

Impact of individual risk factors on German life expectancy

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Introduction

Individual risk factors such as smoking, alcohol consumption and lack of physical activity contribute importantly to early mortality. Meta-analyses have documented the effects of several individual risk factors on mortality, summarizing results of several prospective cohort studies. For most risk factors, several meta-analyses have been published and over time insights about the mortality risks associated with exposure to the risk factors have changed for some risk factors, including alcohol consumption. An overview of recent meta-analyses summarizing the current evidence on the effect of individual risk factors on mortality is lacking. The first aim of this study was to assess which individual factors have an impact on mortality and to quantify the size of the effect in terms of relative risks (RR).

In addition to quantifying the effect of a risk factor on mortality in terms of relative risks, quantifying the loss in life expectancy associated with exposure to the individual risk factors is important. The reason being that individual risk factors may affect at what age persons die but not whether or not a person dies. It is therefore more meaningful to assess the impact on life expectancy, which is a measure of the age at death. Moreover, the relevance of a given relative risk depends on the absolute mortality level. For instance, if mortality levels are low, a relative risk of 2 may not relevantly increase the risk to die, whilst a relative risk of 1.2 may increase the mortality risk importantly if mortality levels are high. The second aim of this study was to quantify the impact of individual risk factors on life expectancy in Germany, both for the individual and German male and female population.

In this report, the focus is on the general population, thus not on specific subgroups such as pregnant women, adolescents, chronically ill or persons visiting health care units. Also we focus on risk factors that can be modified by the individual and factors “outside the skin”. We excluded factors such as hypertension, blood pressure, which are more the result of individual and environmental factors and genetic predisposition. We included overweight and obesity. The focus was on risk factors which affect health at the population level, thus not on risk factors that are uncommon and only have a substantial impact on mortality for the few individuals who are exposed.

The report consists of two parts. The first part focusses on the first aim. We start with a short introduction of the role that meta-analyses of prospective studies can play to provide relative risks that quantify the impact of individual risk factors on mortality, including a brief discussion of the major risks of bias and approaches to reduce their impact. Next, we describe the approach we followed to select relative risks from the published meta-analyses and we present the results per risk factor.

The second part focusses on the second aim. We start with a short description of the data we used in addition to the relative risks obtained in part one. Next, we explain the methods to assess the impact of risk factors on life expectancy. We distinguish between the individual impact and the population impact. We then present the results and end the report with a summary and discussion of the results.

Part 1 Relative risks of mortality associated with individual risk factors

Role of meta-analyses of prospective studies

Randomized controlled trials (RTC) give the strongest evidence of a causal relation, but this study design is not feasible to examine the impact of individual risk factors on mortality. Meta-analyses of prospective cohort studies are considered to provide the best evidence of the effect of risk factors on mortality. The advantage of using meta-analyses of prospective studies is that it reduces the risk of noise and accidental confounding, and therefore using meta-analyses is generally considered to give more precise estimates of the effect size than individual prospective studies. Nonetheless, each meta-analysis depends on the quality of the underlying studies, the comparability between the studies included within the meta-analysis and methodological approaches used in the meta-analyses to provide a pooled estimate of the effect of the risk factor. Also when negative findings are not published or less published in individual studies, which is more likely to occur if the effects are small, this may affect the effect estimates of the meta-analyses.

To minimize the possibility that factors other than the one of interest cause the effect on mortality (because of a third factor that is both associated with the risk factor of interest and with mortality, also known as confounding), it is important that studies adjust for potential confounders in multivariate analyses or, if the risk of confounding is high, present stratified analyses, or assess the effect in a subgroup where the effect is least confounded (e.g. assessing the effect of Body Mass Index (BMI) in healthy never-smokers to rule out the effect of smoking as confounder).

For some risk factors, it cannot be ruled out that the risk factor exposure is the consequence of ill health and not the cause (reverse causation). For instance, persons who do not perform physical activity may not do so because of their ill health, or persons may have quit smoking because of health problems. It is important that the studies included in the meta-analyses addressed this issue. Different approaches are used: excluding persons who have a chronic disease or poor health at baseline at the time the risk factor is measured, adjusting in the analyses for the effect of poor health, excluding persons who died close to the baseline measurement (as these individuals might have been already ill at the time of measurement), and avoiding a short follow-up duration.

The published meta-analyses and therefore also our study cannot give answers as to whether there is a causal effect and how strong this causal effect is. It provides insight into the association between the risk factor and mortality, based on prospective studies which measured exposure before the outcome. There is more evidence for a causal relationship if studies controlled maximally for confounding and minimized the risk of reverse causation. The evidence for a causal relation is also stronger in case a dose-response association between the risk factor and mortality can be established and in case the biological pathways through which specific risk factors affects mortality are understood.

The quality of the published meta-analyses differs substantially between the different risk factors for mortality, not only in how many studies are pooled, but also in the comparability of exposure between these studies. Some meta-analyses pool studies that use the same metric for the exposure

measurement (e.g. overweight: BMI in kg/m², sleep in hours). Other meta-analyses pool studies that used different metrics but harmonized exposure (e.g. alcohol in grams, physical activity in METh/week), while for some risk factors there is sometimes no other option than to include different exposure measures to compare high(est) vs. low(est) exposure (e.g. social support).

This report summarizes the current insights. Some of them have been shown to change over time because of methodological improvements in the meta-analyses and in the individual studies, and the growing availability of (large) studies.

Approach to derive Relative Risks

We searched for meta-analyses published since 2010 that summarized evidence from prospective studies with all-cause mortality as outcome. We excluded factors such as hypertension and blood pressure, but included overweight and obesity. We selected per factor one meta-analysis to obtain the relative risks (or hazard ratios which are equivalent) that quantifies the direction and size of the effect on mortality. In general, we selected the most recent meta-analysis for two reasons. First, the most recent meta-analysis generally includes the studies considered in older meta-analyses plus more recent studies (if they meet the inclusion criteria, which can be more restricted in more recent studies for methodological reasons). Second, older studies could not have profited from methodological improvements whilst the most recent studies could have. However, we did not select the most recent study if a prior study was more comprehensive, included more studies and deaths, or was methodologically stronger. We present results of more than one meta-analysis if a second or third meta-analysis had a different focus (such as cycling in addition to physical activity in general), or addressed a different population (such as older persons instead of the general population).

We extract the relative risks (including hazard ratios) from the selected meta-analyses. Sometimes the meta-analyses presented different sets of relative risks, for instance based on different selections (e.g. excluding early deaths). The reason why more options are presented is generally that there is a trade-off between including more subjects, who are less selected and thus more representative, and including fewer subjects reducing heterogeneity and risks of bias. One option could be to present all of them, but that would shift the decision of which ones to use to the reader. We therefore selected the relative risks we considered most suitable for the purpose of this study, considering risks of confounding, reverse causation and number of studies involved.

Relative risks are generally expressed relative to a reference group, or per extra unit of exposure (e.g. reduction in mortality per additional serving of vegetables). The reference group can be the one with the lowest or highest risk. For smoking, never-smokers are generally used as reference group, while for physical activity some studies used the inactive group as reference and other studies the active group. Relative risks above one indicate that the risk factor increases the mortality risk. For instance, a relative risk of 2 for smokers indicates that smokers have a twofold risk to die as compared to never smokers. Relative risks below one indicate that the risk factor reduces the risk. For example, physical activity reduces the risk of dying as compared to the inactive reference group. To allow for an easier comparison of the order of magnitude between relative risks below and above one, we also present the relative risks with the healthy exposure group as reference (physically inactive relative to active)

for significant effects so that all relative risks show the excess risk associated with the unhealthy behaviour.

We include the following risk factors:

1. Smoking
2. Physical activity
3. Sedentary behaviour
4. Alcohol consumption
5. Overweight and obesity
6. Sleep
7. Coffee consumption
8. Diet, including (whole) grain, nuts, fish, fruit and vegetables, dairy products, sugar sweetened beverages
9. Social network and social participation

We present the results per risk factor in a summary table. We specify the reference category in the column and the exposure category(ies) in the row(s). With each relative risk, we present the 95% confidence interval. Only if one is not in the confidence interval, the effect of the risk factor is statistically significant. In a separate column we indicate whether the effect was significant. As mentioned, we added the relative risk with the healthy behaviour as reference to the table if the unhealthy category was the reference in the original study, to allow for a better comparison between the risk factors. Finally, the table gives the source of each relative risk, which are the meta-analyses that reported it. The complete information on the sources is given in the reference list at the end of the document. For some risk factors we present more than one table; the specific reasons are explained with the tables.

