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ROSTOCKER ZENTRUM – DISKUSSIONSPAPIER
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No. 7

The Effect of Sex, Obesity and Smoking on Health Transitions: A statistical meta-analysis based on a systematic literature review

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The Effect of Sex, Obesity and Smoking on Health Transitions:

A statistical meta-analysis based on a systematic literature review

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Abstract:

Context: There is a large and complex body of literature on the effect of various risk factors on health and mortality. This meta-analysis structures and summarizes the knowledge contained in this literature.
Objective: We calculate the average effect-sizes of 55 empirical studies on the impact of sex, obesity and smoking on four different transitions between the statuses of not-disabled, disabled and death. We assess which risk factors and transitions are studied most and whether the impact of theses risk factors differs between the transitions.
Data Source: Expert recommendations, the electronic databases Medline, PsycINFO and SOCA (Sociological Abstracts) and the references in the articles.
Study Selection: The search is confined to the years 1985–2005 and produced a total of 8016 articles. Finally, 55 articles were included in the detailed analysis, selected by two independent researchers according to the study population, a longitudinal design of at least one year, risk factors, the transition and the outcome measures.
Data Extraction: The study characteristics and results were extracted and entered by hand into Excel Tables.
Data Synthesis: The results are presented in groups by risk factor and transition. For each group, we present the average effect size as the result of the statistical meta-analysis, including a fixed effect and a random effect model, and a test for heterogeneity and publication bias. Additionally, a meta-regression was performed.
Conclusions: The results show which risk factors and transitions have not been studied sufficiently to provide significant evidence. They reveal the results expected for the risk factor sex: women have a higher morbidity and a lower mortality. For current smokers, the results show an increased risk, more than for former smokers. Regarding obesity, the evidence shows that for healthy people a higher BMI is associated with a higher risk of disability, but – surprisingly – that for healthy as well as unhealthy people, a higher BMI is associated with a lower risk of dying.

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1 Introduction

There are several pathways to death: someone may die healthy or the trajectory may go from good health to disability, include recovery and finally lead to death. Sex, obesity and smoking are three important risk factors that may have different effects on the various transitions.

To explore this possibility, we study the four transitions (1) not disabled to disabled, (2) disabled to death, (3) disabled to not disabled and (4) not disabled to death. We have two aims: First, we analyze which risk factors have been studied most and for which transition they have been studied. This is because the reliability of research findings among other things depends on the number of high quality studies that have been performed. Second, we aim to reveal differences in the effects of a risk factor on the different transitions. For example, is the effect of obesity on the mortality risk of healthy people as large as it is for disabled persons?

We concentrate on transitions and their determinants instead of the commonly observed prevalence rates of disability. Transition rates especially help to understand the strong associations between the determinants and the prevalence of disability, for example the high prevalence of disability among smokers. Looking at transition rates in addition to prevalence is important because, first, prevalence also reflects experiences in the past, i.e. it is not restricted to current experience. Second, differences in incidence can for example be masked by differences in mortality. Third, looking at transitions is important when the aim is to reduce the burden of disability because transitions are closer to interventions.

2 Literature review

We considered three possible sources for our literature review: recommendations of experts, electronic databases and references in existing articles. The expert recommendations concentrate on certain topics and risk factors, and the electronic search is based on three databases and constitutes the largest part of our search. We used the databases Medline, PsycINFO and SOCA (Sociological Abstracts). The database search was performed during the six months from September 2005 to February 2006.

Our search is confined to the years 1985–2005. The systematic search logic contains the following terms: disability, impairment, limitation, decline, function, activities of daily living and/or mobility. We restricted the search to cohort and longitudinal studies. For the term study, we also used the term trial, for "longitudinal study" we also applied the term follow-up.

To further restrict the search to our risk factors, we looked for the terms life-style, obesity, overweight and Body Mass Index and smoking (including cigarettes or tobacco). We included the term transition as well as demographic characteristics (comprising age, sex or gender). We excluded children and cross-sectional studies, however. The search was performed in titles, keywords and abstracts.

2.1 Processing the articles

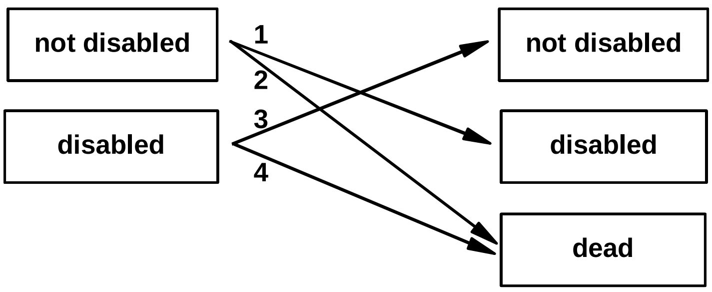
An application of the search strategy to the electronic databases produced 7729 potential results, all of which were shown as abstracts and were read by two persons independently. We considered 287 additional sources. Of these, 78 stem from a literature review by Stuck et al. (1999).[1] Another 49 articles are expert recommendations and 160 articles are taken from references of the articles. Thus, a total of 8016 articles served as the basis for our literature review. Of these, we ordered 561 articles that met our criteria (see section 2.2) to read them in length, 63 articles of these were used for our own detailed analysis. While this article is limited to the risk factors sex, obesity and smoking, our literature research also included the risk factors age, marital status and education. Therefore, of the original selection of 63 articles, we present the results of 55 articles,[2-56] for which details are given in Table 2.

