CORRESPONDENCE

The Morbidity and Mortality Associated with Overweight and Obesity in Adulthood

A Systematic Overview

by Dr. phil. Matthias Lenz, Tanja Richter, Prof. Dr. med. Ingrid Mühlhauser
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Short Period of Observation

In the publication of Lenz et al., the central clinical conclusion is that the overall mortality is not increased "with overweight". However, the authors fail to present an adequate discussion of a problem of all analyzed studies, namely the short periods of observation. For example, many of the studies listed in Table 2 covered observation for periods clearly less than 10 years. Even the meta-analysis of about 900 000 subjects (reference 17), which the authors specially emphasized, had a mean observation period of only 8 years, with a mean subject age of 46 years.

The influence of overweight – starting in early adulthood – can certainly not be reliably evaluated on the basis of such data. For example, it would without doubt be unjustified at the moment to transfer the central conclusion of the study – that overweight does not increase overall mortality – to an overweight subject who is now aged 20.

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Association With Increased Risk of Stroke

The authors have presented an interesting overview of morbidity and mortality in overweight. They come to the conclusion that the generally accepted assumption that overweight is associated with increased risk of morbidity and mortality is no longer tenable and that it must be specified more precisely. Unfortunately, when the authors selected their search terms, they missed some important articles on the association between overweight and cardiovascular or cerebrovascular diseases which have a decisive effect on morbidity and mortality. Hu et al. (1) reported a population-based study with about 50 000 participants. They demonstrated an association between body mass index (BMI) of 25–29 kg/m^2 and an increased risk of stroke. Our research group has recently reported the result of a case-control study with 1137 participants, which demonstrated an association between abdominal overweight and increased risk of stroke (2).

It follows that the statement in the article that there is "no association with stroke risk" is untenable. This is based on a study in the Asia-Pacific area and cannot be directly transferred to the European population. We refer you to Yusuf et al. (3) for the association between overweight and myocardial infarction.

We agree with the authors that the morbidity associated with overweight must be specified more precisely. Nevertheless, the important role of overweight in cerebrovascular and cardiovascular diseases should not be neglected, as, taken together, these are the most important causes of mortality and handicap in adults.

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Inappropriate Interpretation of the Data

This topic and the evaluation of the meta-analyses and cohort studies from Germany is an important task which the authors have set themselves. However, they have failed to include the most important and largest meta-analysis – with 900 000 participants from 28 March 2009 – in their study (1); they just mention it. Although the authors report many facts more or less correctly, particularly in relation to mortality, their selection of topics and their occasionally inappropriate interpretation of the data are striking.

The authors repeatedly state that the overall mortality is not raised in overweight. Neither the WHO nor professional societies consider that this weight class presents serious problems with respect to mortality. Although the assertion that "a BMI of 27 kg/m^2 in middle ages is now associated with the lowest

mortality" is supported in the presented study, this is in disagreement with the current scientific evidence, as has been established for decades: "[...] mortality was lowest at about 22·5–25 kg/m^2" (1).

The systematic analysis only included studies in which the BMI was used as the measure of obesity. More recent studies record waist circumference or the "waist-to-hip ratio" (WHR) as well as the BMI. These show a clear increase in mortality with increased waist circumference, even at normal BMI (2, 3). The authors' conclusion must therefore be qualified as follows: Overall mortality is not increased in overweight – as measured by the BMI.

It is incomprehensible why the authors only use meta-analyses to evaluate comorbidities, as there are numerous studies of high level of evidence on many diseases associated with obesity. The assertion that "other diseases could not be identified" is a gross disregard of the current state of knowledge. A comprehensive presentation of obesity-associated diseases would have shown how frequent and severe the secondary diseases of obesity can be. Suitable parameters for the overall evaluation of morbidity include inability to work, premature retirement and the direct and indirect costs. Many comorbidities of obesity do not influence mortality, even though they are important diseases and greatly impair the quality of life.

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Quintessence Unjustified

We would like to comment on the descriptive analysis of Lenz et al., with their conclusion that overweight – rather than obesity – is not generally associated with increased mortality and morbidity.

It is problematical to define normal weight as corresponding to a BMI between 18.5 and 25 kg/m^2, as it has long been known that a very low BMI is linked to increased risks of mortality and morbidity. It would be better to take the lower limit of the normal range as being 20 kg/m^2, even though this is not implemented in the current recommendations of the professional societies or the WHO.

