



## The combined effect on survival of four main behavioural risk factors for non-communicable diseases



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### ABSTRACT

**Objective.** To quantify and illustrate the combined effects of WHO's four behavioural risk factors for non-communicable diseases (NCDs) on mortality.

**Methods.** Participants ( $n = 16,721$ ) were part of two Swiss population studies conducted between 1977 and 1993. Smoking status, alcohol consumption, physical activity and diet were assessed at baseline. With record linkage in 2008, up to 31 years of follow-up with 3,533 deaths could be recorded. Mortality was assessed with Cox proportional hazard models for each risk factor and their combinations. Ten-year survival probabilities for 65- and 75-year-olds were estimated with Weibull regression models.

**Results.** Hazard ratios for the combination of all four risk factors compared to none were 2.41 (1.99–2.93) in men and 2.46 (1.88–3.22) in women. For 65-year-olds, the probability of surviving the next 10 years was 86% for men with no risk factors and 67% for men with four. In women, the respective numbers were 90% and 77%. In 75-year-olds, probabilities were 67% and 35% in men, and 74% and 47% in women.

**Conclusions.** The combined impact of four behavioural NCD risk factors on survival probability was comparable in size to a 10-year age difference and bigger than the gender effect.

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### Introduction

Non-communicable diseases (NCDs) have become a major concern in health care and a priority of global health policy (United Nations, 2011). In its current Action Plan for the Global Strategy for the Prevention and Control of Non-Communicable Diseases, the World Health Organization (WHO) has identified four main groups of NCDs (cardiovascular diseases [CVD], cancers, diabetes and chronic respiratory diseases) and four main behavioural risk factors (tobacco use, unhealthy diet, physical inactivity and harmful use of alcohol) (World Health Organization, 2009). The Global Burden of Disease Study 2010 has quantified the impact of those four and other risk factors on global health as population attributable fractions (Lim et al., 2012; Murray et al., 2012). For Western Europe, the eight risk factors with the highest shares on attributable burden of disease were, in descending order, tobacco smoking, high blood pressure, high body mass index (BMI), alcohol use, physical inactivity, high fasting plasma glucose, diet low in fruits and high total cholesterol (Lim et al., 2012). Thus, the top eight of all risk factors for NCDs include four modifiable lifestyle factors

and four biological parameters that are associated with at least some of these four behaviours.

An accumulation of clinical risk factors increases morbidity and mortality; particularly for CVD, risk score charts and guidelines for diagnostic and therapeutic procedures in clinical decision making or for risk prediction have been developed based on combinations of clinical parameters (Cooney et al., 2009). However, not only clinical parameters but also unhealthy behaviours are often clustered (Heroux et al., 2012), and it has been shown that mortality increases with an accumulation of unfavourable lifestyle factors including measures of body fatness (Behrens et al., 2013; Carlsson et al., 2012; Dobson et al., 2012; Loeff and Walach, 2012). Since behavioural counselling in primary care is an important element of both prevention and therapy, a comprehensive system illustrating directly the effect of behavioural factors could be of particular value for health professionals. Such an illustration could also become an important communication tool for health policy. To our knowledge, risk charts based on the four main behavioural risk factors for NCDs have not been developed so far.

This study therefore aimed at quantifying and illustrating the combined effects of the WHO's four behavioural risk factors for NCDs on total, CVD and cancer mortality, using observational and recent population specific routine data from Switzerland. For this purpose, data from two Swiss population studies were linked to the Swiss National Cohort (SNC), a record linkage project of data from census, death and migration registers.