2.2 Criteria of included and excluded articles

We included all studies that either examined community-dwelling or institutionalized people older than 25 years and studies that analyze both groups combined. We intended to include hospitalized people, but studies concentrating on this risk group are either short in follow-up time – usually not more than six weeks after hospital release – or they consider hospitalization as a risk factor for predicting disability. Moreover, they often focus on chronic conditions and clinical outcomes, such as knee impairments, arthritis, surgeries, etc.

Only studies from industrialized countries were considered. Entirely non-white populations in industrialized countries were excluded from our analysis. We only considered studies that clearly distinguish the disability status at baseline and explore the four transitions shown in Figure 1 below. Studies that look at mixed populations at baseline, i.e. disabled and non-disabled people together in one examination unit, are excluded from our analysis.

Figure 1: Transitions



Studies that did not contain any transitions were excluded. We only considered articles in which the outcome was age-related disability. Consequently, we excluded studies that focus on disability caused by injuries, chronic conditions or surgeries, Alzheimer's disease, Parkinson's disease and stroke. All studies that did not contain odds ratios (OR), rate ratios, relative risks (RR), or incidences as statistical measures were excluded, too. Note that we considered articles in German, French and English.

3 Description of risk factors

A distinction is made between proximate and distal determinants. The former are risk factors causing a disease and the latter are those that cause exposures to and determinants of the disease. This paper reports the results for the risk factors sex, obesity/BMI and smoking. Sex, next to age, is the most important predictor of health and mortality. Obesity and smoking are the two most important behavioral/life style factors that are likely to determine present and future mortality trends and mortality differences between men and women and between social groups.

Other important risk factors of disability and mortality, for example the education /social status, the marital status and age have been included in our literature review. However, they can not be presented in this paper due to the quantity of results.

Both obesity and smoking have a large impact on public health and are a core issue of public health policy. They are also two important behavioral factors that determine gender differences in health and mortality, as mentioned above.

4 Measurements

4.1 Measures of risk factors

Sex is a dichotomous variable and in our analysis men are the reference group.

Generally, in terms of obesity, people with a Body Mass Index (BMI) below 18.5 are regarded as underweight, those with a BMI between 18.5 and 25 are considered as being of normal weight. Persons with a BMI ranging from 25 to 29.9 and a BMI above 30 are regarded as overweight and obese, respectively. Different categorizations are possible, however. Thus, the BMI variable is divided into four categories. For the purpose of our analysis, we recalculated the reference groups into standardized groups with a normal BMI as the reference group.

The variable smoking has different categories. Most frequently, people who have never smoked are compared with current and former smokers. Sometimes, however, smoking is coded as a dichotomous variable. In this case, smokers are often compared to non-smokers. Where applicable, those who never smoked are considered as reference group in our analysis.

4.2 Measures of outcome

Disability is either established through self-reported data or through objective measurements. The measures and definitions are often modified, combined and/or developed further. As a result, a multitude of disability measures arises, which are hard to relate to a single basic disability definition. We generated four categories of disability measures representing the most frequently used concepts in our analysis.

The first category is based on the Katz concept of Activities of Daily Living (ADL).[57]

As a second category, we adapt the concept of Instrumental Activities of Daily Living (IADL) according to Lawton and Brody[58].

A third group, consisting of a mixture of the two basic concepts above, was constructed by Nagi[59] and Rosow and Breslau[60]. In our study, this category is called Combined Mobility/ Physical Performance Category (M/PP).

Some studies use a mixture of the four underlying basic concepts described here. Thus, the fourth disability category we created is called Combined Disability Measure (CDM). It combines three or four of our basic disability concepts. Information on all of the measured items in each study is provided in Table 2.

Possible outcome measures in the selected studies are the rate ratio, the relative risk, the odds ratio and incidence rates. We transformed the incidence rates into rate ratios and, where possible, odds ratios into rate ratios. For criteria and the method used, see Zhang and Yu[61].

5 Statistical Meta-Analysis

We estimated fixed and random effect models, using the Statistic Q Test devised by Cochran[62] to test for the presence of additive between study variance. Both the fixed effect and the random effect model are estimated by using weighted least squares. The weights are defined as the inverse of the variance of the effect sizes of the individual studies. Publication bias is identified by exploring funnel plots and the test suggested by Egger et al[63] and Begg[64]. Sensitivity analyses are performed to test the influence of a single study on the pooled meta-analysis estimate. The effect sizes of the individual studies are defined as odds ratios, hazard ratios from survival analysis, ratios of discrete rates and continuous measures. Only studies that give the standard errors of the effect sizes or provide information to permit the calculation of standard errors (confidence intervals, p-values) are included in the meta-analysis. When a study reports several models with different covariates, only the most extensive model is included. Separate models are estimated (a) when more than two treatments are reported (e.g., medium and low education versus high education), (b) when the effect size takes the form of a continuous measure (c) and for the different transitions. The meta-regression accounts for the definition of the treatment effect, the form of treatment as well as the definition of disability, the inclusion of institutionalized population, sex and the age range of the study.

5.1 Presenting the results

Our results are presented on three different levels and with two different representations (figures and tables). The figures in section 5.2 show every single effect-size of each study included, together with the average effect-size (see the bottom of each figure) resulting from the meta-analysis. Owing to the large amount of data and because different meta-analyses were performed, we had to select the most important meta-analyses to be represented by a figure. However, all analyses are shown in Table 1 at the end of section 5.2. The table displays the average effect sizes estimated by the fixed and random effect models of sex, obesity and smoking on the four transitions, completed by a number of statistical tests. The third level of our analysis constitutes a meta-regression, for which we do not present a detailed outcome. The results and the interpretation of the outcome are covered in the discussion, however.

