SMR = 1.13 (0.5 to 2.1)	Cohort study (7)
CVD mortality	BMI >30	BMI ≥18.5 to 25	RR = 1.53 (1.38 to 1.69)	RR = 1.45 (1.33 to 1.59)	Meta-analysis (6)
	BMI 36 to 39.9	Overall German population	SMR = 1.51 (1.2 to 1.9)	SMR = 2.24 (1.6 to 3.1)	Cohort study (7)
	BMI >40	Overall German population	SMR = 2.77 (2.3 to 3.3)	SMR = 4.36 (3.2 to 5.8)	Cohort study (7)
CHD mortality	BMI >30	BMI ≥18.5 to 25	RR = 1.62 (1.46 to 1.81)	RR = 1.51 (1.36 to 1.67)	Meta-analysis (6)
Mortality in type 2 diabetes	BMI 36 to 39.9	Overall German population	SMR = 3.95 (2.0 to 6.9)	SMR = 14.2 (6.5 to 27.0)	Cohort study (7)
	BMI >40	Overall German population	SMR = 7.58 (4.8 to 11.4)	SMR = 2.41 (0.1 to 13.5)	Cohort study (7)

BMI, body mass index (in kg/m^2); CI, confidence interval; CVD, cardiovascular disease; CHD, coronary heart disease; RR, relative risk
SMR, standardized mortality ratio (The reference population is the population of North Rhine-Westphalia.)

increases by about 100%; at a BMI ≥29.4 kg/m^2 the risk increases by about 300% (e9, e10) (*eSupplement, Table 3*). Data for the mortality risk in type 2 diabetes are only available for morbidly obese individuals (*Table 4*).

Orthopedic complications—A higher BMI is associated with a lower risk of suffering bone and hip fractures (e11) (*eSupplement, Table 3*). The relationship is not linear: Fractures most frequently occur in the lower BMI ranges; at a BMI around 30 kg/m^2 the risk for bone fractures is neither increased nor reduced while it is lower for hip fractures. Upon eliminating (adjustment) the factor bone density, the results are not significant (e11).

Neoplastic diseases—Men who are overweight have about a 7% lower overall risk of developing cancer (*Table 3*); no significant association exists for women. No relationship exists between obesity and overall cancer mortality (*Table 4*) (6). In morbid obesity (BMI >40 kg/m^2), overall cancer mortality in men is not increased; in women it is about 1.5 times as high as in the German total population (7). To evaluate the association between overweight/obesity and the morbidity and mortality risks of specific cancers, we analyzed 19 meta-analyses (6, e12–e29) and 3 cohort analyses (7, e30, e31) relevant to the German population (*Tables 1 and 2*). One review includes 20 meta-analyses of the association between overweight/obesity and a range of cancers (e26). The anthropometrically related morbidity and mortality risks are either lower, the same, or higher depending on the type of cancer (*eSupplement, Table 4*).

Other disease-specific risks—When compared to individuals of normal weight, overweight and obese individuals are at higher risk of developing asthma (e32, e33) (*eSupplement, Table 3*). Overweight and obese individuals have a higher risk of developing renal diseases (excluding renal cell carcinoma) with certain sex-specific differences (e29). According to a multicenter cohort study (Germany, Austria, and Switzerland) (e34), the risk for gastroesophageal reflux disease (GERD) is significantly increased at larger BMI values.

No meta-analyses were identified for the association between overweight/obesity and health-related quality of life, nor for diseases for which generally positive or negative relationships are assumed to exist (e.g., mental disorders, gallbladder diseases, hyperuricemia/gout, infertility, infectious diseases, sleep apnea syndrome, and tooth decay).

Discussion

Interpreting these results is challenging. According to the analyses performed by the authors, all cause mortality is not increased in overweight. On the other hand, the

TABLE 5

Waist circumference– and waist-to-hip ratio–associated all cause mortality risk* (5)