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## Methods

### Study populations and record linkage

The sample population, aged 16–90 years at baseline, consisted of participants of two studies on cardiovascular health in Switzerland: the National Research Programme 1A (NRP 1A) (Gutzwiller et al., 1985) and the Swiss Monitoring of trends and determinants in Cardiovascular disease (MONICA) study (Bothig, 1989). The NRP 1A was conducted from 1977 to 1979 in five towns situated in the three main language regions of Switzerland (Aarau, Lugano, Nyon, Solothurn and Vevey) (Bopp et al., 2012). Measurements included a health examination (body weight and height, blood pressure, blood lipids and other biological parameters) and a questionnaire (socio-demographic variables, smoking, alcohol consumption, physical activity and general eating patterns, dietary intake on the day preceding the examination and eating behavior). The Swiss MONICA study included the French- and Italian-speaking but not the German-speaking part of Switzerland, and it was conducted in three waves in 1984–1986, 1988–1989 and 1992–1993 (Wietlisbach, 1987; Wietlisbach et al., 1997). Again, measurements included a health examination and a self-administered questionnaire. We used only variables that were identical or quasi identical in both studies.

In neither of these two studies a mortality follow-up was planned. In order to obtain survival information, data from the SNC, which includes also information on cause of death, were linked to NRP 1A and MONICA participant records in 2008. Details on linkage procedure and success were reported elsewhere (Bopp et al., 2009, 2010, 2012). Briefly, 8008 out of 8539 eligible participants of NRP 1A (93.8%) (Bopp et al., 2012), and 9853 out of 10,160 eligible MONICA participants (97.0%) could be linked with the SNC (Bopp et al., 2010).

For the present analyses, the NRP 1A and MONICA data sets with linked mortality data were then combined. After deleting individuals with missing covariate information ( $n = 1140$ ), data of 16,721 participants remained for analysis, with a total of 357,045 person-years of follow-up and 3,533 deaths. The analyses for this paper were conducted in 2013.

### Measurements

All-cause mortality and cause-specific mortality were used as outcome variables. In Switzerland, causes of death were defined according to the 8th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-8) until 1994, and afterwards based on ICD-10. CVD deaths were defined as ICD-8 codes 410–438 and ICD-10 codes I00–I99. Cancer mortality corresponds to ICD-8 codes 140–239 and ICD-10 codes C00–C99 and D00–D48.

The health behaviours included as covariates (see electronic Supplementary material file 1 for questionnaires) in the models were smoking status (current smoker [regular or occasional]; current non-smoker [never or former smoker]), alcohol consumption on the previous day (no; moderate [MONICA: drinking either wine or beer or cider; NRP1A: women drinking less than 20 g/d, men drinking less than 40 g/d]; high [MONICA: drinking spirits or more than one sort of alcohol on the previous day; NRP1A: women drinking more than 20 g/d, men drinking more than 40 g/d]), leisure-time physical activity (LTPA: (low [light physical activity, mostly sedentary]; high [frequent walking or cycling; other frequent activities such as gardening; or regular vigorous physical activity]), and fruit intake on the previous day (no; yes). As an indicator for a healthy diet, we chose fruit intake because of its ranking in the Global Burden of Disease project (Lim et al., 2012). In addition, the following covariates were included: sex, age (years), education (according to the International Standard Classification of Education ISCED: mandatory school [ISCED 0–2], vocational education [ISCED 3], higher vocational education [ISCED 4], university [ISCED 5–6]), marital status (single, married, widowed, divorced/separated), survey (NRP1A, MONICA waves 1–3) and nationality (Swiss, non-Swiss).

### Ethical approval

Approval (No. 13/06) for record linkage and the analyses of the resulting data base was obtained from the Ethics Committee of the Canton of Zurich. Written informed consent had been obtained from participants in MONICA (Bothig, 1989), but this procedure was not customary at the time the NRP 1A was conducted.

### Statistical analyses

For descriptive analyses, means and standard deviations of the continuous variables and frequencies and proportions of categorical variables were calculated. Hazard ratios describing relations between independent variables and total, CVD and cancer mortality were estimated with Cox proportional hazards models for both sexes separately and combined. All models include the four behavioural factors as well as sex (where appropriate), age, indicators for socio-economic status and survey. The proportional hazards assumption was tested and was sufficiently fulfilled for eight of the nine models presented, the only exception being the model for total mortality in both sexes combined.