The following figures read as follows: the left-hand side of the figures contains the name and year of the study. The "datapoints" in the figure itself are shown as squares. The size of the square indicates the precision (inverse of the variance) of the effect size. A horizontal line shows the width of the confidence interval of each single study. The result of the meta-analysis is shown as a dashed vertical line. A trapezoid at the bottom of each graph represents the confidence interval for the results of the meta-analysis. The log-scaled x-axis reveals the relative risk for the group in question.

Table 2 displays detailed information on the study design and the special features of each of the 55 studies.

In the following, the results are discussed for each risk factor from Transition 1 to Transition 4 (or to the transition applicable).

5.2 Results of Meta-Analysis

5.2.1 Risk factor sex

We limited our presentation of the results on the risk factor sex to Transition 1 and Transition 3 because the results may be less obvious and less clear than for the other transitions (where it is already well-known that women have a lower mortality than men).

Figure 2: Risk factor sex, Transition 1, from not disabled to disabled

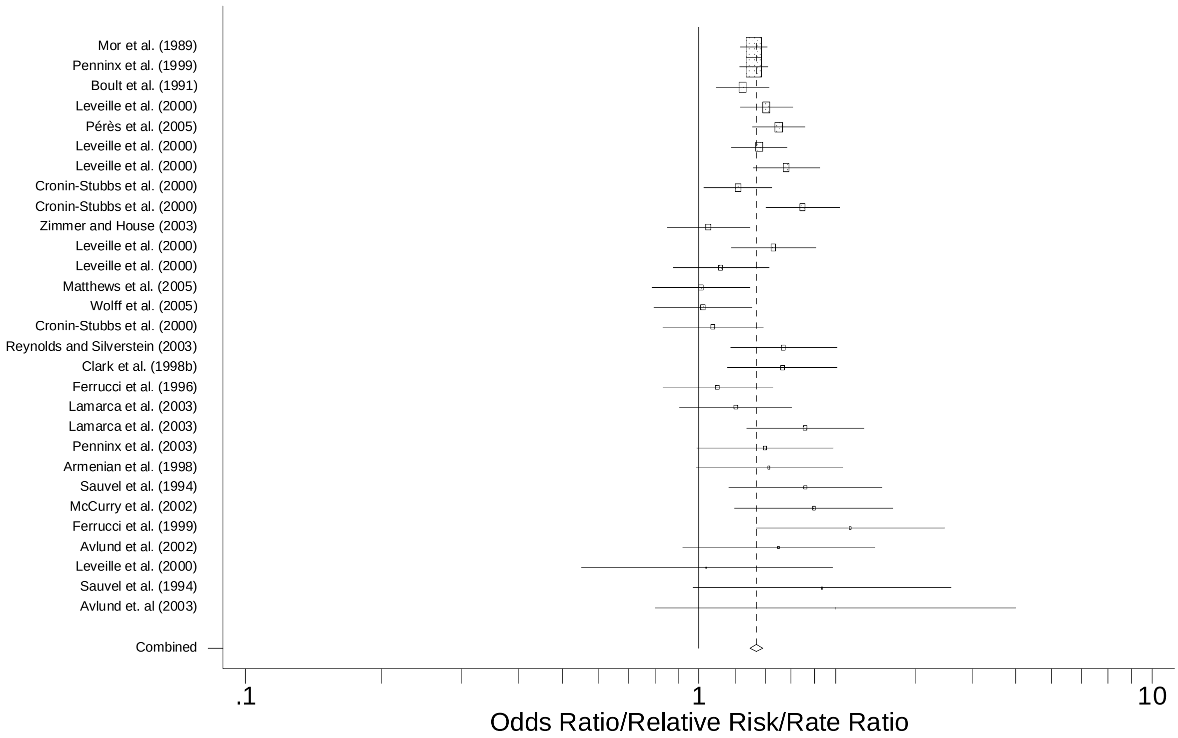
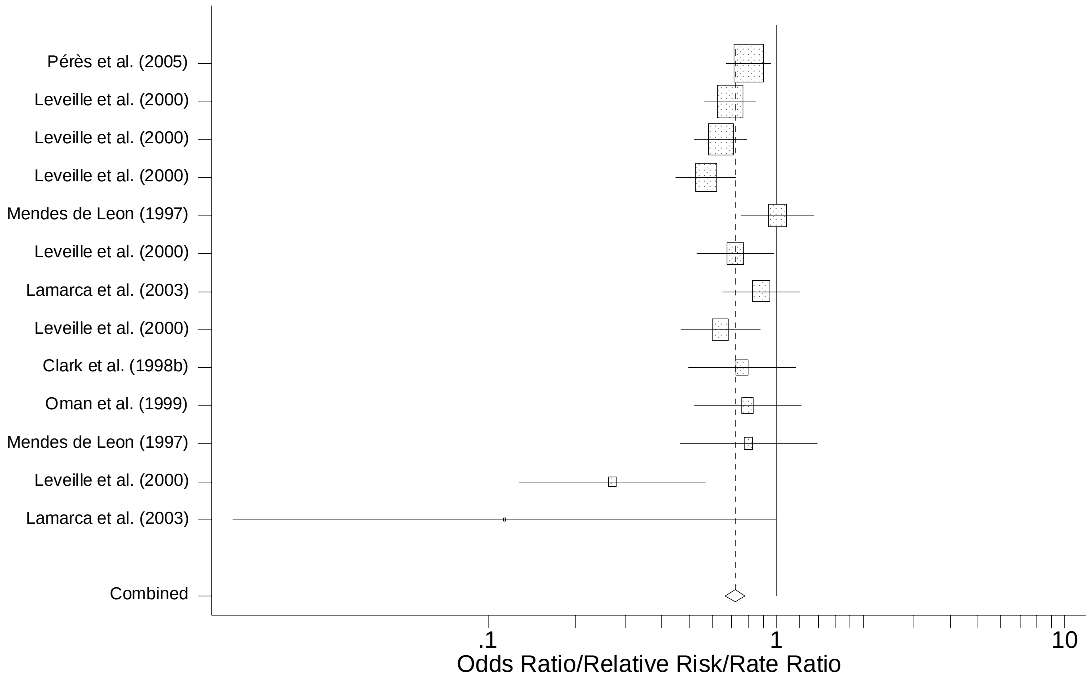