Results per risk factor

Smoking

Meta-analyses

We found four publications with meta-analyses devoted to smoking (1-4) and one publication with meta-analyses for 7 risk factors, including smoking (5). Two of these publications were restricted to persons aged 60 years and older (1, 4), one to second-hand smoking (3) and one focused on the difference between menthol and non-menthol cigarettes (2). We report relative risks from the study of Stringhini (5) for the general population. In addition we report relative risks for the elderly from the publication of Muezzinler (4) being the most recent and comprehensive study of the two studies for the elderly. Both selected meta-analyses were based on re-analysis of data from the original prospective studies, which allowed for maximum possible harmonization of the exposure and control variables. Because the selected meta-analysis for the total population was less detailed, we also used the study of Thun (6) including more than 950.000 individuals from five cohort studies in the United States and the study of Pirie (7) including more than one million women in the United Kingdom (7).

Effects and interpretation

Current smoking	vs. never smokers (95% CI)	Significant (Y/N)	Source	Reference: healthy exposure
Current smoking	HR 2.21 (2.10–2.33)	Y	Stringhini 2017 (5)	2.21
Current smoking (60+)	HR 2.03 (1.77-2.32)	Y	Muezzinler 2015 (4)	2.03
Former smoking	vs never smokers			
Former smokers	HR 1.25 (1.20-1.31)	Y	Stringhini 2017 (5)*	1.25
Former smoking (60+)	HR 1.32 (1.21-1.44)	Y	Muezzinler 2015 (4)	1.32

*Obtained from authors on request

Effect: Smoking increases the risk of mortality strongly, with a factor of 2.2 for the total population and with a factor of 2 for persons aged 60+. Relative risks of smoking have increased over time. Recent studies in the UK (7) and US (6) report relative risks of around 2.8. Relative risks are similar for men and women (4, 6, 7). There is a clear dose response relation between the number of cigarettes smoked and the mortality risk (4, 7, 8) and persons who started smoking at younger ages have higher relative risks (7). The relative risks among former smokers decrease with time since quitting (4, 7, 8) and are lower for person who stopped at younger ages (7).

Confounding: The relative risks from the selected meta-analyses for the total population were adjusted for important potential confounders, including: BMI, education, alcohol consumption and physical activity. The study of Muezzinler (4) presented sensitivity analyses, showing that excluding studies that did not adjust for physical activity, alcohol consumption, or both did not alter the results substantially, nor did the adjustment for the history of diabetes, blood pressure, and total cholesterol level.

Reverse causation: Ill health affecting smoking exposure is plausible, as it is known that ill health is one of the reasons for smokers to quit smoking. These quitters could have a higher mortality than continuing smokers (sick-quitter bias), which may have resulted in an underestimation of the presented relative risk for current smokers.

Conclusion: Cigarette smoking increases the risk for all-cause mortality in men and women.

Physical activity

Meta-analyses

We found six publications with meta-analyses devoted to physical activity (9-14), and one publication with meta-analyses for 7 risk factors, including physical activity (5). One of these meta-analyses was restricted to the elderly (9). As there was considerable variation in the effect of physical activity, we presented relative risks for different types of physical activity depending on the type and intensity of physical activity. We selected the meta-analysis of walking and cycling published in 2014 by Kelly (11) and the meta-analysis of non-vigorous physical activity published in 2011 by Woodcock (12). For comparison we present also the relative risk for walking from this study. For moderate to vigorous physical activity (MVPA) we presented results from the meta-analysis by Samitz (14) in 2011, and we presented the results of a meta-analysis restricted to the elderly published in 2015 by Hupin (9). All selected meta-analyses converted physical activity, measured in different ways in the underlying individual studies, into MET hour per week (METh/w) or MET minutes per week (METm/w) to make exposure comparable and to examine dose-response effects. MET refers to metabolic equivalent tasks, and is a unit of energy expenditure adjusted for body mass, with the reference category of 1 MET being the energy expenditure of an individual at rest. In addition to these detailed meta-analyses, we also report the relative risks from the meta-analysis by Stringhini (5). This study did not convert physical activity to METS nor made a distinction by type of physical activity, but categorized physical activity as the presence or absence of physical inactivity. Nonetheless, the reason to include this relative risk is to provide also an overall estimate, as often detailed exposure data are not available and then a general estimate is needed.

Effects and interpretation

Walking and cycling	vs. 0 MET	Y/N significant	Source	Reference: healthy exposure
Walking (11.25 METh/w)	HR 0.89 (0.83-0.96)	Y	Kelly 2014 (11)	1.12
Cycling (11.25 METh/w)	HR 0.90 (0.87-0.94)	Y		1.11
Non-Vigorous Physical activity- (METh/w)	vs. 0 MET			
NVPA for 11.25 METh/w	HR 0.81 (0.76-0.85)	Y	Woodcock 2011 (12)	1.23
NVPA for 30 METh/w	HR 0.76 (0.71-0.81)	Y		1.32
(Walking 11.25 METh/w)	HR 0.89 (0.82-0.96)	Y		(1.12)
Moderate to Vigorous Physical activity (MVPA) in METh/w	vs. 0 MET			
Moderate to vigorous activity 150m/w	HR 0.86 (0.80-0.92)	Y	Samitz 2011 (14)	1.16
Moderate to vigorous activity 300m/w	HR 0.74 (0.65-0.85)	Y		1.35
Elderly (60+): MVPA in METm/w	vs. 0 MET			
MVPA 1-499 METm/w	RR 0.78 (0.71-0.87)	Y	Hupin 2015 (9)	1.28
MVPA 500-900 METm/w	RR 0.72 (0.65-0.80)			1.39
All levels combined	Vs. active			
Physical inactivity	HR 1.28 (1.19-1.37)	Y	Stringhini 2017 (5)	1.28

* Walking (11.25 METh/w) is about 2.5 h/w brisk walking; 11 METh/w of non-vigorous physical activity is about 2.5 h/week; MVPA 500-900METm/w in elderly is about 2.5 h/w.

Effect: Physical activity reduces the risk of mortality. The relative risk for all levels combined, which compares persons who engage in physical activity against those that do not, shows that inactive persons have a 1.28 times higher risk of dying. The size of the effect depends on the type of physical activity (intensity) and duration. 11.25METh/week of non-vigorous activity, which is about the recommendation of 2.5 hours per week, reduces the mortality risk with a factor of 0.81 (equivalent

to a 1.23 times higher risk of non-active persons as compared to active persons) and walking with a factor of 0.89. The relative risk for 30 METS/h week is 0.76 (equivalent to a 1.32 higher risk for persons with no physical activity as compared to ≥ 30 METS h/week). There is a dose response relation between physical activity and mortality (9, 11, 12, 14). Higher intensity or longer durations increase the effects, but this relation is not linear; largest benefits of physical activity are found in moving from inactivity to moderate physical activity. The effects are generally larger in women than men (9, 12, 14).

Confounding: The studies in the selected meta-analyses mostly corrected for potential confounding from other life style factors, such as smoking, BMI, education and alcohol consumption. It is noteworthy that adjustment for BMI may involve an over-adjustment, as BMI is in the causal chain between physical activity and death. Residual confounding by other factors or imperfect correction for these factors may have overestimated the relative risks.

Reverse causation: Low or no physical activity may be the result, rather than the cause of ill health and mortality. To avoid bias, the majority of the studies included the general population, excluded unhealthy people or adjusted for baseline health status. Excluding deaths that occurred soon after measurement of baseline data showed to have little effect on the relative risks (12).

The literature describes several mechanisms how physical activity contributes to lower mortality (14).

Conclusion: Physical activity reduces the risk for mortality in men and women, including among the elderly.

Sedentary behaviour

Independent of physical activity, sedentary behaviour is considered a risk factor for mortality. Sedentary behaviour refers to activities with less than 5 metabolic equivalents, and is often measured as sitting time or TV watching time. Two relative risks are reported in the literature for the independent effect of sedentary behaviour: 1) relative risks for different levels of physical activity, and 2) relative risks controlled for physical activity.

Meta-analyses

For sedentary behaviour we found 5 meta-analyses (15-19). The meta-study of Ekelund (17) published in 2016 is the largest and most comprehensive study that re-analysed data of the original cohort studies using common categories of sitting time and TV-watching time and converting these into METh/week. This study provided relative risks for the effect of sedentary behaviour for different levels of physical activity for the table. In addition, we report relative risks for TV watching hours corrected for physical activity, based on the study of Sun (19) published in 2015. This study reports relative risks for the highest as compared to the lowest TV watching and presents a summary relative risk based on 4 studies with similar exposure categories. We did not select the meta-analyses of Biwas (15) published in the same year, as the relative risks in this study were adjusted minimally for confounders.