Time to event or censoring was defined as time difference between study entry (date of baseline interview) and date of death, or the possible censoring dates of emigration, or end of the study (December 31, 2008), respectively. Model selection was performed based on Akaike's information criterion (AIC) and the Bayesian information criterion (BIC).

In analogy to the SCORE project (Conroy et al., 2003), we then calculated the 10-year probability of survival at ages 65 and 75 years for different combinations of risk factors. For the calculation of such absolute risks, an estimation of the baseline hazard is needed. This cannot be obtained using a Cox proportional hazards model; therefore, a Weibull regression model was used (Faeh et al., 2013). The included covariates were the same as in the Cox proportional hazards models.

We chose  $\alpha = 0.05$  as level of significance. The calculations were done with STATA 12.1 (StataCorp LP, College Station, Texas, 2011) and R 2.15.2 (R Foundation for Statistical Computing).

## Results

### Characteristics of participants

Characteristics of participants at study entry (baseline) are shown in Table 1. Mean age was 45.1 years (SD = 13.5), and the proportion of women was 51.4%.

### Risk behaviours and mortality

Cox proportional hazards models were calculated and the hazard ratios (HR) for mortality derived from the multivariate analysis are given in Table 2. In both sexes combined, total mortality was increased

**Table 1**  
Baseline characteristics of participants (MONICA and NRP 1A, Switzerland, 1977–2008).

	Men	Women
N	8132	8589
Mean age in years (SD)	44.9 (13.1)	45.2 (13.8)
Person-years	167,508	189,537
Number of deaths	All causes	1566
	CVD	666
	Cancer	705
	Other causes	596
Educational level	Mandatory (%)	27.5
	Vocational (%)	50.2
	Higher vocational (%)	13.2
	University (%)	9.1
Marital status	Single (%)	16.2
	Married (%)	77.8
	Widowed (%)	1.2
	Divorced/separated (%)	4.8
Nationality	Swiss (%)	78.8
	Non-Swiss (%)	21.2
Current smoking status	Non-smoker (%)	60.1
	Smoker (%)	39.9
Alcohol consumption yesterday	No (%)	29.6
	Moderate (%)	49.3
	High (%)	21.1
Leisure time physical activity	High (%)	72.6
	Low (%)	27.4
Fruit consumption yesterday	Yes (%)	65.2
	No (%)	34.8

CVD = cardiovascular disease; SD = standard deviation.

**Table 2**  
Hazard ratios (HR) for four risk behaviours and total, CVD and cancer mortality (MONICA and NRP 1A, Switzerland, 1977–2008).

		Total mortality			CVD mortality			Cancer mortality		
		Men and women	Men	Women	Men and women	Men	Women	Men and women	Men	Women
		HR	HR	HR	HR	HR	HR	HR	HR	HR
		(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Sex	Female	1			1			1		
	Male	1.74 (1.61, 1.87)	–	–	2.00 (1.75, 2.28)	–	–	1.48 (1.30, 1.68)	–	–
Current smoker	No	1	1	1	1	1	1	1	1	1
	Yes	1.57 (1.46, 1.69)	1.63 (1.48, 1.78)	1.52 (1.34, 1.72)	1.56 (1.37, 1.78)	1.66 (1.42, 1.95)	1.39 (1.09, 1.77)	1.63 (1.44, 1.84)	1.67 (1.43, 1.95)	1.57 (1.29, 1.92)
Alcohol consumption yesterday	No	1	1	1	1	1	1	1	1	1
	Moderate	1.01 (0.94, 1.09)	1.02 (0.92, 1.14)	0.99 (0.89, 1.10)	0.91 (0.80, 1.03)	0.86 (0.73, 1.03)	0.94 (0.78, 1.13)	1.14 (1.00, 1.29)	1.20 (1.00, 1.44)	1.06 (0.88, 1.27)
	High	1.15 (1.03, 1.28)	1.13 (0.99, 1.29)	1.21 (0.98, 1.50)	0.96 (0.78, 1.17)	0.85 (0.66, 1.08)	1.20 (0.81, 1.78)	1.32 (1.11, 1.58)	1.34 (1.08, 1.68)	1.40 (1.01, 1.93)
Leisure time physical activity	High	1	1	1	1	1	1	1	1	1
	Low	1.16 (1.08, 1.25)	1.12 (1.01, 1.23)	1.22 (1.10, 1.36)	1.15 (1.01, 1.30)	1.04 (0.88, 1.24)	1.25 (1.04, 1.50)	1.13 (1.01, 1.28)	1.15 (0.98, 1.36)	1.13 (0.94, 1.36)
Fruit consumption yesterday	Yes	1	1	1	1	1	1	1	1	1
	No	1.15 (1.07, 1.24)	1.18 (1.07, 1.30)	1.09 (0.97, 1.24)	1.15 (1.01, 1.31)	1.17 (0.99, 1.38)	1.10 (0.88, 1.36)	1.20 (1.06, 1.36)	1.23 (1.05, 1.45)	1.16 (0.95, 1.43)
Number of risk factors	None	1	1	1	1	1	1	1	1	1
	All four	2.42 (2.07, 2.81)	2.41 (1.99, 2.93)	2.46 (1.88, 3.22)	1.98 (1.50, 2.60)	1.72 (1.22, 2.43)	2.30 (1.40, 3.75)	2.93 (2.29, 3.75)	3.18 (2.31, 4.39)	2.89 (1.90, 4.39)