Figure 2 shows that women have a higher risk of changing from the status of not disabled to the status of disabled than men. All 29 effect sizes point into this direction; however, 13 of them are not significant. Nevertheless, the results of our meta-analysis are highly significant and show an increased risk of 1.35 for women. The most important differences between the multiple effect sizes of a single study are explained as follows: The first entry for Lamarca et al[32] is for the transition "not disabled" to "having difficulties" and the second is for the transition from "not disabled" to "becoming dependent". The sex difference in the transition to "becoming dependent" seems to be greater. The two studies by Sauvel et al[50] use disability type IADL and the second belongs to our mixed category Combined Disability Measure (CDM) (see section 4.2.)

In the study by Armenian et al.,[3] only very few studies look at younger ages, for example at the age group 18+. There are six entries for Leveille et al[34] that represent ascending 5-year age groups from 65-69 to 90-95. The three results by Cronin-Stubbs et al[15] represent three different concepts of disability. Here, we see substantial differences in the results: a small difference between men and women in physical performance, a large difference in a mobility-based measure, and an insignificant one when we look at ADL.

The studies by Beckett et al.,[6] Crimmins et al.,[14] Maddox et al.[36] and Dunlop et al[16] are excluded because they neither provide confidence intervals nor the information to compute these intervals, the provision of which, however, is necessary for the meta-analysis.

Figure 3: Risk factor sex, Transition 3, from disabled to not disabled (recovery)



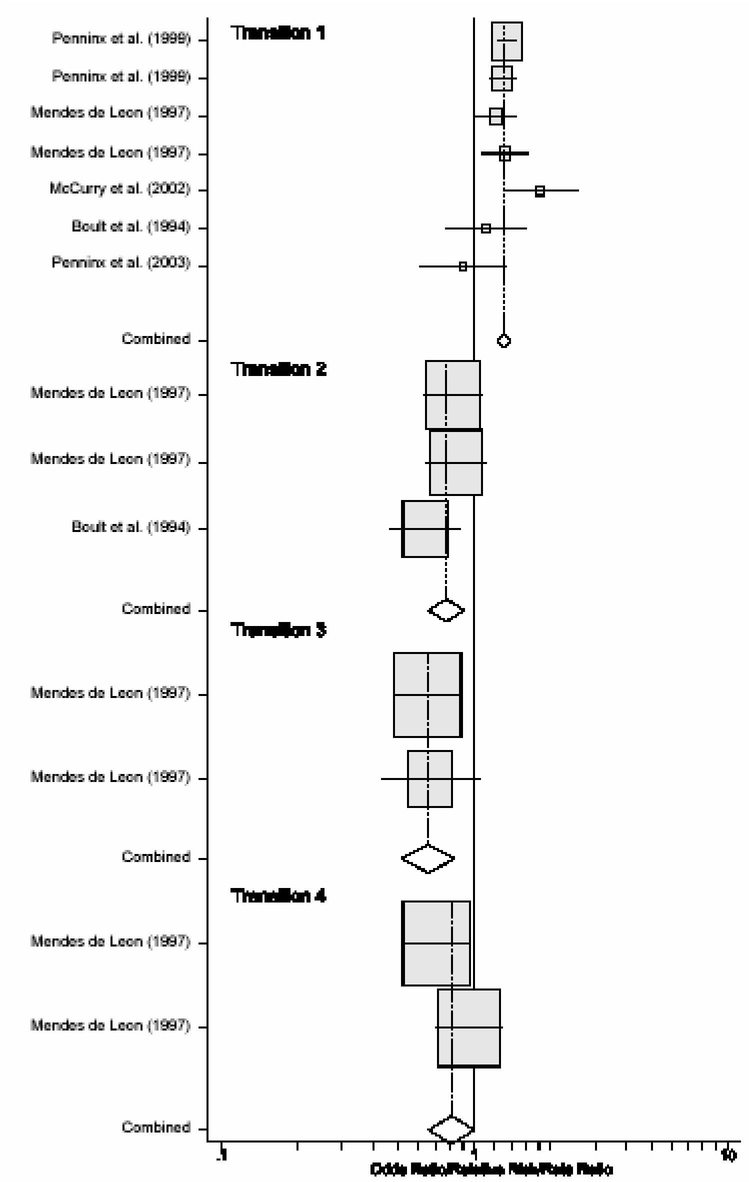
The chance to recover from disability is lower for women than it is for men. All but one effect size point into this direction and the majority of effect sizes is significant. Again,