Effects and interpretation

Sitting	vs. , 4 h/day sitting time	Y/N significant	Source	Reference healthy exposure
Sitting & Low PA (<2.5 METh/week)				
-4-6 h/day sitting	HR 1.08 (1.04-1.12)	Y	Ekelund 2016 (17)	1.08
-6-8 h/day sitting	HR 1.09 (1.05-1.14)	Y		1.09
-8 h/day sitting	HR 1.27 (1.22-1.32)	Y		1.27
Sitting & High PA (>35.5 MET h/week)				
-4-6 h/day sitting	HR 1.00(0.96-1.04)	N	Ekelund 2016 (17)	
-6-8 h/day sitting	HR 1.01 (0.97-1.06)	N		
-8 h/day sitting	HR 1.04 (0.98-1.10)	N		
TV watching time	vs. , < 1 h/day TV	Y/N significant	Source	Unhealthy vs. healthy exposure
TV & Low PA (<2.5 METh/week)				
- 1-2 h /day TV	HR 1.00 (0.94-1.08)	N	Ekelund 2016 (17)	
- 3-4 h/day TV	HR 1.10 (1.02-1.18)	Y		1.10
->5 h/day TV	HR 1.44 (1.34-1.56)	Y		1.44
TV & High PA (>35.5 MET h/week)				
- 1-2 h /day TV	HR 0.96 (0.88-1.04)	N	Ekelund 2016 (17)	
-3-4 h/day TV	HR 1.01 (0.93-1.10)	N		
->5 h/day TV	HR 1.15 (1.05-1.27)	Y		1.15
Sedentary behaviour, corrected for physical activity	vs. low sedentary time	Y/N significant	Source	Unhealthy vs. healthy exposure
High sedentary time (TV and sitting time)	HR 1.22 (1.08–1.38)	Y	Sun 2015 (15, 19)	1.22
Highest TV watching time	HR 1.33 (1.20-1.47)	Y	Sun 2015 (19)	1.33
T watching time (summary HR)*	HR 1.23 (1.08-1.39);	Y	Sun 2015 (19)	1.23

*based on 3 categories <2, 2-4, >=4 hour

Effect: sedentary behaviour is associated with a higher risk on mortality for all physical activity levels. High levels of physical activity (about 60-75 minutes moderate intensity per day) eliminate the increased mortality risks associated with long sitting time (8 h day), but do not eliminate the elevated risk of TV watching (>=5 h). Independent of physical activity, there is a non-linear dose-response relation for TV watching: more than two hours TV watching as compared to less than two hours TV watching is associated with an 1.23 times increased mortality risk. TV watching was significantly associated with all-cause mortality in a j-shaped fashion (19).

Confounding: In the meta-analyses of Ekelund (17), all studies corrected for age, sex and smoking, the majority also for alcohol consumption and BMI and some included more control variables (17). The studies in the meta-analysis of Sun were controlled for risk factors such as smoking and education. Studies that additionally adjusted for other possible confounding factors (e.g., alcohol consumption, energy intake, diabetes, hypertension, or ethnicity) tended to find slightly weaker associations than those that did not adjust for those variables (19).

Reverse causation: Reverse causation is an important risk as persons in ill health are likely to be more sedentary and ill health is associated with mortality. The studies in the meta-analysis of Ekelund (17) included in the most part apparently healthy participants at baseline or excluded early deaths. In de meta-analysis of Sun (19) the effect of excluding early deaths was examined and the results were similar.

The literature describes several mechanisms how sedentary behaviour contributes to lower mortality (19).

Conclusion: sedentary behaviour increases the risks for mortality.

Alcohol consumption

Meta-analyses

We found two meta-analyses devoted to alcohol consumption, the study of Stockwell published in 2016 and the study of Wang published in 2014 (20, 21), and one publication with meta-analyses for 7 risk factors, including alcohol consumption (5). The study of Wang focused on differences between men and women (20). We selected study of Stockwell 2016 (21) as this was the most recent and methodologically strongest study. This study converted alcohol intake into grams per day and distinguished occasional drinkers, lifetime abstainers and former drinkers and presented relative risks corrected for confounders and excluded former drinkers from the reference group as this introduces bias (21). The publication provided different sets of relative risks to document the impact potential sources of bias. We report the relative risks with as reference group lifetime abstainers (i.e. excluding former drinkers) and adjusted for all identified confounders.

Effects and interpretation

Alcohol	Vs. life time abstainers	Y/N significant	Source	Reference healthy exposure	
all drinkers combined	RR 1.15 (0.97-1.36)	N	Stockwell 2016 (21)		
Former drinker	RR 1.38 (1.24-1.54)	Y	Stockwell 2016 (21)	1.38	
Occasional (<1.3 g/day)	RR 0.95 (0.85-1.05)	N			
Low volume (1.30–<25 gr /day)	RR 0.97 (0.88-1.07)	N			
Medium volume (25-45 gr/day)	RR 1.07 (0.97-1.18)	N			
High volume (45-65 gr/day)	RR 1.24 (1.12-1.37)	Y			1.24
Higher volume (>65 gr/day)	RR 1.44 (1.30-1.60)	Y			1.44

Effect: Low levels of alcohol consumption do not protect against mortality (which was found in earlier studies). Both former and high-volume drinking are associated with about 1.4 times higher mortality risks. According to the study of Wang (20) and several prior studies, women have higher mortality risks, but because these studies may suffer from abstainer bias and the study of Woodcock did not report gender differences, we refrain from any conclusion on gender differences at this moment.

Reverse causation: Persons who become unhealthy may be more likely to quit or substantially reduce their alcohol consumption, leading to poor health profiles of abstainers. The often used practice of including former drinkers with the lifetime abstainer reference group will bias drinking risk estimates downward, thereby magnifying the appearance of health benefits from low-level drinking. For alcohol this is called “abstainer bias”. (21)

Confounding: The study of Stockwell (21) presented different sets of relative risks and indicated the importance of controlling for confounders. The relative risks in the table are from the maximally adjusted models.

The literature describes several mechanisms how alcohol consumption contributes to lower mortality.

Conclusion: High alcohol consumption increases the risks of mortality. Low alcohol consumption is not beneficial for mortality.

Overweigh and obesity

Meta-analyses

For overweight and obesity we found seven meta analyses (22-28), including one study focusing on the elderly (28). In addition, the publication of Stringhini 2017 included a meta-analysis for obesity (5). We did not consider studies focusing on the effect of weight change. Two meta-analyses were published in 2016: the meta-analysis of Aune (22) and of Di Angelantio for the “The Global BMI mortality consortium” (24). Both studies included more than 3.7 million deaths, presented different sets of relative risks with successively stricter correction for bias, and included results for never smokers without chronic disease. We consulted both publications and we present the relative risk from the study of Di Angelantio because it included both relative risks for the generally used categories of normal weight, overweight and obesity and more detailed BMI categories. We did not include the results the study of Winter for the elderly, as it does not provide separate results for never smokers and the recent meta-analyses have shown that only controlling for smoking may not be sufficient to reduce bias.

Effects and interpretation

BMI	vs normal weight BMI 18.5-<25.0 kg/m ² *¶	Y/N significant	Source	Reference healthy exposure
Underweight BMI 15.0-<18.5 kg/m ²	RR 1.47 (1.39-1.44)	Y	Di Angelantio 2016 (24)	1.47
Overweight BMI 25.0-<30.0 kg/m ²	RR 1.11 (1.10, 1.11)	Y		1.11
Obesity grade 1 BMI 30.0-<35.0 kg/m ²	RR 1.44 (1.41-1.47)	Y		1.44
Obesity grade 2 BMI 35.0-<40.0 kg/m ²	RR 1.92 (1.86-1.98)	Y		1.92
Obesity grade 3 BMI 40.0-<60.0 kg/m ²	RR 2.71 (2.55-2.86)	Y		2.71

* in never-smokers without known chronic disease at baseline—excluding the first 5 years of follow-up

Effect: Overweight increases the mortality risk by a factor 1.11 and obesity grade 1 by a factor 1.44. There is a j-shaped dose-response relation between BMI and mortality. Without adequate control for smoking and ill health, this j shape becomes a u shape form, with higher risk of mortality for underweight. The association between BMI and mortality is stronger among people younger than 65 years than for people aged 65 and over.

Confounders: smoking is associated with lower body weight and smoking is a strong risk factor of mortality. The adverse effects of smoking are so strong that controlling for smoking as confounder is not sufficient to remove the confounding effects. The relative risks presented in the table are relative risks for healthy never-smokers.

Reverse causation: persons with ill health often experience weight loss. In the recent meta-analyses, included in the table, the relative risks are presented for healthy non-smokers.

The deleterious effects of excess body weight on chronic diseases have been well documented.

Conclusion: overweight and obesity increase the risk of mortality. The increase in risk in underweight persons might be at least partly due a non-causal association reflecting weight loss associated with disease.

