

Factors predicting 31-year survival among a population cohort in Northern Finland

Yrjö Perkkio^{a,b}, Juha Auvinen^{a,c}, Markku Timonen^{a,d}, Jari Jokelainen^{d,e}, Nihkolas Valkeapää^f, Markku Koironen^a, Juha Saltevo^g and Sirkka Keinänen-Kiukaanniemi^{a,h}

^aCenter for Life Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland; ^bDepartment of Primary Health Care in Lapland Central Hospital, Health Centre of Muonio-Enontekiö, Rovaniemi, Finland; ^cHealth Center of Oulunkaari, Ii, Finland; ^dUnit of General Practice, Oulu University Hospital, Oulu, Finland; ^eInfrastructure for Population Studies, University of Oulu, Finland; ^fLapland Central Hospital, Rovaniemi, Finland; ^gCentral Finland Central Hospital, Jyväskylä, Finland; ^hHealth Center of Selänne, Pyhäjärvi, Finland

ABSTRACT

We evaluated the survival of a subarctic population and the significance of traditional risk factors for mortality, causes of death and their seasonal variation from the period of 1984–2014. By the end of 2014 (follow-up), 644 (34.4% from 1,869) participants had died (42.1% of cardiovascular causes, 22.4% of neoplastic diseases). The average age at death \pm SD was 74.6 \pm 11.4 years for women (n=284) and 70.2 \pm 12.0 years for men (n=360). After adjusting for baseline age, the major risk factors predicting death were male sex (hazard ratio [HR] 1.80; 95% confidence interval [CI] 1.54–2.10), current smoking (HR 1.85; 95% CI 1.58–2.17), obesity (HR 1.75; 95% CI 1.45–2.12), high blood pressure (HR 1.46; 95% CI 1.24–1.72), cardiovascular disease (HR 1.62; 95% CI 1.36–1.93) and depression (HR 1.61; 95% CI 1.21–2.14) at baseline.

The most common causes of death and the main risk factors predicting death in this population were the same as reported globally. Lifestyle factors had an important impact in predicting survival. The most common causes of death were the same for men and women. There was no significant difference in overall mortality rate between winter and summer, but cerebrovascular and pulmonary causes of death were more common during winter.

ARTICLE HISTORY

Received 28 August 2020
Revised 22 March 2021
Accepted 23 March 2021

KEYWORDS

Mortality; risk factors predicting death; causes-of-death

Introduction



In 2016, as many as 54% of the 56.9 million deaths worldwide were due to the top 10 causes with the top 2 (ischaemic heart disease and stroke) together accounting for 15.2 million deaths [1,2]. Among non-communicable diseases, the next most common causes of death were chronic obstructive pulmonary disease, lung cancer, diabetes and dementia. Deaths due to diabetes and dementia markedly increased from the year 2000 to 2016 [1].

In Finland, the most common causes of death in 2017 were cardiovascular diseases, followed by neoplastic disorders, dementia, injuries and respiratory diseases [3]. However, little is known about the factors resulting in death in a rural, subarctic district.

We evaluated the survival rate of a subarctic (Muonio-Enontekiö, Finland) population and the significance of traditional cardiovascular, including social and lifestyle-related, risk factors for all-cause mortality, causes of death and their seasonal variation, (the

follow-up time was 31 years). This population differs in many respects from the main Finnish population living in the Southern Finland. Number of people in the Muonio-Enontekiö district in 1984 earned their living by physical labour, such as by agriculture, forestry, reindeer herding and hunting. There are also cultural and genetic differences compared to the main population in Finland. The ethnic Sámi people comprised about 9% of the study population [3]. The education level of the population is low and the geographic area (150–400 km above the Arctic Circle) is large (10,431 km²) and sparsely populated (4,145 inhabitants: 0.4–0.5 inhabitants/km²). Distances from remote villages to health stations can be over 100 km, and no public transportation is available.

The Muonio-Enontekiö District is located between the Norwegian and Swedish borders. The climate is harsh: The mean annual average temperature is as low as -2°C [4]. During summer the sun does not set for weeks, while in winter, it does not rise for about the

CONTACT Yrjö Perkkio  yrjo.perkkio@fimnet.fi  Health Centre of Muonio-Enontekiö, Kätkäjärventie 75, Kätkäsvanto 99320, Finland

Abbreviations: BMI: body mass index; HR: hazard ratio; SD: standard deviation; CI: confidence interval.

© 2021 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

same period. The environment is the cleanest in the world based on the World Health Organization Follow-up Report 2008–2014 [5].

Materials and methods

Study design and participants

The study cohort (see Figure 1) consisted of the population born between 1915 and 1958 living in the Muonio–Enontekiö district of Northern Finland and participating in health surveys between 1974 and 1984. Of the 2,750 individuals invited to health survey 1,923 (69.9%) agreed. Due to incomplete information on identification code, 54 participants were excluded from the analysis thus leaving 1,869 participants who were included in this study. The baseline characteristics of the study population were collected between 1974 and 1984.

Health survey

Health check-ups and blood samplings for laboratory analyses were conducted by trained primary healthcare nurses at Muonio–Enontekiö Health Centre between 1974 and 1984. The nurses also provided information on lifestyle interventions to the study participants and sent them for a general practitioner consultation if needed.