the difference between the two studies by Lamarca et al[32] consists of different kinds of disability. Leveille et al[34] use different age groups. Mendes de Leon[40] studies two different regions, North Carolina and New Haven. The result of the meta-analysis shows that women have a lower chance of recovery of 0.71 compared to men (CI: 0.63-0.81).
There are two outliers; one is the age group 90-95 in the study by Leveille et al.,[34] suggesting that at very advanced ages, women have a much lower chance to recover than men. However a gradient over the whole age range of his study (65-95) can only be assumed and is far from being significant. The second outlier (Mendes de Leon[40], studying North Carolina) points into the opposite direction and suggests that there are no sex differences. Note that the confidence intervals of most studies largely overlap. Thus, even if two specific studies (out of 10 or 20) are significantly different, this does not necessarily imply or require an explanation.
Again, several studies that offer effect sizes for this transition and the risk factor sex could not be included in the meta-analysis because there were no confidence intervals.[6,12,29,14,37,25,7]

5.2.2 Risk factor obesity

For this risk factor, we present figures comparing obesity with normal weight (Figure 4) and comparing obesity with normal weight/overweight (Figure 5). The third categorization (overweight versus normal) will be neglected because there are no studies on Transition 4. The results for all comparisons and all available transitions are shown in Table 1.

Figure 4: Risk factor obesity (obese vs normal/overweight), Transitions 1 to 4



Transition 1: Among the healthy, the risk to become disabled is significantly increased for obese persons. The average effect size is 1.30 (CI: 1.19-1.41).

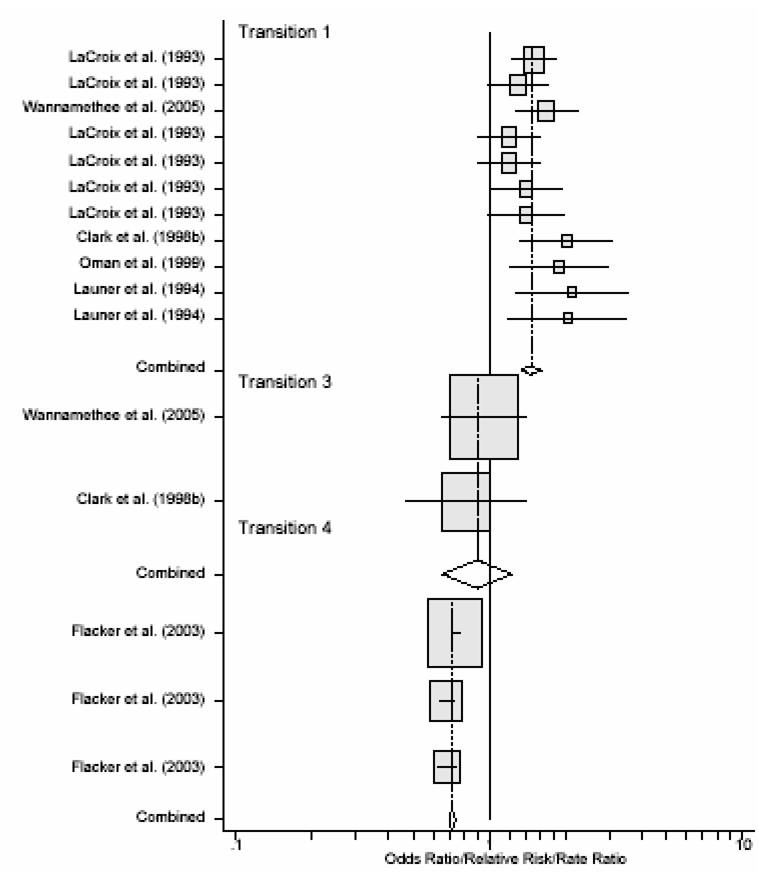
Transition 2: Surprisingly, the risk of dying for healthy persons seems to be lower for obese persons than for those with a normal weight or those overweight. The average effect size of 0.78 (CI: 0.66-0.91) from the meta-analysis is based on a study by Boult et al[8] and two different populations in the study by Mendes de Leon[40] whose results are as such not significant. However, the overall result of the meta-analysis is significant.

Transition 3: The same study by Mendes de Leon[40] provides evidence that the chances of recovery stands at 0.66 (CI: 0.51-0.84) for obese persons compared to persons with normal weight or those who are overweight.

Transition 4: The two populations in New Haven and North Carolina in the same study confirm surprising results for Transition 2, one result is significant and the other is not: on average, disabled obese persons have a lower mortality risk of 0.82 (CI: 0.61-1.09). The significant result from the fixed effects model becomes insignificant in the random effects model (see Table1).

Figure 5 below shows the results for Transitions 1, 3 and 4 for the comparison of obese persons with persons with normal weight.

Figure 5: Risk factor obesity (obese vs normal), Transitions 1, 3 and 4



Transition 1: the effect of obesity versus normal weight on the risk of health decline is clearly significant. The random effect model estimates an increased risk of a transition

of 1.49 (CI: 1.33-1.66). However, Begg's test as well as Egger's test suggest the presence of a publication bias, i.e. taking into account that studies with significant results are more likely to be published, the risk would be lower.

Trans 3: The fixed effect model based on two studies with two effect sizes suggest a slightly lower chance of recovery for obese persons, but this effect is far from being significant.