Sleep

Meta-analyses

We found 7 meta-analyses for sleep (29-35). Two meta-analyses were published in 2017. We present the relative risks derived from the recent meta-analysis published by Yin (29) and not the meta-analysis of Liu, because the first included more studies and excluded studies who did not derive the participants from the general population. In addition we present results from the meta-analysis of Da Silva that was restricted to the elderly (32).

Effects and interpretation

Sleep	vs 7 hours	Y/N significant	Source	Reference. healthy exposure
Shorter sleeping	RR 1.13 (1.09–1.17),	Y	Yin 2017 (29)	1.13
Longer sleeping	RR 1.35 (1.29–1.41),	Y	Yin 2017 (29)	1.35
Elderly 60+	vs 7 hours			
Shorter sleeping	RR 1.07 (1.03 -1.11)	Y	Da Silva 2016 (32)	1.07
Longer sleeping	RR 1.33 (1.24 -1.43)	Y	Da Silva 2016 (32)	1.33

Sleep	Per hour more/less than 7 h	Y/N significant	Source	Reference healthy exposure
Shorter sleep per hour per day	RR 1.06 (1.04 -1.07)	Y	Yin 2017(29)	
Longer sleep per hour per day	RR 1.13 (1.11- 1.15)	Y	Yin 2017(29)	

Effect: There is a u-shaped association: sleeping for shorter and longer periods than 7 hours is associated with higher mortality. Shorter sleep increases the risk of mortality by a factor of 1.13 (all ages) and 1.07 (persons age 60+). The effects of longer sleep are stronger, increasing mortality by a factor of 1.35. Within the segments below 7 hours and above 7 hours of sleep, there is a dose-response effect. The recent meta-analyses are not consistent as to whether the u-shape is found both for 24h of sleep and night sleep ((31, 34).

Confounding: In prior studies long sleep time was associated with poor health, high depression scores, low BMI, low education, low physical activity, smoking and alcohol consumption, all risk factors of mortality (reference in (30)). The meta-analyses of Liu (30) used adjusted risk estimates from each contributing study. The relative risks for the elderly in the study of Da Silva (32) were very similar when based on studies and models that corrected for a large number of confounders, including diseases and health status.

Reverse causation: in particular, longer sleep may be the consequence of ill-health rather than the cause. The study of Yin (29) excluded studies if participants were not recruited from a generally healthy population. Nonetheless, residual confounding by imperfect correction for ill health may have overestimated the relative risks for longer sleep duration.

Mechanisms for short and long sleep duration are discussed in the literature (29, 30). The explanations for long sleep duration are considered more speculative and may represent the confounding effects of sub-healthy status or uncontrolled chronic illness (29).

Conclusion: short and long sleep duration increase the risk of mortality. The increase in risk of long sleep duration might at least partly a non-causal association reflecting longer sleep associated with disease.

Coffee consumption

Meta-analyses

For coffee, we found 5 meta-analyses (36-40). We present the relative risks from the study of Grosso (39), because this was the most recent and largest study, and this study stratified by smoking status and tested for the effect of potential confounders and effect modifiers.

Effects and interpretation

Coffee	vs. 0 cups	Y/N significant	Source	Reference healthy exposure
Up to 4 cups/day	RR 0.86 (0.82-0.89)	Y	Grosso 2016 (39)	1.16

Effect: Coffee intake is inversely associated with all-cause mortality. Consumption of up to 4 cups/day of coffee was associated with a reduction in mortality by a factor 0.86. Higher intake was associated with no further lower risk in for smokers, while for non-smokers the effect was slightly larger and showed a linear dose response relationship with higher intakes associated with lower risks.

Confounding: Smoking is considered an important confounder for the effect of coffee on mortality. The study of Grosso stratified by smoking and corrected for several other confounders.

The literature describes the biological mechanism of how coffee consumption can contribute to lower mortality (39)

Conclusion: coffee consumption of up to four cups reduces the risk of mortality.

Diet

Meta-analyses

We found four meta-analyses for whole grain (41-44), two for fruit and vegetable intake (45, 46), five for nut consumption (47-51), four for dairy intake (52-55), two for fish intake (56, 57), and two for meat intake (58, 59). All these risks factors were included in the recent study by Schwingshackl (60), published in 2017, except the combination of fruit and vegetable consumption. This study included meta-analyses for 12 food groups: whole grain, refined grain, vegetable, fruit, legumes, nuts, eggs, dairy. To provide a broad overview, we report the relative risks from this study as it included the largest number of deaths, and selected results in individual studies with the maximum correction for confounders. Moreover, it provided both effects for the highest vs. lowest category and the dose-response effect and included quality assessments for the meta-analyses for each dietary factor. We report the relative risks for each additional serving and for highest vs lowest intake.

The meta analyses of Wang (46) provides Relative Risks with the combination of fruit and vegetable consumption and using the group that had no daily consumption of fruit and vegetables as comparison group. Compared with people who had no daily consumption of fruit and vegetables, the estimated hazard ratios of mortality were 0.92 (95% confidence interval 0.90 to 0.95) for one serving/day of fruit and vegetables, 0.85 (0.81 to 0.90) for two servings/day, 0.79 (0.73 to 0.86) for

three servings/day, 0.76 (0.69 to 0.83) for four servings/day, 0.74 (0.66 to 0.82) for five servings/day, and 0.74 (0.65 to 0.82) for six or more servings/day.

Effects and interpretation

Diet	Quality of meta-evidence rated by author	For each additional serving	Y/N significant	Source	unhealthy vs. healthy exposure*
Whole grain	High	RR 0.92 (0.89, 0.95)	Y	Schwingshackl 2017(60)	
Refined grain	Low	RR 0.99 (0.97-1.01)	N	Schwingshackl 2017(60)	
Vegetable	Low	RR 0.96 (0.95, 0.98)	Y	Schwingshackl 2017(60)	
Fruits	Low	RR 0.94 (0.92, 0.97)	Y	Schwingshackl 2017(60)	
Legumes	Moderate	RR 0.96 (0.90, 1.01)	N	Schwingshackl 2017(60)	
Nuts	Moderate	RR 0.76 (0.69- 0.84)	Y	Schwingshackl 2017(60)	
Dairy	Moderate	RR 1.03 (0.98-1.07)	N	Schwingshackl 2017(60)	
Fish	Moderate	RR 0.93 (0.88, 0.98)	Y	Schwingshackl 2017(60)	
Red meat	Moderate	RR 1.10 (1.04, 1.18)	Y	Schwingshackl 2017(60)	
Processed meat	Moderate	RR 1.23 (1.12, 1.36)	Y	Schwingshackl 2017(60)	
Eggs	Very low	RR 1.15 (0.99-1.34)(N	Schwingshackl 2017(60)	
Sugar sweetened beverages	Low	RR 1.03 (0.91-1.18)	N	Schwingshackl 2017(60)	

*with dose response, 0 is reference

Diet	Quality of meta-evidence rated by author	Highest vs lowest intake	Y/N significant	Source	unhealthy vs. healthy exposure*
Whole grain	High	RR 0.88 (0.84,0.92(Y	Schwingshackl 2017(60)	
Refined grain	Low	RR 0.99 (0.94,1.05)	N	Schwingshackl 2017(60)	
Vegetable	Low	RR 0.93 (0.90, 0.95)	Y	Schwingshackl 2017(60)	1.08
Fruits	Low	RR 0.91 (0.89, 0.94)	Y	Schwingshackl 2017(60)	1.10
Legumes	Moderate	RR 0.96 (0.93, 1.00)	N	Schwingshackl 2017(60)	
Nuts	Moderate	RR 0.80 (0.74-0.86)	Y	Schwingshackl 2017(60)	1.25
Dairy	Moderate	RR 1.03 (0.98,1.07)	N	Schwingshackl 2017(60)	
Fish	Moderate	RR 0.95 (0.92-0.98)	Y	Schwingshackl 2017(60)	1.05
Red meat	Moderate	RR 1.10 (1.00,1,22)	Y	Schwingshackl 2017(60)	1.10
Processed meat	Moderate	RR 1.21 (1.16,1.26)	Y	Schwingshackl 2017(60)	1.21
Eggs	Very low	RR 1.06 (1.00-1.12)	N	Schwingshackl 2017(60)	1
Sugar sweetened beverages	Low	RR 1.02 (0.97,1.06)	N	Schwingshackl 2017(60)	

Effect: Increasing intake (for each daily serving) of whole grains, vegetables, fruits, nuts, and fish decreases the risk of mortality with a factor of 0.92, 0.96, 0.94 0.76 and 0.93 respectively. Higher intake of red meat and processed meat was associated with a 1.10 and .1.23 times higher risk of mortality, respectively. A clear indication of nonlinearity was seen for the relations between vegetables, fruits, nuts, dairy and mortality, with no further increase in protective effect for vegetables above 300 gr, fruits above 250-300 gram, and nuts above 15-20 gram. For dairy, high intakes (above 750 gr/d) were associated with higher mortality.