The surveys included a self-administered questionnaire, a clinical examination, and blood sampling. The questionnaire asked about marital status, education level, chronic diseases, medications, smoking habits, physical activity and consumption of alcohol, coffee and fish.

In the clinical examinations, each participant's weight (without shoes and with light underwear) was measured in kilograms using a personal scale (SECA, Espoo, Finland), and height was measured in centimetres using a wall scale. Body mass index (BMI) was calculated based on the measured height and weight

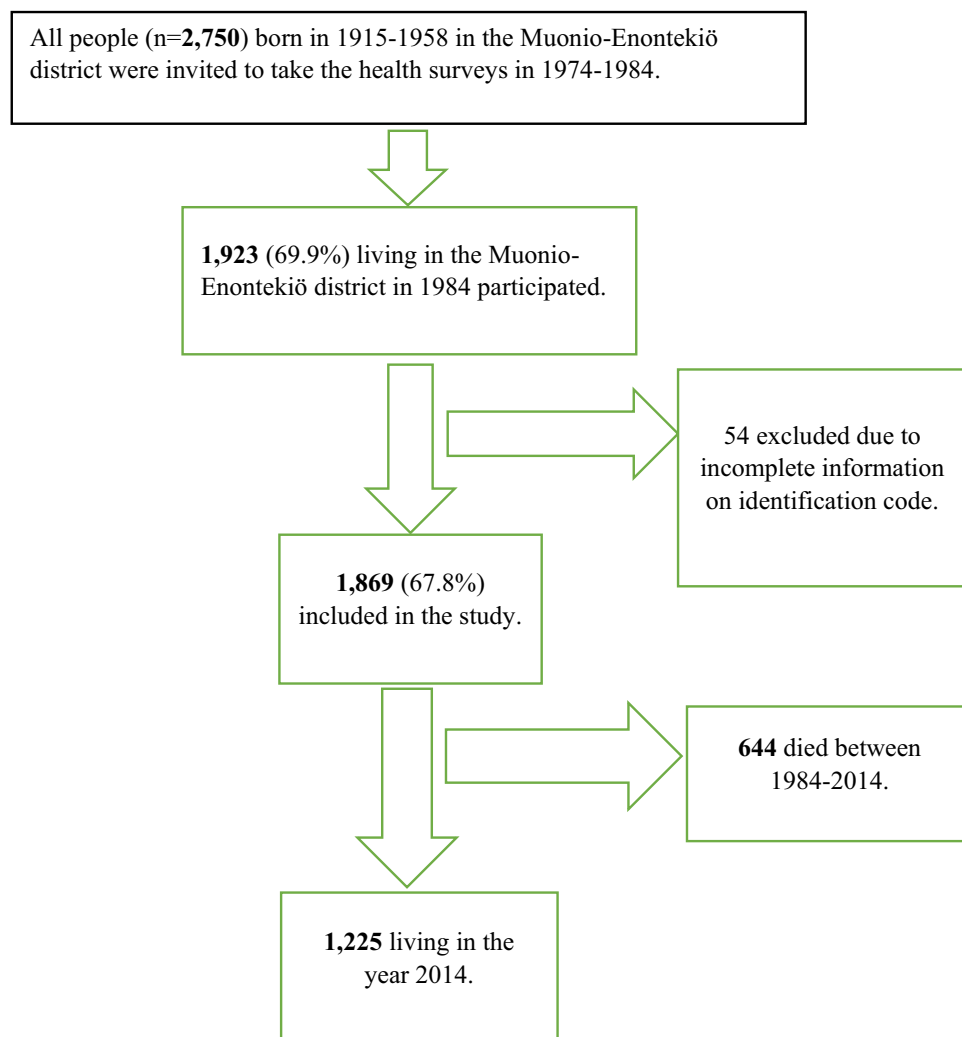


Figure 1. Flow chart of the Muonio–Enontekiö district study population.

(in kg/m²). Participants with a BMI of at least 30 kg/m² were classified by the WHO definition as obese [6]. Blood pressure was measured with a mercury manometer (Erka, Germany) and classified as normal (systolic blood pressure <140 mmHg and diastolic <90 mmHg) or high (systolic at least 140 mmHg and/or diastolic at least 90 mmHg) [6].

Blood samples for laboratory analyses were taken after an overnight fast. Serum total cholesterol was analysed in the laboratory of Muonio Health Centre by photometer and classified into quartiles. Haemoglobin was also analysed locally by photometry (following the health centre's regular procedures) and classified based on the current Finnish normal upper and lower limits for haemoglobin (men: 134–167 g/l and women: 117–155 g/l) [7].

Smoking status was categorised as either smoker (daily smoking) or non-smoker. Consumption of alcohol was assessed by responses to the question: "Do you drink alcohol more often than once a week?" Fish eating was evaluated by asking, "Do you eat plenty of fish weekly?" Coffee drinking was determined by answers to the question: "How many cups of coffee do you drink daily?" The extent and variety of leisure time physical activities was determined. Based on weekly frequency, type of physical activity and time used for the corresponding activity, the weekly energy used for leisure time physical activities was calculated and categorised according to published Finnish data [8]: physically inactive, <1000 kcal and active, at least 1000 kcal per week. Education was classified as primary school or less (≤ 7 years) or more than primary school (> 8 years). Marital status was categorised as married or single (including unmarried, divorced and widower).