The statement about mortality is evidently derived from the study of the EPIC cohort, including evaluated data from 359 387 subjects (1). It must first be said that there is in fact an increase in the overall mortality in the EPIC cohort between a BMI of 23.5–25 kg/m^2 and a BMI of 28–30 kg/m^2. This corresponds to 11% for women and 8% for men. Even though these changes sound small, they correspond to a considerable loss in life expectancy for a cohort with an average age on entry of 51.5 years. Moreover, the BMI is greatly influenced by smoking and consumptive diseases. In almost all studies, smokers have a lower BMI than nonsmokers. The formulation "Whether it is smoking alone or the associated lower weight that contributes to the increased risk [of bronchial carcinoma]" implies that obesity may protect smokers from bronchial carcinoma.

As it is generally accepted that smoking is the predominant cause of bronchial carcinoma, it is difficult to establish whether there is also an effect of BMI. Consumptive diseases also regularly lead to low BMI values. It follows that a very low number of patients with consumptive diseases could enormously distort the results – particularly in age groups with low mortality.

We therefore conclude that the authors' quintessence on overweight and mortality is not justified on the basis of the available data and is even dangerous.

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In Reply:

Vogeser sees a problem in the periods of follow-up. In most of the studies included in our analysis, the periods of follow-up were between 5 and 10 years Vogeser writes that "The influence of overweight ….can certainly not be reliably evaluated on the basis of such data". It is generally true that causal relationships can be established by cohort analyses only to a limited extent. Observational studies do only permit statements about correlations. Our article addressed the question of whether morbidity and mortality are correlated with the BMI and not whether they are caused by it. The question as to whether periods of follow-up are

appropriate is complex. Aside from the period of follow-up, the number of observed persons and the exposure parameter are of decisive importance. With large cohorts, periods of follow-up may be shorter. For example, if it were possible to observe the whole population of Germany, a few months would presumably be enough to identify associations. This is the case for the exposure parameter BMI, as BMI values are stable even over relatively long periods. Thus, we can assume that subjects who are now 50 had similar BMI values in past years. On the other hand, very long periods of follow-up present problems, as confounding by factors such as co-morbidities, changes in the social environment et cetera can not appropriately be controlled.

Winter and Back allege that we missed important studies with the search terms we used. They specifically mention the article of Hu et al. (1) and two case-control studies (2, 3). This is not the case. Because of the very large number of publications, we restricted our analysis to meta-analyses and to cohort studies related to the German population. The meta-analysis we included on stroke (4) does not support the results of the individual studies selected by Winter and Back (4). Our statement that "there is no association with stroke risk" is based on the analysis of the cohorts in the meta-analysis, who were Caucasian (from Australia and New Zealand) (4). In our opinion, these results can be transferred to the European population.

Wirth criticized the lack of scientific evidence for the statement that "a BMI of about 27 kg/m^2 in midlife is now associated with the lowest mortality". These results are based on the NHANES data from the USA. Wirth's statement that only the BMI was used as a measure of obesity in our study is not correct. WC (waist circumference) and WHR (waist to hip ratio) were also analyzed, in so far as we managed to identify corresponding meta-analyses or German population-based cohort studies. Please refer to the results and discussion section, as well as Table 5 and Tables 1, 3 and 4 in the Web Appendix.

According to Wirth, "other diseases could not be identified". This sentence has been wrongly quoted. The correct wording is: "No meta-analyses focusing on the risk of myocardial infarction were identified.". Wirth also writes that "A comprehensive presentation of obesity-associated diseases would have shown how frequent and severe the secondary diseases of obesity can be". There seems to be a misunderstanding here. We have emphasized the risk of **obesity** – rather than **overweight**. However, no meta-analyses or German population-based cohort studies could be identified for various diseases or target parameters. Our article contained an adequate discussion of any possible study or publication bias for diseases caused by overweight or obesity.

Orth and Dierkes are mistaken in their assumption that "there is in fact an increase in the overall mortality in the EPIC cohort for a BMI of 28–30 kg/m^2". The relative risks they mention are not statistically significant (see Table 3 in our article). The EPIC data (5) show that the overall mortality is increased when BMI is under 21 kg/m^2 or over 30 kg/m^2 – relative to the overall mortality with BMI between 23.5 and 25 kg/m^2. Orth and Dierkes write that our phrase "whether smoking alone or, in addition, the resulting decrease in body weight increases the risk of bronchial carcinoma" implies that obesity may protect smokers. We did not intend to imply this. The meta-analysis from 13 individual studies (6) was included in our article and shows that an increase of 5 kg/m^2 in the BMI is associated with a decrease of 20% in the risk of lung cancer for women and of 30% for men. We agree that the BMI-associated risk of lung cancer is difficult to identify in the context of the high risk of smoking.

We would like to take the opportunity of making a necessary correction in the literature list. Reference 5 (Lee CM et al.) has been cited wrongly. The correct reference is: Pischon T et al.: General and abdominal adiposity and risk of death in Europe. NEJM 2008; 359: 2105–20.

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