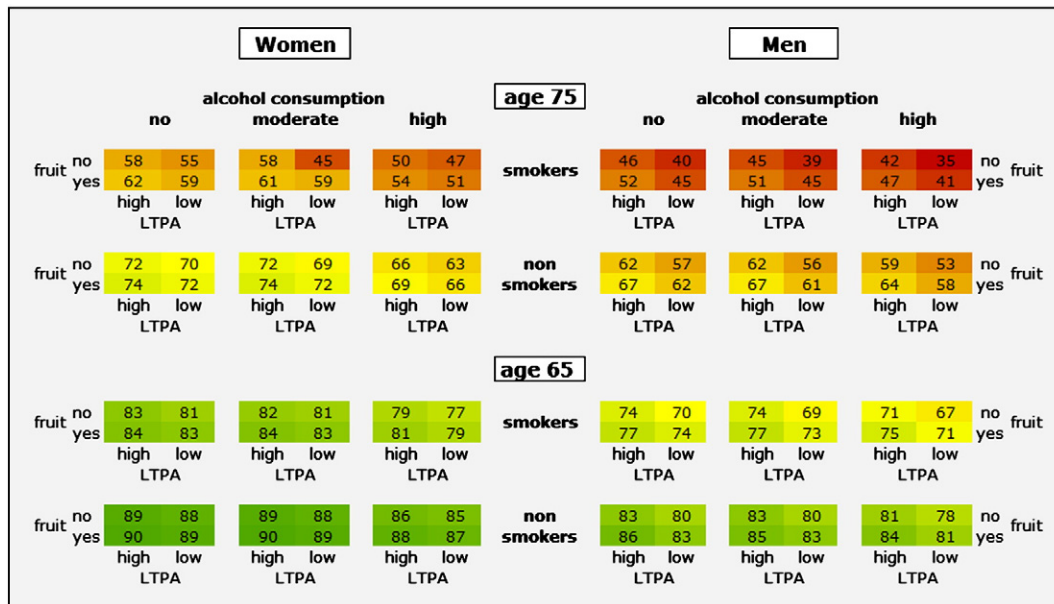
CVD = cardiovascular disease; HR = hazard ratio.  
All HRs adjusted for age, sex (when applicable), socio-economic variables (education, marital status, nationality), survey and the other behavioural variables listed in the table.

by each one of the four risk factors independently. Also in the sex-specific analysis, six out of the eight associations reached the level of statistical significance. The combination of all four risk factors increased total mortality about 2.5-fold in comparison to no risk factors. Also cause-specific mortality (in both sexes combined) was independently associated with the four risk factors—except that alcohol consumption did not significantly increase the risk of CVD mortality.