Confounders: people with a high intake of whole grains, fruits, vegetables, fish, nuts, or legumes may have different lifestyles (see prior sections) or a different socioeconomic status as compared to those with lower intakes. The study Schwingshackl (60) confirmed the results in a sensitivity analyses including only studies adjusted for important lifestyle factors, such as smoking, physical activity, and BMI.

The author rated the quality of meta-evidence as “very low” for eggs; “low” for refined grains, vegetables, fruits, and sugar sweetened beverages “moderate” for nuts, legumes, dairy, fish, red meat, and processed meat; and “high” for whole grains.

Conclusion: consumption of whole grains, nuts, fish, vegetables, fruits are likely to reduce the risk of mortality and consumption of red processed meat are likely to increase the risk of mortality.

Social network and social participation

In addition to the individual health behaviours presented in the prior sections, lack of a social network and social participation are also considered a risk factor for mortality. These factors can have a direct effect on mortality, but can also operate through the individual health behaviours. One of the possible mechanisms is that social networks and social participation stimulate persons to adopt and keep healthier life styles. This direct and indirect effect, and the large heterogeneity in concepts, instruments, measures and categorizations of exposure complicate the assessment of the effect of these risk factors on mortality.

Meta-analyses

We found one meta-analyses on social relationships by Holt-Lunstad (61) published in 2010, one meta-analysis on social isolation, living alone, and loneliness also by Holt-Lundstad (62) published in 2015 and one meta-analysis on social contact frequency by Shor (63) published in 2015. In addition we found one meta-analysis by Sher that compared the effect of religious and nonreligious participation (64).

We selected the most recent meta-analysis published in 2015 by Shor (63) on the effect of contact frequency on mortality, as the exposure was clearly defined, and the study selected estimates from prior studies with maximal correction for confounders. We also present for comparison the results from the meta-analyses by Shor (61) on the effect of religious and non-religious participation, although the study did not clarify for which confounders the underlying studies controlled. We do

not present the results from Holt-Lundstad published in 2010 (61) on social relationships as the results were minimally corrected for confounders and presented as odds ratios which cannot be directly compared with relative risks. Nor do we present the study of the same author on social isolation, living alone and loneliness (62) as the original studies used in the meta-analysis included participants from medical settings and used very different exposure measures. Also the effects were presented in Odds Ratios (derived from various metrics).

Effects and interpretation

Social contacts	Higher vs. lower contact levels	Y/N significant	Source	Reference healthy exposure
Social contacts (excluding contacts measures that include marital status)	HR < 1.11 (p value: 0.0168)	Y	Shor 2015 (63)	1.11
Social participation	Higher levels of participation			
Lower levels of participation	HR 1.26 (1.21-1.31)	Y	Shor 2013 (64)	1.26

Effects: Frequent social contact tends to be associated with lower mortality, but the magnitude of the effect was quite small (<1.11) and not consistent for all subgroups (63). Low levels of group participation were associated with an increased risk of death with a factor 1.26; the specific form of participation (i.e., religious vs. nonreligious) did not have a significant effect on the magnitude of the relative risk.

Confounding: factors such as health and socio-economic status are considered potential confounders. The study of Shor (63) showed that correcting for confounders largely reduces the effect of network size on mortality. Other health behaviours such as smoking, healthy diets can be both confounders and in the causal pathway between social networks and health.

Reverse causation: unhealthy people may be less able to participate in social activities and contacts and hence a low participation in activity can be the result of ill health.

The literature describes different mechanisms on how social network and support can contribute to lower mortality, including facilitation of healthy behaviours (63)

Conclusion: social network and also social participation may reduce the risk of mortality.

Part 2 Loss in German life expectancy associated with individual risk factors

Data

We used the European Social Survey (ESS) as data source for the prevalence of the individual risk factors in Germany by age and gender. ESS is a cross-national survey that is organized every two years from 2002 onwards. The survey looks into beliefs, attitudes and behaviour patterns of populations of more than 30 countries. It is conducted through face to face interviews to newly selected cross-sectional samples. The survey includes representative samples of non-institutionalized populations aged 15 years without an upper limit. In the 7th round of the ESS in 2014, a large set of risk factors was included. The number of respondents for Germany is 3045 and the response rate is 34%. More information on the ESS survey can be found in Eikemo et al, 2017 (65) and Fitzgerald and Jowell, 2010 (66).

The ESS 2014 included information about smoking, physical activity, sedentary behaviour, alcohol consumption, overweight and obesity, fruit and vegetable consumption and social contacts. The survey does not provide information on hours sleep, coffee consumption and other dietary factors than fruit and vegetable consumption.

Data on the number of deaths and person-years by single year of age and gender for the year 2015 were obtained from the Human mortality database (<http://www.mortality.org/>).

Individual risk factors

We classified information on the individual risk factors into two to three exposure categories.

Smoking was classified as never, former and current smokers. Current smokers include occasional smokers.

Alcohol consumption was classified as low, medium and high alcohol consumption, with less than 25 gram alcohol per day as low, between 25 and 45 gram alcohol per day as medium and 45 gram per day or more as high.

Fruit and vegetable was assessed as less than once a day fruit and vegetable consumption versus at least once a day fruit and vegetable consumption.

Overweight was assessed as normal weight (BMI between 18.5-25 kg/m²), overweight (BMI between 25-30 kg/m²), obesity (BMI>30 kg/m²).

Physical activity was classified in two groups: at least 5 days a week 30 minutes of walking quickly, doing sports or other physical activity versus less than 5 days per week 30 minutes of physical activity. 5 days 30 minutes non-vigorous physical activity is equivalent to 11.25 METS.

Sedentary behaviour was measured by TV watching time. Sedentary behaviour was classified into less than 2 hours TV per day as non-sedentary versus at least two hours TV watching per day as sedentary.

Social contact was classified as meeting more than once a week socially with friend or colleagues versus not meeting at least once a week socially with friend or colleagues.

Hours sleep, coffee consumption and other dietary factors than fruit and vegetable consumption factors are excluded from the further analyses.

Relative risks

Relative risks estimates quantifying the association between exposure to each risk factor and mortality and presented in Table 1 were based on the literature review in Part 1. For obesity we combined the relative risks for obesity grade 1, 2 and 3 into one class. For alcohol consumption we combined the RR from the literature review for high and highst level into one class for high alcohol consumption (≥ 45 grams/day).

We used the same relative risk for all ages and both genders because for most factors the meta-analyses did not provide age- and gender-specific relative risks. To allow for comparisons between the risk factors, we used that same approach for all risk factors.

Table 1 Relative risks for different factors based on the literature review

	Relative Risks
Smoking	
-never smoker	1
-former smoker	1.25
-current smoker	2.21
Physical activity (PA)	
Low PA ≤ 11.25 MET (5 days 30 min)	1.28
High PA ≥ 11.25 MET	1
Sedentary behaviour (TV)	
Less than 2 hours TV watching	1
Two hours or more TV watching	1.23
Alcohol consumption	
Low (< 25 gram)	1
Medium (25- < 45 gram)	1.07
High (≥ 45 gram)	1.35
Overweight obesity	
Normal weight (18.5- 25 kg/ m ²)	1
Overweight (25- < 30 kg/ m ²)	1.11
Obesity (≥ 30 kg/ m ²)	1.65
Fruit and vegetable consumption	
Not at least daily fruit and vegetable consumption	1.22
At least daily fruit and vegetable consumption	1
Social contact	
Less than once a week meeting with a friend or colleague	1.10
At least once a week meeting with a friend or colleague	1

Methods

Prevalence of the risk factors

For descriptive analyses we calculated the prevalence of each risk factor for age 15 years and over.

As input for the calculations of loss in life expectancy we calculated prevalence by single year of age and gender. We smoothed the age-specific prevalence using restricted cubic splines (5 knots), using a binomial logistic regression model for risk factors with two exposure categories (e.g. no physical activity vs. physical activity), ordinal logistic regression for risk factors with ordinal exposure categories (e.g. normal weight, overweight, obesity) and multinomial logistic regression for risk factors with nominal exposure categories (e.g. never smoking, former smoking, current smoking).

Life expectancy

We used standard life table techniques to calculate life expectancy by age and gender for the year 2015 using death counts and the population at risk in single-year age groups. We closed the life tables at age 100.

Losses in life expectancy associated with the risk factor

Using information on the relative risks, the smoothed prevalence of the risk factor, and mortality rates by single year of age we estimated two measures of the effect of the risk factors on total life expectancy: 1) the loss in average life expectancy associated with the risk factor (“population loss” and 2) the loss in life expectancy for persons who are exposed to the risk factor (“individual loss”).