Trans 4: In Figure 5, we see the same surprising result as in Figure 4: all three effect sizes in the study by Flacker and Kiely[21] indicate a lower risk of dying for disabled obese persons compared to disabled persons of normal-weight. The meta-analysis shows a lower mortality risk of 0.70 (CI: 0.67-0.75). The three effect sizes in the study are based on different cohorts, i.e. different samples.

Although information is limited we have two studies with five effect sizes that indicate a protective effect of obesity on mortality for disabled persons. Statistical tests indicate the presence of between study variance but reject any publication bias (see Table 1).

When the BMI is measured as a continuous variable, there is no significant effect on the risk of becoming disabled (see Table 1).

5.2.3 Risk factor smoking

Figure 6: Risk factor smoking (current vs never), Transition 1 from not disabled to disabled

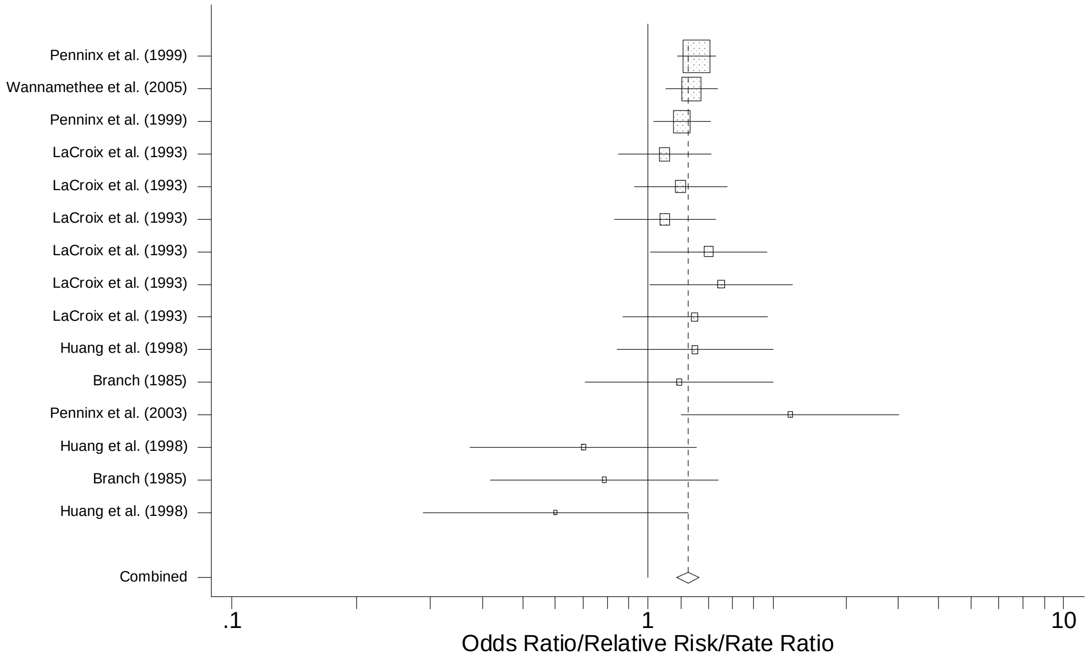


Figure 6 shows an increased risk of becoming disabled for current smokers compared to those who have never smoked. In the following, we will explain the multiple effect sizes provided by the same author: The author Branch[10] studies women and men separately and so do LaCroix et al[31] (however, focusing on three different regions). Penninx et al[45] use ADL and M/PP as two different disability measures. All confidence intervals of the studies overlap and only one effect size is significantly lower than the average computed in the meta-analysis. This average shows an increased risk of 1.24 (CI: 1.14-1.33). We excluded the studies by Liu et al[35] and Reynolds and Silverstein[40] because there were no confidence intervals.

Taking into account the different measurements for smoking, we see that current smoking versus never having smoked or being a former smoker is also associated with a higher risk of becoming disabled (1.02; CI: 1.01-1.03). Additionally, former smokers have a higher risk than non-smokers but this excess risk is reduced from 1.24 (see Figure 6) to 1.08 (CI: 1.02-1.14). Statistical tests do neither suggest the presence of a publication bias nor of outliers affecting the overall result.

Table 1: Results of the Statistical Meta-Analysis of the Effect of Sex, Obesity and Smoking by Type of Transition

					Fixed Effects Model			Random Effects Model			Heterogeneity		Publication Bias		
						Confidence Interval			Confidence Interval		Q Test	Between Study	Begg's Test	Egger's Test	
Risk factor	Transition	Number of Included Effect Sizes	Number of Excluded Effect Sizes	Number of Studies	Mean	Lower	Upper	Mean	Lower	Upper	P-Value	Variance τ^2	P-Value	Bias	P-Value
Sex females vs males	**1**	29	0	20	**1.34**	**1.30**	**1.38**	**1.35**	**1.28**	**1.43**	0.01	0.01	0.30	0.34	0.44
	2	13	0	7	**0.41**	**0.37**	**0.45**	*	*	*		*	0.58	-0.24	0.78
	3	13	2	7	**0.72**	**0.66**	**0.78**	**0.71**	**0.63**	**0.81**	0.02	0.02	0.50	-1.08	0.27
	4	18	2	9	**0.58**	**0.57**	**0.60**	**0.56**	**0.51**	**0.62**	0.00	0.03	0.94	-0.57	0.54
Weight															
Overweight vs normal	1	2	0	2	1.13	0.93	1.38	*	*	*	*	*	n.a.	n.a.	n.a.
	3	2	0	2	0.82	0.61	1.11	0.81	0.74	1.22	0.19	0.04	n.a.	n.a.	n.a.
Obese vs normal & overweight	**1**	7	0	5	**1.31**	**1.23**	**1.39**	**1.30**	**1.19**	**1.41**	0.17	0.00	0.23	-0.63	0.53
	2	3	0	2	**0.78**	**0.66**	**0.91**	*	*	*	0.39	*	n.a.	-9.69	0.19
	3	2	0	1	**0.66**	**0.51**	**0.84**	*	*	*	0.91	*	n.a.	n.a.	n.a.
	4	2	0	1	0.81	0.66	1.00	0.82	0.61	1.09	0.17	0.02	n.a.	n.a.	n.a.