About 98% of the total sample also had complete data on BMI, blood pressure and serum cholesterol. Adjusting for these biological parameters changed the associations presented in Table 2 only marginally (see electronic Supplementary material Table 1).

*Probabilities of surviving the next 10 years, at ages 65 and 75*

Fig. 1 shows the probabilities of surviving the next 10 years for 65 and 75-year-old men and women depending on their risk profile derived from Weibull regression models. The chances of surviving another 10 years varied between 90% in the younger women with no risk factors and 35% in the older men with all four risk behaviours. Survival probability was higher in women than in men, with the largest differences (up to 10%) in those individuals with three or four risk factors. Remarkably, 75-year-old men with no behavioural risk factors had the same probability of surviving the next 10 years as those men who were still



**Fig. 1.** Charts for probabilities (%) of surviving the next 10 years, at ages 65 and 75 years, by sex (MONICA and NRP 1A, Switzerland, 1977–2008). Green shades = highest survival probabilities; yellow shades = medium survival probabilities; red shades = lowest survival probabilities. Probabilities for all combinations of risk factors estimated with Weibull regression models controlled for survey, education, marital status and nationality. LTPA = leisure time physical activity; fruit = fruit consumption yesterday. Men: N = 8132 (of which 1967 cases); women: N = 8589 (of which 1566 cases).

10 years younger but had all four risk factors (67%). Among women, the respective pattern was similar.

## Discussion

In this study using baseline data from two population studies linked to the SNC, the accumulation of the four behavioural NCD risk factors tobacco smoking, high alcohol consumption, low levels of leisure time physical activity and poor diet indicated by no reported fruit consumption on the previous day increased all-cause mortality about 2.5-fold. All four behaviours contributed to this overall effect. For risk communication, charts for the probability of 10-year survival for 65 and 75-year-old men and women were developed for all possible combinations of the four risk factors. We chose to visualise the probability of survival for these two age groups because at this age, effects of unhealthy behaviours on mortality become apparent in Switzerland (see electronic Supplementary material Fig. 1 for 45- and 55-year-olds).

The relevance of WHO's four behavioural risk factors for overall, CVD and cancer mortality in a population based linkage study was clearly shown. Given the limitation of crude exposure measures, the main aim of this study was not to refine effect estimates of single or combined health behaviours on mortality but to translate our findings into information accessible to a broader audience. Nevertheless, a comparison of our results shows that effect estimates for the single risk factors were in the same order of magnitude as in other studies: They were comparable or somewhat smaller for smoking (Gellert et al., 2012; Mucha et al., 2006), comparable (Dauchet et al., 2009) or somewhat stronger (Leenders et al., 2013) for fruit consumption and comparable to the effect of a healthy diet assessed with an alternate Mediterranean diet score (Behrens et al., 2013). For moderate alcohol consumption, there was only a suggestion of the expected protective effects on CVD mortality, as described in a review and a meta-analysis (Ronksley et al., 2011). Effect estimates for alcohol consumption on cancer mortality were at least as high as in other studies (Jin et al., 2012). For physical activity, effect estimates were comparable for CVD mortality, but lower for cancer and total mortality than in a recent re-analysis of cohort studies (Lee et al., 2012). In the present study, estimates for LTPA were lower in men than in women. We had in fact also tested a variable for the frequency of sports activities (at least one sports session per week vs. less than one) as an indicator of physical activity which had shown stronger associations with mortality outcomes in men. However, based on face validity, we chose the leisure time physical activity indicator for the final model.