Mortality data

The total mortality data of the study cohort were gathered from 1 January 1984 up to 31 December 2014 for those participants who were alive on 1 January 1984. Data were retrieved from the Central Population Register, which keeps a record of all Finnish citizens. The causes of death were obtained from the national Cause of Death Register, maintained by Statistics Finland [3].

Seasonal variation of causes of death was calculated comparing causes of death during winter (November–April) to summer (May–October). This was based on the long-term average monthly temperatures under 0°C from the period of 1981–2010 [4].

Statistical analyses

Variables are presented as means and standard deviations for continuous variables and as frequencies and

proportions for categorical variables. The statistical differences in group proportions of categorised variables were analysed by Chi-squared test and differences in group means of continuous variables by t-test. Mortality rates before specific age-related cut-off points are presented in cases in which the baseline age after that cut-off point is censored. Left- and right-truncated proportional hazard Cox models were used to study the association of baseline factors with mortality. The hazard ratios (HRs) are presented as one-by-one baseline-adjusted and as a saturated model in which the HRs were adjusted for all other exposures in the model. HRs and confidence intervals (CIs) are illustrated as forest plots. The HR can be interpreted as a follow-up time risk ratio of mortality of cases having a specific exposure compared to those that do not. The risk factor specific mortality was calculated using the Kaplan–Meier method, and the log-rank test was used to estimate the significance of differences between the groups. Statistical analyses were performed using SAS 9.4 statistical package (Cary, NC) considering $p < 0.05$ as significant.

Results

Baseline characteristics of the study population

Of the 1,869 subjects, 863 (46.2%) were men and 1,006 (53.8%) women (Table 1). The prevalence of cardiovascular disease diagnosis or medication was 17.7% (men: 18.7% and women: 16.7%), self-reported depression 8.6% (men: 7.9% and women: 9.3%), and high blood pressure 40.7% (men: 46.6% and women: 35.7%).

Among the study participants who had answered the question about smoking ($n=1,784$), 37.6% were smokers (49.2% of men and 27.0% of women). Study participants drank an average six cups of coffee daily.

Mortality

During the 31-year follow-up (from 1984 to 2014), 644 of the participants died. Of them 55.9% ($n=360$) were men and 44.1% (284) were women. The mean age at death for men and women was 70.2 (SD: 12.0) and 74.6 (SD: 11.4) years, respectively. The most common cause-of-death was cardiovascular diseases in 42.1% of all deaths (men: 44.4%, women: 40.1%), followed by neoplastic diseases 22.4% (men: 22.2%, women: 20.8%), dementias 7.0% (men: 6.4%, women: 8.5%), injuries and accidents 5.3% (men: 5.8%, women: 4.2%) and respiratory diseases 4.5% (men: 2.8%, women: 5.6%).

Those participants who died had significantly higher mean total cholesterol at baseline than those who

Table 1. Baseline anthropometric, laboratory measurements and self-reported sociodemographic and lifestyle characteristics in the Muonio–Enontekiö study population.

	All		Men		Women	
	N	Mean (SD) or %	N	Mean (SD) or %	N	Mean(SD) or%
Baseline age, years	1869	40.8 (11.0)	863	42.2 (10.4)	1006	39.5 (11.3)
Weight, kg	1858	70.5 (12.8)	863	76.5 (11.0)	995	65.2 (11.8)
Height, m	1854	166.0 (8.7)	857	172.5 (6.5)	997	160.5 (6.0)
BMI, kg/m ²	1840	25.5 (4.0)	855	25.7 (3.3)	985	25.3 (4.5)
≥30 kg/m ²	233/1840	12.7	85/855	9.9	148/985	15
Serum cholesterol	1678	6.9 (1.5)	779	7.1 (1.5)	899	6.8 (1.4)
Lowest quartile: 1.1–5.9 mmol/l	417	24.9	162	20.8	255	28.4
Two middle quartiles together: 6.0–7.7 mmol/l	835	49.8	397	51	438	48.7
Highest quartile: 7.8–13.8 mmol/l	426	25.4	220	28.2	206	22.9
Hemoglobine, g/l	1841	145.2 (14.2)	848	153.3 (12.5)	993	138.3 (11.7)
Low: men <134/women <117	90	4.9	52	6.1	38	3.8
Normal: men 134–167/women 117–155	1578	85.7	684	80.7	894	90
High: men > 167/women >155	173	9.4	112	13.2	61	6.1
Marital status						
Unmarried	126/894	14.1	60/315	19.0	66/579	11.4
Education						
Primary school or less	1659/1882	88.2	781/865	90.3	878/1017	86.3
Smoking						
Current smoker	670/1784	37.6	418/850	49.2	252/934	27
Alcohol use						
More than once a week	39/1122	3.5	36/576	6.3	3/546	0.5
Fish eating: plenty of weekly						
No	418/1069	39.1	204/563	36.2	214/506	42.3
Yes	651/1069	60.9	359/563	63.8	292/506	57.7
Coffee drinking cups a day	1511	6.1 (7.8)	662	6.3(5.5)	849	5.9(9.6)
Leisure time physical activity ≥1000 kcal weekly						
Yes	735/1464	50.2	332/666	49.8	403/798	50.5
No	729/1464	49.8	334/666	50.2	395/798	49.5
Diastolic blood pressure, mmHg	1859	82.8 (12.0)	861	84.2 (11.6)	998	81.6 (12.2)
Systolic blood pressure, mmHg	1860	130.9 (19.0)	861	133.7 (18.0)	999	128.6 (19.6)
Blood pressure ≥140/90 mmHg						
Yes	757/1859	40.7	401/861	46.6	356/998	35.7
Cardiovascular disease or medication						
Yes	317/1794	17.7	161/859	18.7	156/935	16.7
Depression (self-reported)						
Yes	108/1254	8.6	47/595	7.9	61/659	9.3