Loss in average life expectancy associated with the risk factor (“population loss”)

The loss in life expectancy associated with the risks factor is based on the Population Attributable Fraction (PAF) approach (67). This approach combines information on the relative risks and the prevalence of exposure to the risk factor.

$$PAF = \frac{\sum_{i=1}^n P_i RR_i - \sum_{i=1}^n P_i RR_1}{\sum_{i=1}^n P_i RR_i},$$

where P is the prevalence, i the risk factor exposure category (e.g. 1=normal weight, 2 = overweight, 3=obesity) and RR is the relative risk.

The PAF was applied to the age-specific mortality rates. Multiplication with $1-PAF$ gave the mortality rates that would have been observed if the specific risk factor was not present, stated differently, with all persons in the healthiest risk factor category. Using these counterfactual mortality rates in the life table calculation yielded the life expectancy in absence of the risk factor. The average loss in life expectancy caused by the risk factor is the difference between the current life expectancy and the life expectancy without the risk factor.

Loss in life expectancy for persons who are exposed to the risk factor (“Individual loss”)

The loss in life expectancy for persons who are exposed to the risk factor is the difference in life expectancy of the risks factor group with the healthiest exposure (e.g. normal weight) and each exposed group (e.g., overweight and obesity). This is an indirect estimate based on the same

information as in the PAF approach and using in addition the mortality rate by single-year age group (and gender).

The mortality rate is the weighted average of the mortality rates of each exposure group, with the risk factor prevalence as weights ((68, 69).

$$M = \sum_{i=1}^n P_i M_i$$

Where i is the exposure group and $i=1$ the reference group with the relative risk of 1, P the prevalence and M the mortality rate.

For a risk factor with two exposure groups, the equations are as follows:

$$M = P_1 * M_1 + P_2 * M_2$$

$$M = P_1 * M_1 + P_2 * M_1 * RR$$

$$M = M_1 * (P_1 + P_2 * RR)$$

$$M_1 = M / (P_1 + P_2 * RR)$$

Where M is mortality rate, M_1 is mortality rate of reference group which is unexposed, M_2 is mortality rate of exposed. For more classes the approach is similar.

We used single-year age-specific prevalence of each risk factors classified in 1-year age groups starting at age 15. Below age 15 years we assumed no impact of the risk factor on mortality, that is we set all RRs to 1 because mortality below age 15 is extremely low and not caused by exposure to the studied risk factors. For the ease of interpretation, we present life expectancy losses at birth.

Confidence intervals were obtained using bootstrapping (1000 runs). Uncertainty around the Relative risk is not taken into account in these confidence intervals, but is addressed in sensitivity analyses.

Sensitivity analyses

Both the choice of the relative risks and the choice of the survey may impact the results. To assess the sensitivity of the outcomes for uncertainty related to the relative risks and prevalence of the risk factors we conducted two sets of sensitivity analyses. In the first set we varied the relative risks, using 20 and 40 percent higher and 20 and 40 percent lower excess risks as compared to the main analysis (for RR of 2.0 a 20% higher excess risk yields an RR of 2.2, i.e. $((2.0-1.0)*1.20 + 1)$, see Table 2). In the second set of analyses we used 20 % and 40% higher and lower prevalence of all exposed groups (e.g. for overweight and obese).

Table 2. Relative risks used in sensitivity analyses, set 1

	-40%	-20%	Main	+20%	+40%
Smoking					
-former smoker	1.15	1.20	1.25	1.30	1.35
-current smoker	1.73	1.97	2.21	2.45	2.69
Physical activity (PA)					
-Low PA ≤ 11.25 MET (5 days 30 min)	1.17	1.22	1.28	1.34	1.39
Sedentary behaviour (TV)					
-Two hours or more TV watching	1.14	1.18	1.23	1.28	1.32
Alcohol consumption					
-Medium (25-45 gram)	1.04	1.06	1.07	1.08	1.10
-High (≥ 45 gram)	1.21	1.28	1.35	1.42	1.49
Overweight obesity					
-Overweight (25-30 kg/ m ²)	1.07	1.09	1.11	1.13	1.15
-Obesity (≥ 30 kg/ m ²)	1.39	1.52	1.65	1.78	1.91
Fruit and vegetable consumption					
-Not at least daily fruit and vegetable consumption	1.13	1.18	1.22	1.26	1.31
Social contact					
-Less than once a week meeting with a friend or colleague	1.06	1.08	1.10	1.12	1.14

Results

Prevalence of the risk factor by gender

Table 3 presents the prevalence of Germany by gender for 2014. About one third of the German population smoked, 33 percent of men and 27 percent of women. About 60 percent of the German population was physically active (at least 11.25 METS/w). The percentage of persons spending at least 2 hours of TV watching was about 40 percent. 11 percent of men and 3 percent of women consumed between 25 and 45 grams alcohol per day, and 6 and 1 percent respectively consumed more than 45 grams of alcohol per day. 43 percent of the men had overweight and 17 percent was obese, and 28 percent of women had overweight and 17 percent was obese. 54 percent of the men and 38 percent of the women did not eat at least once a day both fruit and vegetables. 46 percent of men and 43 percent of women did not meet at least once a week with a friend or colleague.

Table 3 Prevalence of the risk factors for Germany, age 18+, by gender, based on ESS wave 7

	Men prevalence (CI)	Women Prevalence (CI)
Smoking		
Former smokers	0.28 (0.25-0.30)	0.19 (0.15-0.20)
Current smokers	0.33 (0.30-0.36)	0.27 (0.24-0.30)
Physical activity		
Less than 11.125 MET, 5 d/30m min.	0.59 (0.56-0.62)	0.61 (0.58-0.64)
Sedentary behaviour		
Less than 2 hours/day	0.38 (0.35-0.40)	0.43 (0.40-0.47)
Alcohol consumption		
Medium	0.11 (0.09-0.12)	0.03 (0.02-0.04)
High	0.06 (0.05-0.07)	0.01 (0.00-0.01)
Overweight/Obesity		
Overweight	0.43 (0.41-0.46)	0.28 (0.26-0.31)
Obesity	0.17 (0.15-0.19)	0.17 (0.14-0.19)
Fruit and vegetable consumption		
Less than once a day	0.54 (0.51-0.57)	0.38 (0.35-0.41)
Social contact		
Less than once a week	0.46 (0.43-0.49)	0.43 (0.40-0.46)

Loss in average life expectancy associated with the risk factor

Life expectancy of men in was 78.1 (95% CI 78.1-78.2) years and life expectancy of women was 83.0 (82.9-83.0) years 2015.

Table 4 shows the average losses in life expectancy associated with each risk factor at the population level.

Of all the risk factors considered, smoking yielded the largest loss in the average life expectancy in Germany, reducing life expectancy of men with 2.7 (95% CI 2.5-2.8) years and of women with 1.5 (95% CI 1.3-1.7) years. Overweight/obesity was the second largest contributor, reducing life expectancy with 1.7 (95% CI 1.5-1.8) year in men and 1.4 (95% CI 1.2-1.6) in women. Physical activity

reduced life expectancy of men with more than one year and life expectancy of women with less than one year. Sedentary behaviour and fruit and vegetable consumption, reduced life expectancy of men with almost one year and of women with 0.5 year. Alcohol consumption yielded the smallest losses in average life expectancy.

Table 4 Loss in average life expectancy (LE) associated with risk factor exposure in the German population

	Men loss LE, in years (95% CI)	Women loss LE, in years (95% CI)
Smoking	2.66 (2.50-2.83)	1.53 (1.33-1.74)
Physical activity	1.14 (1.02-1.25)	0.78 (0.67-0.89)
Sedentary behaviour	0.90 (0.82-0.98)	0.62 (0.53-0.71)
Alcohol consumption	0.30 (0.25-0.36)	0.04 (0.02-0.07)
Overweight/obesity	1.65 (1.52-1.80)	1.37 (1.17-1.59)
Fruit and vegetable consumption	0.91 (0.83-1.00)	0.57 (0.49-0.66)
Social contact	0.59 (0.55-0.62)	0.44 (0.40-0.49)

Loss in life expectancy for persons who are exposed to the risk factor

Table 5 shows the losses in life expectancy for persons who are exposed to the risk factor. Largest losses were found for smoking, with a loss of 6.85 (95% CI 6.78-6.92) years for current smokers for men and of 5.86 (95% CI 5.81-5.93) years for women as compared to never smokers. The estimated loss for overweight was 1.03 (1.02-1.04) years for men and 0.89 (95% CI 0.88-0.90) years for women and for obesity 5.01 (95CI 4.97-5.05) years for men and 4.34 (95% CI 4.30-4.40) for women. For persons with an average daily alcohol consumption of more than 45 grams, the loss was 3.01 (95% CI 3.00-3.02) years for men and 2.61 (2.60-2.62) for women. For the other risk factor exposure groups the losses were smaller.