To our knowledge, our study is the first one that exclusively used behavioural factors in the models and that estimated the probability of survival for all combinations of factors. One study reported absolute risks of death for risk factor combinations using BMI but not an indicator for poor diet (Dobson et al., 2012). Effect estimates were comparable to our results. Others have investigated the effects of combinations of lifestyle factors on total mortality using scores by counting numbers of risk factors (Behrens et al., 2013; Carlsson et al., 2012; Loef and Walach, 2012) or by additionally defining some specific risk factor combinations (Behrens et al., 2013). In a meta-analysis of 15 studies (Loef and Walach, 2012) obesity was also included as a lifestyle factor in addition to the behavioural factors investigated in the present study. The pooled estimate of the effect of four factors compared to none ( $RR = 3.12$ ) (Loef and Walach, 2012) was slightly stronger than the effects found in our study. The same was true for a large cohort study including also abdominal fat as a risk factor (Behrens et al., 2013). Another recent study used seven modifiable lifestyle factors of which four were food intake factors (fruit, vegetable, meat and fish); the impact of risk factor accumulation was comparable to our study (Carlsson et al., 2012). Scoring concepts based on the number of risk factors have also been used to assess the effects of an accumulation of lifestyle risk factor on incident cases of specific cancers (Jiao et al., 2009; Odegaard et al., 2013) or CVD (Carlsson

et al., 2012; Myint et al., 2009), showing effect estimates in the same order of magnitude as in our mortality study.

CVD risk charts based on clinical parameters have been used for risk stratification by specialists or primary care physicians in clinical decision making for some time already (Conroy et al., 2003). Our charts complement these classic risk charts. They are based exclusively on behavioural risk factors and on total and not only CVD mortality. In its current Global Action Plan 2013 to 2020 for the Prevention and Control of Non-Communicable Diseases, WHO defines "To strengthen and orient health systems to address the prevention and control of noncommunicable diseases and the underlying social determinants through people-centred primary health care and universal health coverage" as an important objective (World Health Organization, 2013). In this context, the survival charts presented in this paper could be used to directly address lifestyle habits in behavioural counselling situations, either by primary health care professionals and their patients (Neuner-Jehle et al., 2013) or other health professionals and their clients. WHO also points out the need to create health-promoting environments (World Health Organization, 2013). With this perspective, the self-explanatory nature of risk charts and the use of absolute instead of relative risks could help in communication with decision makers in public health and other stakeholders, in addition to measures already used in communication such as population attributable fractions (Lee et al., 2012).

## Strengths and limitations

The main strength of this study is that it had a long follow-up period and the loss-to-follow-up was small (6.2% in NRP 1A and 3% in MONICA). Record linkage in this study was very successful (Bopp et al., 2010); therefore, linkage dropout does not have to be considered a relevant source of selection bias. We also do not expect recall bias because of the prospective nature of the analyses. An additional strength is that the associations between mortality and behavioural risk factors were observed in a country with a high quality health care system accessible to the entire population which might have compensated some of the effects on mortality.

The main limitation of the study is its set of rather crude exposure measures, e.g., fruit consumption on the previous day as an indicator of a healthy diet. In addition, only baseline assessments of exposures have been conducted and changes over time, and lifetime exposures have not been assessed. It is remarkable that the effect of the behavioural risk factors on mortality could be shown so clearly because these limitations in exposure assessment are likely to lead to non-differential misclassification, which would result in an underestimation of mortality risks in the Cox proportional hazards models. Also in the Weibull regression models, this phenomenon would result in an underestimation of differences in survival between exposed and unexposed groups. We adjusted for socio-economic variables and mutually controlled for all other behavioural factors in the model. Because assessment of behaviours was crude, some residual confounding cannot be excluded.

## Conclusions

In conclusion, this study clearly showed the impact of NCD risk accumulation on overall, CVD and cancer mortality exclusively based on behavioural factors. The survival charts with absolute probabilities provide a tool that could be used for risk communication with health professionals and their patients or clients, policy makers or other stakeholders. The usefulness of the survival charts for these tasks should be evaluated. Future research should investigate not only the dose-response relationship between single and combined behavioural risk factors with mortality, but also their effects on morbidity as well as the role of lifetime accumulation of risk factors and changes in exposure.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ypmed.2014.05.023>.



**Conflict of interest statement**

The authors declare that there are no conflicts of interest.

**Contributors**

All authors contributed to the conception and design of the study and to the interpretation of the data, and they approved the final version to be published. JM, JB and ST analysed the data. EM and BM drafted the article. DF and SR critically revised the manuscript for important intellectual content. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. BM is the guarantor.

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