Baseline age = age in health survey; SD, standard deviation; BMI, body mass index.

stayed alive during the follow-up (in men 7.2 (SD 1.5) mmol/l vs. 7.0 (1.4) mmol/l, $p=0.049$; in women 7.3 (1.6) mmol/l vs. 6.6 (1.4) mmol/l, $p<0.001$).

At baseline, weekly consumption of fish was significantly less common among those who died during follow-up (in men 36.8% vs. 63.2%, $p=0.034$, in women 23.4% vs. 76.6%, $p=0.010$).

Mortality among all participants before 60, 70, 80 and 90 years of age according to baseline factors is presented in Table 2. The mortality of men was higher in every ten-year age range window, i.e. before 60, 70, 80, and 90 years of age compared to the mortality of women. The mortality rates in smokers before the ages of 60, 70, 80, and 90 years were significantly greater than those in non-smokers. Obesity decreased survival before the ages of 60, 70 and 80 years. High blood pressure significantly shortened survival before 60 years of age.

Those participants not living in a relationship had increased risk for mortality at the age period before 70 years. Cardiovascular disease diagnosis or

medication increased mortality among the participants before 60 and 70 years of age, and self-reported depression increased mortality before 70 and 80 years of age. Use of alcohol more than once a week shortened survival in the participants before 70 and 80 years of age. The mortality of participants with high haemoglobin was significantly increased before 80 years of age. Coffee drinking had no significant effect upon survival.

Survival curves

Kaplan–Meier curves (Figure 2) indicate significant shortening of survival with the following risk factors: smoking, high blood pressure, male gender, obesity, cardiovascular disease or medication, and high haemoglobin.

Table 3a and Figure 3a show the left- and right-censored Cox regression model HRs for each variable adjusted one-by-one for baseline age. The following risk

Table 2. Mortality at 60, 70, 80, and 90 years of age.

Exposure	Mortality before 60 years			Mortality before 70 years			Mortality before 80 years			Mortality before 90 years			
	No. at risk	No. of deaths	% of deaths	No. at risk	No. of deaths	% of deaths	No. at risk	No. of deaths	% of deaths	No. at risk	No. of deaths	% of deaths	p
Sex													
Men	713	79	11.1	630	181	28.7	487	292	60.0	394	374	94.9	<0.000
Women	807	31	3.8	636	93	14.6	430	185	43.0	318	269	84.6	
Marital status													
Not married	101	9	8.9	87	26	29.9	66	38	57.6	58	51	87.9	1.000
Married	643	33	5.1	564	96	17.0	382	173	45.3	285	249	87.4	
Education													
Primary school or less	1316	93	7.1	1121	248	22.1	843	441	52.3	661	598	90.5	0.621
More than primary school	204	17	8.3	145	26	17.9	74	36	48.6	51	45	88.2	
Cardiovascular disease or medicine													
Yes	224	25	11.2	263	76	28.9	246	134	54.5	211	192	91.0	1.000
No	1238	85	6.9	957	195	20.4	636	333	52.4	483	438	90.7	
Depression													
Yes	84	8	9.5	83	25	30.1	67	43	64.2	57	55	96.5	0.201
No	940	64	6.8	732	145	19.8	498	249	50.0	369	335	90.8	
Smoking													
Smoker	554	68	12.3	430	141	32.8	336	228	67.9	289	275	95.2	0.000
Non-smoker	904	41	4.5	778	126	16.2	532	234	44.0	396	347	87.6	
Use of alcohol													
More than once a week	31	5	16.1	30	12	40.0	21	17	81.0	19	19	100.0	0.240
Less than weekly	910	63	6.9	833	165	19.8	602	291	48.3	457	409	89.5	
Fish eating weekly													
No	373	23	6.2	301	67	22.3	187	104	55.6	146	126	86.3	0.095
Yes	525	44	8.4	521	102	19.6	408	195	47.8	309	283	91.6	
Leisure time physical activity^a													
Inactive	579	42	7.3	497	117	23.5	375	198	52.8	294	274	93.2	0.086
Active	613	38	6.2	473	79	16.7	310	150	48.4	228	202	88.6	
BMI, kg/m²													
≥30	176	26	14.8	187	63	33.7	165	103	62.4	145	133	91.7	0.636
<30	1314	81	6.2	1050	206	19.6	731	365	49.9	550	496	90.2	
Blood pressure, mmHg													
≥140/90 or more	577	50	8.7	586	138	23.5	486	252	51.9	405	365	90.1	0.897
<140/90	921	55	6.0	663	131	19.8	421	219	52.0	298	270	90.6	
Cholesterol													
Lowest quartile: 1.1–5.9 mmol/l	352	28	8.0	232	53	22.8	140	80	57.1	106	101	95.3	0.036
Mid quartiles: 6.0–7.7 mmol/l	694	40	5.8	597	120	20.1	426	207	48.6	331	291	87.9	0.155
Highest quartile: 7.8–13.8 mmol/l	343	24	7.0	339	77	22.7	278	142	51.1	213	191	89.7	1.000
Haemoglobin, g/l													
Low: men <134, women <117	50	6	12.0	47	9	19.1	38	18	47.4	27	26	96.3	0.504
Mid: men 134–167, women 117–155	1338	91	6.8	1115	239	21.4	797	406	50.9	616	551	89.4	0.061
High: men > 167, women >155	132	13	9.8	104	26	25.0	82	53	64.6	69	66	95.7	0.134

Bold indicates that the observed proportion is significantly greater than the expected proportion. BMI, body mass index.