Exposure	Reference	Risk (95% CI)	
		Women	Men
WC 70.1 to <75.6	WC <70.1	RR = 1.16 (1.05 to 1.28)	
WC 75.6 to <81.0	WC <70.1	RR = 1.21 (1.09 to 1.35)	
WC 81.0 to <89.0	WC <70.1	RR = 1.46 (1.30 to 1.64)	
WC ≥89.0	WC <70.1	RR = 1.78 (1.56 to 2.04)	
WC 86.0 to <91.5	WC <86.0		RR = 1.15 (1.05 to 1.26)
WC 91.5 to <96.5	WC <86.0		RR = 1.35 (1.22 to 1.50)
WC 96.5 to <102.7	WC <86.0		RR = 1.63 (1.46 to 1.83)
WC ≥102.7	WC <86.0		RR = 2.05 (1.80 to 2.33)
WHR 0.73 to <0.77	WHR <0.73	RR = 1.09 (0.99 to 1.20)	
WHR 0.77 to <0.80	WHR <0.73	RR = 1.12 (1.02 to 1.22)	
WHR 0.80 to <0.85	WHR <0.73	RR = 1.23 (1.12 to 1.34)	
WHR ≥0.85	WHR <0.73	RR = 1.51 (1.37 to 1.66)	
WHR 0.89 to <0.92	WHR <0.89		RR = 1.15 (1.05 to 1.26)
WHR 0.92 to <0.95	WHR <0.89		RR = 1.26 (1.16 to 1.38)
WHR 0.95 to <0.99	WHR <0.89		RR = 1.36 (1.24 to 1.49)
WHR ≥0.99	WHR <0.89		RR = 1.68 (1.53 to 1.84)

CI, confidence interval; RR, relative risk; WC, waist circumference (in cm); WHR, waist-to-hip ratio (in units)
*adjusted to body mass index

mortality risks for several diseases are increased while they are reduced or unchanged for others. In obesity, all cause mortality is about 20% higher than in normal weight individuals. In morbid obesity, all cause mortality can be more than 200% higher. Whether a role is played by fat distribution patterns (WC and WHR) and what this role may be remains essentially unknown due to insufficient data.

For various diseases or target parameters it was impossible to identify any data. A possible reason for this is the restriction of our study to an evaluation of meta-analyses and German population-related cohort studies. In addition, the medical literature primarily analyzes those diseases for which an effect through overweight or obesity is plausible to exist. Thus, there is a suspected investigational and publication bias for diseases that appear to be favored by overweight or obesity.

This assumption is supported by the results of the mortality analyses: all cause mortality is not increased in overweight individuals. This parameter is made up of disease-specific mortality risks for each disease. Many of the diseases analyzed here yield elevated risks. Accordingly, there must also be still unidentified diseases with a reduced risk.

The problem in interpreting the morbidity risks is similar. Whether reduced risks for diseases exist for which the authors have not identified any data or that have so far not been investigated cannot be evaluated.

A higher BMI can be advantageous for severely ill patients: It is plausible that overweight may be associated with reduced risks in consumptive diseases such as cancer and this is partially confirmed by the available analyses. International meta-analyses (e35–e38) show that patients with heart failure, after myocardial infarction or percutaneous transluminal angioplasty are protected by overweight/obesity against reinfarction and death by myocardial infarction. Patients in the ICU exhibit a lower mortality with a BMI 25 to 29.9 kg/m^2 versus a BMI 18.5 to 24.9 kg/m^2 (e39). Meta-analyses which only summarize the already known mortality or morbidity risks can be misleading, because of the investigational and possible publication bias (e40).

An additional area of uncertainty is the significance of the reported associations. To interpret the clinical relevance (relative risks [RR], odds ratios [OR], etc.) the particular population-related incidence of a target parameter must be known. In rare diseases even high relative risks can be marginally relevant. For example, each year 15 out of 100 000 people in Germany are diagnosed with non-Hodgkin's lymphoma (e41). In obesity the risk is about 20% higher. This means that out of 100 000 obese people approximately 18 are annually diagnosed with non-Hodgkin's lymphoma.

The information discovered by the authors is based on cohort analyses. Only information on associations

can be provided, because an adjustment of the many interfering factors is only possible on a limited basis. Whether the presented associations are causal remains open. For example, mortality and morbidity are also determined by age, sex, SES, smoking, and other factors such as body fat distribution which for the most part interact with one another.

In the elderly, the number of competing risk factors increases (9). Thus, individual risk factors are less significant for the overall risk. Bias also can result from age-related diseases which are frequently associated with weight loss (e4).

As in most international studies (10, 11), the German population exhibits an association between SES and overweight/obesity (12, 13), with education (14), work, income (15), and birth weight (10) playing an important role. The lowest cardiovascular risk is observed in socially well positioned young individuals (10).