Obese vs normal	**1**	11	0	5	**1.47**	**1.34**	**1.62**	**1.49**	**1.33**	**1.66**	0.24	0.01	**0.07**	**2.34**	**0.05**
	3	2	0	2	0.90	0.66	1.24	*	*	*	0.64	*	n.a.	n.a.	n.a.
	4	3	1	1	**0.72**	**0.69**	**0.74**	**0.70**	**0.67**	**0.75**	0.06	0.00	0.71	4.18	0.22
Weight continuous	1	9	0	4	1.01	0.99	1.03	*	*	*	0.50	0.00	0.53	0.76	0.43
Smoking															
Smoking current vs never smoked	**1**	15	0	5	**1.25**	**1.17**	**1.33**	**1.24**	**1.14**	**1.33**	0.26	0.01	0.15	-0.67	0.21
	3	2	0	2	0.76	0.61	0.94	0.79	0.58	1.08	0.19	0.02	n.a.	n.a.	n.a.
Smoking current vs former/non-smoker	**1**	10	0	8	**1.02**	**1.01**	**1.03**	**1.15**	**1.08**	**1.22**	0.00	0.00	**0.1**	**1.71**	**0.03**
Smoking former vs never smoked	**1**	12	0	4	**1.08**	**1.02**	**1.14**	*	*	*	0.33	*	0.45	0.06	0.92
smoking former vs never/non-smoker	3	2	0	1	1.05	0.79	1.39	*	*	*	*	*	n.a.	n.a.	n.a.

*: moment, restricted Maximum-Likelihood and Maximum-Likelihood estimates of the between study variance are zero, significant effects are indicated in bold

n.a. not applicable

5.3 Results of meta-regressions

Additionally to our meta-analysis of the numerous effect sizes of different studies, we performed a meta-regression analysis to find out whether the average effect size systematically depends on the characteristics of the selected studies. We only performed meta-regressions for transitions and risk factors that have a sufficient number of effect sizes: i.e. all transitions for sex and the transition from not disabled to disabled for smoking and obesity. The different models contain different numbers of study characteristics in order not to over-parameterize the models. Since the number of studies is limited, we restricted the explaining variables to the most relevant ones, that is the age range of the study, whether the outcome is measured as relative risk or whether it is measured as odds ratio, the four types of disability, the sex of the respondents (both sexes, males, females) and the household type (private, institutions, both). Due to space limitations, we will only mention the most important results. In terms of the risk factor sex, the measure of disability clearly influences the effect size. For all transitions, CDM measures result in larger sex differences than do ADL/IADL measures. Concerning the risk factors overweight and obesity, the number of effect sizes only permitted us to study the transition from not disabled to disabled. The risk of becoming disabled due to obesity is much larger among the young and middle aged than among the elderly. Studies based on males only lead to lower effect sizes than studies based on both sexes. The risk of becoming disabled is significantly increased for current smokers compared to those who have never smoked. Whether current smokers compared to former smokers have an increased risk and whether the effect of smoking depends on age can not be resolved conclusively because these results are confounded by the measure of the effect size. In other words, they depend on whether the risk is defined in terms of odds ratios or relative risks.

6 Discussion

In this meta-analysis, we documented first that the four transitions and the three risk factors are studied to a very different degree. The transition from healthy to disabled received much more attention than the other transitions, thus opening future areas of research. Second, we summarized numerous different findings on health transitions and their risk factors in terms of means estimated by fixed and random effects models and by meta-regressions that include the most important study characteristics. However, we are aware that most of our studies are non-experimental and observational studies and that they are prone to a greater degree of bias than randomized control trials. We therefore placed a very strong emphasis on sensitivity analyses, publication bias and a careful analysis of the original studies concerning their methodological and statistical properties. We used this detailed information for a description of the results and for the purpose of interpretation, but we refrained from quality scoring of individual studies.

Within a transition, we find different numbers of results for our three risk factors. There are more studies on the risk factor sex than there are on obesity and smoking. We assume that the latter are rarely analyzed because appropriate data is difficult to find. Note that in the design of our literature analysis, we set high standards for the quality of the study, including the standard of a longitudinal perspective, which as such requires longitudinal and therefore more expensive and rare data sets. Obesity and smoking are more often analyzed in shorter clinical cross-sectional studies and are thus excluded from our specific literature review. In addition, the measurement of health behavior, such as smoking and personal information or the Body Mass Index, is more difficult. Interpreting the relative frequency of our risk factors, we come to the conclusion that there is a lack of representatives of proximate and modifiable risk factors, such as smoking and obesity.