Statistical significance and bounded text means that parameter is statistically significant

^aActive ≥1000 kcal weekly.

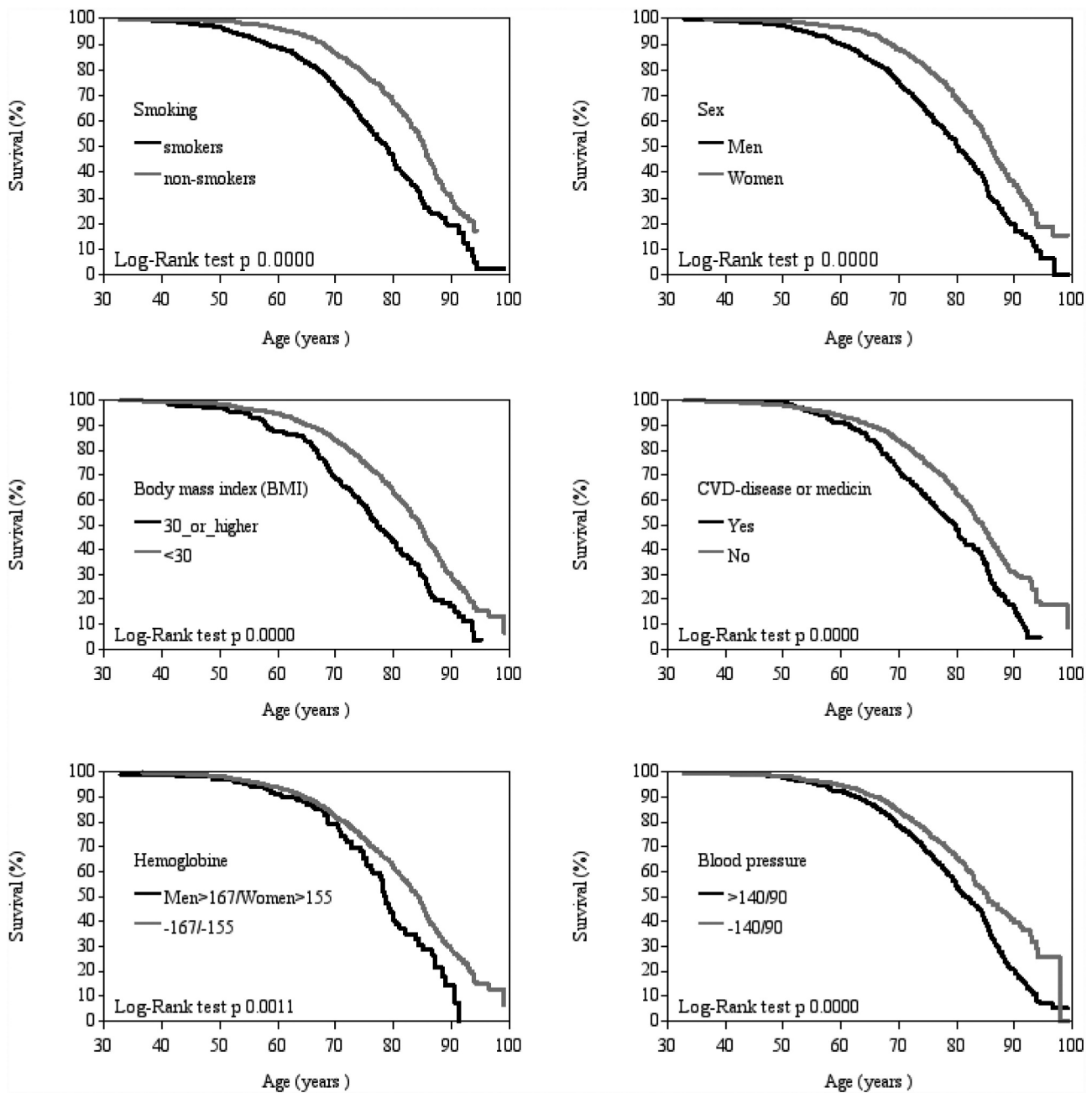


Figure 2. Kaplan–Meier survival curves according to smoking, sex, body mass index (BMI), cardiovascular disease (CVD) or medication, haemoglobin (HB) and blood pressure (RR).

factors were found to significantly negatively impact on mortality risk: male sex, high blood pressure, smoking, obesity, cardiovascular disease or medication, depression, at least weekly use of alcohol for all participants, low education for all participants, leisure time physical inactivity for all participants and women, for all participants and men not living in a relationship.