Table 5 Loss in life expectancy (LE) associated with risk factor exposure as compared to healthiest category, Germany

	Men loss LE in years, (95% CI)	Women loss LE in years, (95% CI)
Smoking		
Former smokers	2.45 (2.42-2.47)	2.10 (2.09-2.13)
Current smokers	6.85 (6.78-6.92)	5.86 (5.81-5.93)
Physical activity		
High activity	2.47 (2.45-2.49)	2.10 (2.08-2.11)
Sedentary behaviour		
Sedentary	2.02 (2.01-2.03)	1.75 (1.74-1.76)
Alcohol consumption		
Medium	0.67 (0.67-0.67)	0.58 (0.58-0.58)
High	3.01 (3.00-3.02)	2.61 (2.60-2.62)
Overweight		
Overweight	1.02 (1.02-1.04)	0.88 (0.88-0.90)
Obesity	5.01 (4.97-5.05)	4.34 (4.30-4.40)
Fruit and vegetables		
Less than once a day	1.96 (1.95-1.97)	1.70 (1.69-1.71)
Social contact		
Less than once a day	0.95 (0.95-0.96)	0.82 (0.81-0.82)

Sensitivity analyses

Table 6 shows the average loss in life expectancy associated with each risk factor in the main analysis and in the two sets of sensitivity analyses. Table 7 provides the sensitivity analyses for the individual loss. As expected, scenarios with larger relative risks than in the main analyses, yielded larger average and individual losses and scenarios with smaller relative risks yielded smaller average losses. Scenarios with larger prevalence of exposure yielded larger average losses and scenarios with smaller prevalence of exposure yielded smaller losses, but the individual losses did not change. The overall picture did not change.

Table 6 Sensitivity analyses varying relative risk and prevalence, average loss in life expectancy (in years)

	Smoking	Physical activity	Sedentary behaviour	Alcohol consumption	Overweight/obesity	Fruit and vegetable consumption	Social contact
Men							
Main (Baseline)	2.7	1.1	0.9	0.3	1.7	0.9	0.6
Relative Risk decrease by 20%	2.3	0.9	0.7	0.2	1.3	0.7	0.5
Relative Risk decrease by 40%	1.8	0.7	0.6	0.2	1.0	0.6	0.4
Relative Risk increase by 20%	3.2	1.4	1.1	0.4	1.9	1.1	0.7
Relative Risk increase by 40%	3.6	1.6	1.2	0.4	2.2	1.3	0.8
Prevalence increase by 20%	3.1	1.4	1.1	0.4	1.9	1.1	0.7
Prevalence increase by 40	3.4	1.6	1.2	0.4	2.2	1.3	0.8
Prevalence decrease by 20%	2.2	0.9	0.7	0.2	1.3	0.7	0.5
Prevalence decrease by 40	1.7	0.7	0.6	0.2	1.0	0.6	0.4
Women							
Main (Baseline)	1.5	0.8	0.6	0.0	1.4	0.6	0.4
Relative Risk decrease by 20%	1.4	0.6	0.5	0.0	1.1	0.5	0.4
Relative Risk decrease by 40%	1.1	0.5	0.4	0.0	0.9	0.4	0.3
Relative Risk increase by 20%	1.9	0.9	0.7	0.1	1.6	0.7	0.5
Relative Risk increase by 40%	2.1	1.1	0.8	0.1	1.9	0.8	0.6
Prevalence increase by 20%	1.8	0.9	0.7	0.1	1.6	0.7	0.5
Prevalence increase by 40	2.0	1.1	0.8	0.1	1.9	0.8	0.6
Prevalence decrease by 20%	1.3	0.6	0.5	0.0	1.1	0.5	0.4
Prevalence decrease by 40%	1.0	0.5	0.4	0.0	0.9	0.4	0.3

Table 7 Sensitivity analyses varying relative risk and prevalence, for individual loss in life expectancy (in years)

	Former smokers	Current smokers	Low physical activity	Sedentary behaviour	Medium alcohol	Low alcohol consumption	Overweight	Obesity	Low fruit & vegetable	Low social contact
Men										
Main (Baseline)	2.4	6.9	2.5	2.0	0.7	3.0	1.0	5.0	2.0	1.0
Relative Risk decrease by 20%	2.0	6.4	2.0	1.7	0.5	2.5	0.8	4.2	0.8	0.8
Relative Risk decrease by 40%	1.6	5.2	1.6	1.3	0.4	1.9	0.6	3.3	0.6	0.6
Relative Risk increase by 20%	2.8	8.3	2.9	2.4	0.8	3.5	1.2	5.8	1.1	1.1
Relative Risk increase by 40%	3.2	9.1	3.3	2.7	0.9	4.0	1.4	6.5	1.3	1.3
Prevalence increase by 20%	2.4	6.8	2.5	2.0	0.7	3.0	1.0	5.0	1.0	1.0
Prevalence increase by 40%	2.4	6.7	2.5	2.0	0.7	3.0	1.0	5.0	1.0	1.0
Prevalence decrease by 20%	2.5	6.9	2.5	2.0	0.7	3.0	1.0	5.0	1.0	1.0
Prevalence decrease by 40%	2.5	7.1	2.5	2.0	0.7	3.0	1.0	5.0	1.0	1.0
Women										
Main (Baseline)	2.1	5.9	2.1	1.7	0.6	2.6	0.9	4.3	1.7	0.8
Relative Risk decrease by 20%	1.7	5.5	1.7	1.4	0.5	2.1	0.7	3.6	1.4	
Relative Risk decrease by 40%	1.4	4.5	1.3	1.1	0.4	1.6	0.5	2.8	1.1	0.5
Relative Risk increase by 20%	2.4	7.2	2.5	2.1	0.7	3.1	1.0	5.0	2.0	1.0
Relative Risk increase by 40%	2.7	7.9	2.8	2.3	0.8	3.5	1.2	5.6	2.3	1.1
Prevalence increase by 20%	2.1	5.8	2.1	1.7	0.6	2.6	0.9	4.3	1.7	0.8
Prevalence increase by 40%	2.1	5.7	2.1	1.7	0.6	2.6	0.9	4.3	1.7	0.8
Prevalence decrease by 20%	2.1	5.9	2.1	1.8	0.6	2.6	0.9	4.4	1.7	0.8
Prevalence decrease by 40%	2.2	6.0	2.1	1.8	0.6	2.6	0.9	4.4	1.7	0.8

Discussion

Summary of the results

Based on the literature review, we found several individual factors increasing the risk of mortality. Strongest effects were found for smoking with relative risks between two and three and obesity with relative risks between 1.5 and 2. Sedentary behaviour, lack of physical activity, alcohol consumption, insufficient fruit and vegetable consumption have been shown to increase the risks of mortality with a factor between 1.2 and 1.5. Having no social contacts and several dietary factors have been shown to increase the mortality risk with a factor of about 1.1.

Using additional data on mortality and the prevalence of the risk factors for the German male and female population by age, we estimated the loss in average life expectancy caused by each factor. Comparing the actual life expectancy with the life expectancy in the counterfactual scenario with all persons in the healthiest exposure category showed that of all factors considered smoking yielded the highest loss in the average life expectancy in Germany, reducing life expectancy of men with 2.7 years and of women with 1.5 years. Overweight/obesity was the second largest contributor, reducing average life expectancy by more than one year. Physical activity, sedentary behaviour and fruit and vegetable consumption, reduced average life expectancy of men with about one year and of women with about 0.5 year. Alcohol consumption reduced life expectancy with slightly less than 0.5 year in men and showed virtually no effect on life expectancy of women.

The losses in average life expectancy are the losses for the total population, including both persons who are in the healthiest exposure category (e.g. normal weight) and persons in exposure categories with increased mortality risks (e.g. overweight and obesity). This is the loss at the population level. Using the same data, we estimated life expectancies by exposure group and compared life expectancies between these groups, with the healthiest category as the reference. For men, we found largest differences for smoking with a difference of 7 years between current and never smokers. For men with obesity life expectancy was 5 years less as compared to persons with normal weight. For men with an average daily alcohol consumption of more than 45 gram, life expectancy was about 3 year less as compared to persons drinking less than 25 gram (<2 drinks). For the other risk factors, the differences were smaller. For women the differences were slightly smaller than for men.

Strengths and limitations

The major strength of our study is that it provided relative risks estimates of the effect on mortality for several individual risk factors based on recent meta analyses, and that these estimates were used to quantify losses in life expectancy due to the risk factors in Germany. Meta-analyses can be considered as the best available evidence of the effect of risk factors on mortality. Using life expectancy measures in addition to relative risks has advantages because life expectancy is a metric that is commonly used and easily understood by the broader audience. Moreover, the measures of life expectancy loss for the population and the individual takes into account the German mortality levels and the German risk factor exposure levels.