Smoking modifies the BMI-associated risk of developing lung cancer. A BMI that is 5 kg/m^2 higher in smokers is associated with a reduced risk of developing lung cancer (RR: 0.76; 95% confidence interval [CI]: 0.67– 0.85); in non-smokers the relationship is not significant (RR: 0.91; 95% CI: 0.76–1.10) (e26). Smokers frequently weigh less than non-smokers (e42) and this can contribute to distortions in studies (e43). Whether it is smoking alone or the associated lower weight that contributes to the increased risk, remains open.

There are also confounding factors the effect of which are plausible, but cannot be quantified. In the risk of developing diabetes these include undiagnosed cases that are more frequently discovered in overweight and obese persons (e44). It is suspected that greater attention is paid to diabetes in these groups.

Ethnic origin modifies the association between overweight/obesity and a type 2 diabetes risk (e45). A quantification and ethnic specification is hardly possible because of the heterogeneity of the observed participants and the diversity of the exposure parameters.

Potential sources of error are also non-standardized methods for measuring the hip and abdominal circumference (e46).

External validation studies on the comparative predictive performance of the BMI, WHR, and WC could not be identified by the present analysis. Thus, the reliability of individual risk prognoses based on these parameters remains unclear.

Body weight as well as the associated risks are subject to temporal trends (16). Since the 1970s in the USA, the body weight with the best life expectancy has shifted to higher BMI values (16). Today, a BMI of 27 kg/m^2 in middle age is associated with the lowest mortality. At more than 70 years old, a BMI 27 to 35 kg/m^2 is associated with the lowest mortality (16).

Similar findings also hold for the German population (8). Thus, the significance of obesity for mortality has been reduced.

After the present systematic review was completed, an additional meta-analysis was published (17). It included individual data from approximately 900 000 study participants in 57 international cohort studies. The mortality risk was evaluated according to BMI categories. The study essentially confirms the results of our own analysis. All cause mortality in overweight (BMI 25–30 kg/m^2) compared to normal weight individuals (BMI 18.5 to 25 kg/m^2) is not, or only slightly, elevated. However, this study defines unusual categories which limits data comparability. An important result of the analysis is the pronounced parabolic distribution of the mortality risk. Especially in the category of a "low normal" BMI (18.5 to 22.5 kg/m^2) the mortality risk versus a BMI of 27.5 to 30 kg/m^2 is even increased. The increased risk above a BMI of 28 kg/m^2 is especially due to vascular diseases and in the lower BMI ranges it is the result of neoplastic diseases. Therefore, these results fundamentally cast doubts on the classification of BMI categories such as normal weight or overweight.

Conclusion

Anthropometrically related morbidity and mortality risks are not linear: The risk increase is steepest in morbid obesity. Obesity is a risk factor for many diseases, while for a few identified diseases the risks are reduced. Overweight, however, is associated with an increased risk for some diseases and with a reduced risk for others. All cause mortality is not increased in overweight individuals. The risks associated with being underweight are not part of this literature analysis. However, an increased morbidity and mortality risk has been confirmed for being underweight. The assumption that overweight versus normal weight is associated with an increased morbidity and mortality risk must be stated more specifically (17).

The question whether all persons above a defined BMI should lose weight cannot be answered by these analyses. This requires randomized controlled trials that examine the efficacy of weight-reducing interventions. Depending on the intervention or the intervention group, weight loss can have desirable or undesirable effects (e47-e52). Long-term effects are unclear (e50). Therefore, general recommendations for weight loss cannot be derived from this review.

Conflict of interest statement
The authors declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

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KEY MESSAGES

- Overweight is associated with an increased risk for some diseases and a reduced or unchanged risk for others.
- The all cause mortality is not increased in overweight. It is increased for individual diseases; for others it is reduced or unchanged.
- Obesity is associated with an increased risk for more diseases and with a reduced or unchanged risk in fewer diseases.
- In obesity the all cause mortality is increased by approximately 20%; in morbid obesity this can be more than 200%.
- The assumption that overweight is associated with an increased morbidity and mortality risk versus normal weight must be stated more specifically.

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REVIEW ARTICLE

The Morbidity and Mortality Associated With Overweight and Obesity in Adulthood

A Systematic Review

Matthias Lenz, Tanja Richter, Ingrid Mühlhauser

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