HRs adjusted for baseline age and other variables based on the left- and right-censored Cox regression model are shown in [Table 3b](#) and [Figure 3b](#). Due to the small data subsets concerning marital status, fish

consumption and depression, statistical analyses were not feasible in this model for these variables. Significant adjusted HRs were found for male sex, smoking, obesity, cardiovascular disease or medication and high blood pressure for all participants and for women and in addition for low education.

Seasonal proportions of death and total mortality

We found no significant seasonal difference of total mortality rate between winter and summer months. A total of

Table 3a. Left- and right-censored COX-model with each variable adjusted for baseline age one by one.

	All			Men			Women		
	N	HR (95% CI)	p	N	HR (95% CI)	p	N	HR (95% CI)	p
Male	1678	1.80 (1.54–2.10)	<0.001						
Marital-status unmarried, widow or divorced	848	1.44 (1.08–1.92)	0.014	318	2.06 (1.38–3.06)	0.001	530	1.04 (0.67–1.60)	0.867
Education, primary or less	1678	1.54 (1.13–2.09)	0.006	769	1.37 (0.89–2.10)	0.155	909	1.53 (0.99–2.38)	0.057
Smoker	1592	1.85 (1.58–2.17)	<0.001	757	1.54 (1.25–1.89)	<0.001	835	1.95 (1.48–2.58)	<0.001
Alcohol daily or weekly	1391	1.60 (1.16–2.19)	0.004	708	1.28 (0.91–1.79)	0.154	683	1.16 (0.37–3.63)	0.803
Plenty-of-fish_weekly, no	952	1.18 (0.96–1.46)	0.121	501	1.02 (0.77–1.35)	0.881	451	1.31 (0.94–1.83)	0.117
Weekly-active-exercise-calories <1000 kcal	1305	1.31 (1.10–1.58)	0.003	587	1.21 (0.95–1.54)	0.123	718	1.51 (1.14–1.99)	0.004
Body-mass-index, ≥30 kg/m ²	1642	1.75 (1.45–2.12)	<0.001	761	2.35 (1.77–3.11)	<0.001	881	1.81 (1.38–2.37)	<0.001
Cholesterol-quartile 7.8–13.8 mmol/l ^a	1502	1.08 (0.84–1.37)	0.564	699	1.09 (0.79–1.50)	0.600	803	0.99 (0.68–1.45)	0.974
Cholesterol-quartile 6.8–7.7 mmol/l ^a	1502	1.01 (0.79–1.29)	0.937	699	0.92 (0.67–1.28)	0.619	803	1.02 (0.70–1.49)	0.928
Cholesterol-quartile 6.0–6.7 mmol/l ^a	1502	0.96 (0.74–1.24)	0.744	699	0.84 (0.59–1.18)	0.306	803	1.03 (0.69–1.53)	0.901
Haemoglobin >167/>155	1642	1.40 (1.09–1.80)	0.009	754	1.22 (0.90–1.66)	0.193	888	1.35 (0.85–2.14)	0.198
Blood-pressure 140/90 or higher	1658	1.46 (1.24–1.72)	<0.001	766	1.41 (1.14–1.74)	0.002	892	1.46 (1.13–1.89)	0.004
CVD-disease_or_medicine, yes	1600	1.62 (1.36–1.93)	<0.001	765	1.64 (1.30–2.06)	<0.001	835	1.70 (1.30–2.22)	<0.001
Depression, yes	1118	1.61 (1.21–2.14)	0.001	525	1.59 (1.06–2.40)	0.026	593	1.83 (1.22–2.74)	0.003

^aLowest quartile (1.1–5.9 mmol/l) is the reference group.

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CVD, cardiovascular; baseline age, age in health survey.

333 participants died during winter and 311 during summer. We noted 44 cerebrovascular deaths during winter (November–April) and 19 in summer (May–October) ($p=0.003$); correspondingly, deaths from respiratory diseases were 15 and 5 ($p=0.037$). Deaths from alcohol diseases and accidental injuries were more common during summer ($n=10$) than winter ($n=3$, $p=0.034$).

Discussion

The most common causes of death in the subarctic Muonio–Enontekiö District were the same as among the main Finnish population, namely cardiovascular and neoplastic diseases. Data from the whole of Finland in 2009 found that 40% of all deaths were from cardiovascular diseases, 23% from neoplastic diseases, 10% from dementia and 6% from injuries [3]. Factors predicting all-cause mortality in our study population were male sex, smoking, obesity, high blood pressure, cardiovascular disease and/or medication, depression, not living in a relationship, low education, alcohol use, physical non-activity and high haemoglobin level.

Cardiovascular diseases have been the main cause of mortality in Finland for decades. In 2014, when follow-up of the present study ended, Finland had a population of 5,471,753 inhabitants, and the cardiovascular mortality was 19,555 people with a mortality 3–4 times higher in men than in women [3]. In our study, difference of cardiovascular causes of death was not significant between men and women.

In our study, individuals with high blood pressure had increased risk for all-cause mortality compared to normotensive individuals. This finding is in line with many previous studies, e.g. the study by Strandberg et al. [9].

In the present study, baseline current smoking increased the HR for mortality up to 1.85-fold. The age-adjusted mortality of smokers has also been shown to be twofold compared to non-smokers [10]. In addition, smoking nearly doubled the risk of dying in middle age (35–69 years) from 24% to 42% [10]. Our results are in line with previous studies from the same period.