Several limitations need to be considered.

First, combining data from different sources may introduce a mismatch between the exposure categories used in the calculation of relative risks and those used for the calculation of the prevalence of the risk factor. While we tried to minimize the potential mismatch by making similar exposure categories, this was not possible for all factors. For instance, for alcohol in ESS there was no information on former drinkers.

Second, while we selected those meta analyses which controlled maximally for confounding and minimized the risk of reverse causation and prioritized recent meta-analysis with the highest quality, nonetheless, the quality of the meta-analyses differed, and meta-analyses may have under- or overestimate the true but unknown relative risks. For smoking, relative risks based on more recent studies with longer follow-up time showed higher relative risks than the relative risk we used in our main analyses. Relative risks may also have been overestimated, in particular when there was an incomplete control for confounding factors or reverse causation, which is likely to have occurred in the studies of the effect of social contacts on mortality. The sensitivity analyses showed that 40% higher relative risks for smoking (similar to the relative risk reported in the recent UK (7) and US (6)) would lead average losses in life expectancy associated with smoking of 3.5 years in men and 2 years in women, while the individual losses would increase to 8 years in men and more than 7 in women. For BMI there is more debate on the relative risks, in particular regarding the effect of overweight for the elderly. The sensitivity analyses should that 40 percent lower relative risks would still mean a loss in average life expectancy at the population level of about one year and the loss at the individual level would be about three years for both sexes for obesity. For other risk factors the variations in the relative risk would have a smaller impact on both outcome measures.

Third, using current self-reported exposure data based on a cross-sectional survey, in our case the ESS, is a limitation. Similar to prior studies using the PAF approach (67) we assumed that the reported exposure at the time of the survey was representative for exposure over a longer period of time. In particular for alcohol consumption, general population surveys may largely underestimate real alcohol consumption (70, 71). The same is expected for ESS although an advantage of this survey is that it has very detailed alcohol questions, adapted to each country. Because underestimation of exposure may also be encountered in epidemiological studies that estimated the relative risks, bias may be reduced, because we combined prevalence and relative risks. The sensitivity analyses with 40 percent higher prevalence of alcohol consumption indicated that the average loss in alcohol may be higher than in our main analyses, but that the individual losses are hardly affected. The choice the survey may have affected the outcomes as different survey may yield different estimates of the prevalence of the risk factor because of differences in survey design, survey questions, collection mode (telephone, computer assisted, internet). A rough comparison for selected factors with other published estimates on risk factor prevalence in Germany suggested that our estimates are in line with prior studies, except for the likely underestimation for alcohol consumption and a possible small overestimation of current smokers.

Comparisons with prior studies

For Germany, one prior study by Li (72) assessed the individual loss in life expectancy for different risk factor for persons aged 40 and over. This study was based on the EPIC cohort in Heidelberg, including 22,469 persons 40-year-old or older, recruited from 1994 to 1998 and followed up for mortality until 31 December 2009. This study reported that for 40-year-old adults, similar to our results, the most significant loss of life expectancy was associated with smoking (9.4 years for male

and 7.3 years for female heavy smokers and 5.3 and 5.0 years male and female light smokers). This is in line with our estimates of 6.9 years for men and 5.9 years for women for all smokers. For obesity, the study by Li found a difference between obesity and normal weight of 3.1 years for men and 3.2 years for women and for overweight of 1.1 and 0.6 years respectively. We estimated larger differences (5 years for men and 4.3 years for women for obesity and of 1 and 0.9 years for overweight, respectively). The difference between the EPIC cohort and our study was also reflected in the lower relative risks for obesity in the EPIC study. The higher relative risks in our study, based on recent meta-analyses, may reflect the better correction for smoking. In addition, the relative risk in the EPIC study were adjusted for pre-obesity related conditions, which may have moved away part of the causal effect of overweight/obesity. The EPIC study found a difference in life expectancy between those drinking (>4 drinks/day, comparable with 45 grams/day) and less than 4 drinks of 3.1 years for men and 3.2 years for women. We found a similar differences of 3.2 years in men and 2.8 year in women. The EPIC study found a smaller loss of life expectancy associated with low leisure time physical activity (for men 0.4 years and for women 1.1 years)) as compared to 2.5 and 2.1 in our study. The classification of physical activity was different, making these results hard to compare. A review of Reimer(73) based on 11 cohorts studies (not including Germany), estimated that the difference in life expectancy of physically active compared to inactive persons adjusting for confounding ranged between 0.43 and 4.21 years (mean 2.7 ± 1.1 years).

Conclusion

At the population level individual risk factor cause substantial losses in life expectancy, with smoking having the largest impact on average life expectancy, followed by overweight and obesity and smaller but still relevant impacts by physical activity and fruit and vegetable consumption. The loss due to alcohol was smaller, but this will at least partly reflect the underreporting of alcohol in surveys. The losses in life expectancy for the individual with the unhealthy behaviour are substantially larger, with a loss of 6-7 years for smoking, 4-5 years for obesity, 3 years for heavy drinking and 2 years for physical activity.

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Appendix

Table A1 Comparison prevalence of risk factors in Germany with selected other studies

BMI	Classification	Men	Women	Age	Source	Remark
ESS	Overweight	0.43	0.28	15+	This report	ESS estimates in line with other sources
	Obesity	0.17	0.17		This report	ESS estimates in line with other sources.
Microzensus	Overweight	0.43	0.29	18+	(74)	
	Obesity	0.18	0.18		(74)	
DEGS1	Overweight	0.44	0.29		(75)	
	Obesity	0.23	0.24		(74)	
EPIC	Overweight	0.52	0.29	40+	(72)	Less comparable due different age range
	Obesity	0.16	0.14		(72)	

Smoking	Classification	Men	Women	Age	Source	Remark
ESS	Current smoker, including occasional	0.33	0.28	15+	This report	ESS estimates in line with other sources. Slightly overestimation of prevalence cannot be ruled out.
	Former smoker	0.29	0.19		This report	ESS estimates in line with other sources. Slightly over- or underestimation of prevalence cannot be ruled out.
Microzensus	Current smoker	0.25	0.20	18+	(76)	
	Former smoker	0.24	0.14			
DEGS1	Current smoker	0.33	0.27		(75)	
	Former smoker	0.34	0.23		(75)	
EPIC	Current smoker	0.24	0.23	40+	(72)	
	Former smoker	0.45	0.34		(72)	

Alcohol	Classification	Men	Women	Age	Source	Remark
ESS	25-45 gr/d	0.11	0.03	15+	This report	ESS underestimates alcohol consumption .
	High (>45 gr/d)	0.06	0.01		This	

					report	
DEGS1	Harmful consumption	0.19	0.13	25-69	(77)	
DEGS1	At risk drinking	0.42	0.26	18-79	(78)	
DEGS1	Episodic drinking	0.31	0.10	18-29	(78)	

Physical activity	Classification	Men	Women	Age	Source	Remark
ESS	low (<5 days/30 min; 11.25 Met/w))	0.59	0.61	15+	This report	Comparison hampered by different definitions ESS estimates seem in line with other sources.
	High	0.41	0.39		This report	
Website norm	Not meeting norm	0.55	0.65		(79)	
	Meeting norm	0.45	0.35			
DEGS1				25-69	(77)	
EPIC	Low (< 38 MET/w)	0.53	0.51	40+	(72)	
	High	0.47	0.49			

Fruit and vegetable consumption

Fruit and vegetables	Classification	Men	Women	Age	Source	Remark
ESS-2014	Less 1/day fruit + vegetables vs at least 1	0.54	0.39	15+	This study	Comparison hampered by different definitions In line with result on "not daily fruit and vegetables" for CEDA
CEDA 2014-2015 EHIS	Not Daily fruit and vegetables	0.62	0.46		(80)	
CEDA 2012	Not Daily fruit and vegetables	0.52	0.30		77)	
DEGS1	<3 portion fruit, vegetable, juice vs >=3 portions	0.69	0.61	18+	(76)	
DEGS1	< 5 portions vs >=5	0.95	0.85		(76)	
GEDA	< 5 portions vs >=5	0.93	0.87		(76)	
EPIC	Low <200 gr/day vs >200 gr day	0.51	0.63	40+	(72)	Women deviant pattern, in general opposite gender pattern

Sedentary behaviour	Classification	Men	Women	Age	Source	Remark
ESS-2014	> 2 h/w TV	0.39	0.42	15+		Larger uncertainty. No

						comparable studies found. ESS estimates could be both under or overestimated
NA						

Social contact	Classification	Men	Women	Age	Source	Remark
ESS-2014	No meeting >1/w	0.46	0.43	15+		Larger uncertainty. No comparable studies found. ESS estimates could be both under or overestimated
NA						

For sedentary behaviour and social support, comparison with other studies was not possible.