Concerning the first transition, all studied risk factors (sex, obesity and smoking) significantly increase the risk of transition from not disabled to disabled. The finding that BMI is not significant as a continuous variable may be due to the step sizes. By now, this is no proof against the “dose-response principle” in the relation between obesity and disability.

The transition from the status of not being disabled to death (Transition 2) certainly requires more attention in future research. We confirm the well known finding that women have a lower mortality rate than men, disregarding of whether they have a healthy or unhealthy status. Surprisingly, obesity does not seem to be a risk factor but rather a protective factor that prevents both healthy and unhealthy persons against premature death (Transitions 2 and 4, respectively). The results for the impact of smoking on the transition from not being disabled to death are not conclusive because there are not enough studies to perform a meta-analysis. Transition 2 poses a problem for the analysis because it is not usual (although it is possible) that people die when they have a good health status. There is a risk that this transition suffers from measurement problems in cases when the health decline was too fast to be recorded in an empirical study from one wave to the other, a problem that may differ between studies. However, if we find systematic differences in the impact of a risk factor on healthy versus unhealthy people, this may reveal at which stage and how this risk factor works.

Protective and detrimental factors of recovery (Transition 3) are not well understood. All risk factors in our study have a negative impact on recovery. The detrimental effect of smoking was also found in the review by Stuck et al[1(p459)]. This effect and the effect of obesity should be verified in future studies as many of the results are not significant and based on a limited number of studies.

The transition from the status of being disabled to death (Transition 4) is also understudied. Again, women have a lower mortality risk. For Transition 4, obesity seems to be a protective factor, too. For smoking, there are no studies that could be included in our meta-analysis.

The finding that obesity and not just overweight, as a light form of obesity, decreases mortality is striking. Overweight and obesity seem to increase the risk of becoming or remaining disabled (transitions 1 and 3) but appears to be protective against mortality (Transitions 2 and 4). This finding is supported by a recent study,[65] it reports that it is not a high Body Mass Index but an elevated waist hip ratio that is associated with a greater risk of death. However, a comprehensive study of the interdependence between different transitions possibly would arrive at a different conclusion: in principle it is possible that the fact that obesity increases Transition 1 together with the fact that persons with a disability have higher mortality risks in sum still results in higher mortality for obese persons because first they are more likely to become disabled and as a result, they are more likely to die. This would suggest that for a complete assessment of a risk factor it is important to look at the impact of this risk factor on the whole process of transition, starting from not being disabled to death. Once the (negative) impact of obesity has worsened the health status, its impact on mortality may be smaller or may even reverse; however, the overall impact is still negative.

Current smokers clearly experience an increased risk of mortality and a lower chance of recovery compared to those who have never smoked or are currently not smoking. For former smokers, the effect on recovery is attenuated, which indicates that it pays off to quit smoking.

In general, we do not find an indication of publication bias for the risk factor sex. A possible explanation is that sex may not be the variable of interest per se but rather a control variable. Thus, whatever the result, it has no impact on the likelihood of getting published. This is different with the other two risk factors, smoking and obesity. For the risk factor obese vs normal weight and current smoking vs ever/never smoked, we observe a publication bias for the transition from not disabled to disabled.

A meta-regression analysis usually attenuates or intensifies the effect but rarely changes its direction. For example, the use of CDM as a disability measure results in larger effect sizes for the risk factor sex for all transition. Suffice it to mention another example: the effect of current smoking vs never smoking and obesity is larger at younger ages. The use of odds ratios compared to relative risks usually does not have an impact on the results, with the exception of smoking. That is, models based on odds ratios indicate exactly the opposite of models based on relative risks. The only concordance is that current smokers have a significantly higher risk of becoming disabled than those who have never smoked. Whether this effect increases or decreases with age, whether it is larger or smaller for females and whether the effect is similar when comparing current smokers with former smokers and non-smokers depends on the model specification. A possible explanation is the observed publication bias. In the meta-regression, we did not use information on lifestyle (e.g., smoking, BMI, alcohol consumption), the socioeconomic status (e.g., education, income), variables capturing social relationships (e.g., family status, social integration) and the presence of co-morbidity owing to the limited numbers of effect sizes and the problem of over-parameterization.

7 Conclusion

We consider the existence of a large and sometimes confusing number of different ways to measure disability as a fact that complicates all attempts to unify research findings and to make the existing findings easier to use and to interpret. Our literature review is an attempt to summarize the variety and the large amount of research findings. It puts us into the position to identify areas where more research is needed. In future, research should concentrate more so on the harmonization of the different concepts of health and disability rather than on capturing specific aspects. Our review shows that more studies of risk factors on transition probabilities are needed, particularly on transitions other than from health to disability. In general, more thought should be given to the state-space that exists in disability studies. Many studies that we did not consider eligible for this review, particularly in the area of mortality, are based on populations where at baseline no distinction between disabled and not disabled is made.

Although the transition from not disabled to disabled is the most challenging to public policy makers in terms of prevention measures, we need more information on recovery and the transition from either not disabled or disabled to death. Particularly the latter seems to be under-explored, given that the issue of compression or expansion of disability with increasing life expectancy has not been fully addressed. We generally need more studies on risk factors of transitions other than sex.

In our review, we find that a high BMI has a protective effect in terms of mortality but a negative effect on disability and recovery. The finding is based on a small number of studies, however. We certainly need more studies to confirm this result and to rule out that the protective effect is simply the result of weight loss due to morbidity prior to death.

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Statistical analysis: Doblhammer
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9 Literature

9.1 Literature in the text

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