We also showed that obesity, when adjusted for other risk factors including smoking, increased the risk of mortality, a finding in line with the study by Stokes and Preston [11], who found that, among never-smokers, mortality risks were significantly higher in the overweight/obesity group.

Surprisingly, participants in the highest cholesterol quartile (≥ 7.8 mmol/l) did not have a significant independently increased risk of all-cause mortality. On the other hand, in a Japanese study, hypercholesterolaemia was positively associated with all-cause mortality. Moreover, a positive association was reported between total cholesterol and risk of all-cause mortality in the highest (>6.71 mmol/l) total cholesterol groups [12]. The highest total cholesterol quartile in our study (≥ 7.8 mmol/l) was higher than that of the Japanese study. The total cholesterol levels were exceptionally high in our study, both in men and women. Based on our clinical knowledge, we can say that inhabitants of the Muonio–Enontekiö district used to eat plenty of fatty meat- and milk-products in the 1970s and 1980s, which may be at least part of the reason for their high total cholesterol.

In this present study, high haemoglobin shortened survival, with the baseline age-adjusted HR increasing 1.40-fold. We speculate that this increased mortality risk is mediated, at least in part, by metabolic syndrome. Previous studies have shown that mean haemoglobin is significantly higher in patients with metabolic syndrome

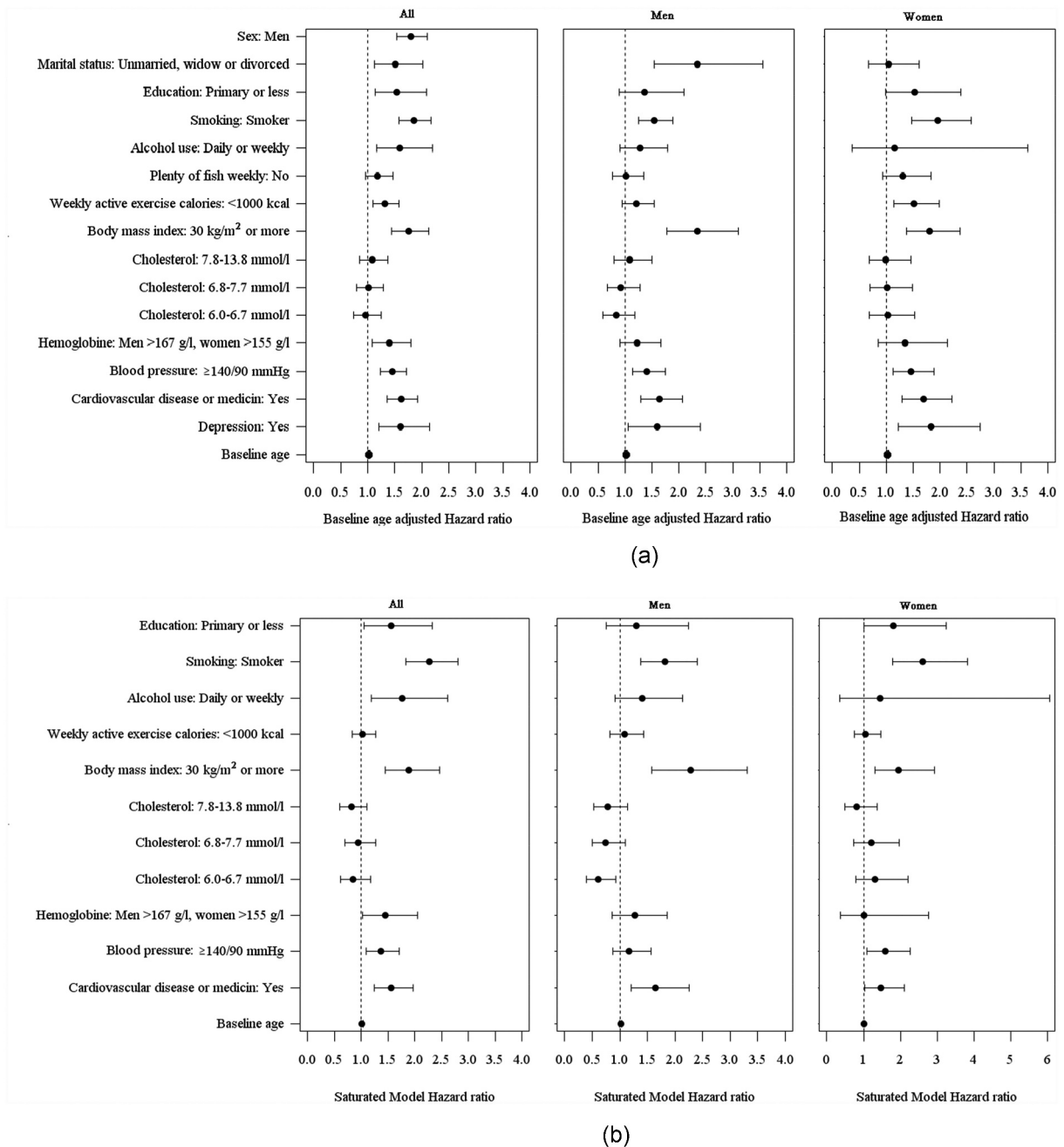


Figure 3. (a) Baseline age-adjusted hazard ratios (HRs) and their 95% confidence intervals (CIs) for mortality. Baseline age = Age in health service. (b) Mortality HRs and their 95% CIs adjusted for baseline age and other variables. Variables marital status, fish-eating and depression not included due to the small number of the available observations. Baseline age = Age in the health survey.

[13]. In addition, both cardiovascular and all-cause mortality is increased in patients with metabolic syndrome [14].

Men had almost twofold higher mortality than women, which is in line with the previous meta-analyses [15,16]. Also in line with previous studies [17], we found that low education reduced survival. Most participants had only primary school level of education. In the Muonio–Enontekiö district, there were no higher educational levels available before the year 1970.

Our finding that leisure time physical inactivity (<1000 kcal weekly energy expenditure) decreased survival is in line with the systematic review and meta-analysis from 2008 showing that physical activity reduced all-cause mortality by 33% [18]. In previous decades, people in northernmost Finland did not have a habit of exercising during their leisure time. Many of the inhabitants in 1984 were living in a rural economy (agriculture, forestry, herding reindeers, hunting, fishing

Table 3b. Cox model adjusted for baseline age and other variables in model.

	All			Men			Women		
	N	HR (95% CI)	p	N	HR (95% CI)	p	N	HR (95% CI)	p
Male	1004	1.57 (1.25–1.98)	<0.001						
Education primary or less	1004	1.52 (1.02–2.26)	0.038	486	1.30 (0.75–2.24)	0.353	518	1.81 (1.01–3.24)	0.045
Smoker	1004	2.00 (1.60–2.50)	<0.001	486	1.82 (1.38–2.40)	<0.001	518	2.61 (1.78–3.82)	<0.001
Alcohol daily or weekly	1004	1.49 (1.00–2.23)	0.051	486	1.40 (0.92–2.14)	0.117	518	1.44 (0.34–6.07)	0.619
Weekly-active-exercise-calories <1000 kcal	1004	1.08 (0.87–1.33)	0.488	486	1.08 (0.82–1.43)	0.566	518	1.05 (0.75–1.48)	0.784
Body-mass-index, ≥ 30 kg/m ²	1004	2.00 (1.53–2.62)	<0.001	486	2.29 (1.58–3.31)	<0.001	518	1.95 (1.30–2.92)	0.001
Cholesterol-quartile 7.8–13.8 mmol/l	1004	0.81 (0.60–1.10)	0.183	486	0.77 (0.53–1.14)	0.193	518	0.82 (0.49–1.36)	0.442
Cholesterol-quartile 6.8–7.7 mmol/l	1004	0.91 (0.67–1.23)	0.523	486	0.74 (0.50–1.10)	0.133	518	1.20 (0.73–1.97)	0.468
Cholesterol-quartile 6.0–6.7 mmol/l	1004	0.80 (0.58–1.11)	0.183	486	0.61 (0.40–0.93)	0.022	518	1.32 (0.79–2.21)	0.295
Haemoglobin >167/>155 g/l	1004	1.28 (0.90–1.82)	0.174	486	1.27 (0.86–1.86)	0.226	518	1.01 (0.37–2.76)	0.987
Blood_pressure $\geq 140/90$ mmHg	1004	1.31 (1.05–1.64)	0.018	486	1.17 (0.88–1.57)	0.287	518	1.58 (1.10–2.27)	0.014
CVD_disease_or_medicine, yes	1004	1.61 (1.27–2.03)	<0.001	486	1.65 (1.21–2.26)	0.002	518	1.48 (1.03–2.12)	0.033
Baseline age	1004	1.01 (1.00–1.03)	0.105	486	1.02 (1.00–1.04)	0.107	518	1.01 (0.98–1.03)	0.529

Variables marital status, plenty of fish weekly and depression not included due to the small number of the available observations. HR, hazard ratio; CI, confidence interval; CVD, cardiovascular disease.

and gathering berries), whereas tourism has gradually increased during the 31-years follow-up.

No seasonal variation in mortality rate was found in our survey. We suppose that rather low temperatures also in summer are the cause of no seasonal difference in mortality. In the Muonio–Enontekiö district mean summer (May–October) temperature from the period of 1981–2010 was +6.1°C and winter (November–April) –9.8°C [4]. Causes of death from cerebrovascular and pulmonary diseases were more common in winter than in summer. Ikäheimo et al. [19] demonstrated that low temperatures increase deaths from cardiovascular and respiratory diseases, causing excess annual deaths in Finland. A previous study also showed that risk of sudden cardiac death was associated with cold temperatures [20]. Usually, cardiovascular deaths increase during the cold season of the year [21] and the same phenomenon could also be seen in our study population. The effect of cold on cardiovascular diseases have been addressed mostly in terms of short-term temporal effects, i.e. days or weeks [21]. We have little knowledge of the association of long-term exposition and survival [21].

In the middle of the follow-up time of our study, in 2000, the mean lifetime of Finnish men and women was 69.6 and 78.8 years, respectively [3]. Life expectancy in the Arctic region overall was 74.7 years in 2012–2016 with intraregional variation: In Quebec (82.2 years) (Canada), Faroe Islands (82.1 years), as well as in Troms and Nordland (Norway), Norbotten (Sweden) and Lapland (Finland), the life expectancy was the longest. The shortest life expectancy was in Chukotka (62.8 years) (Russia) [22]. Life expectancy (2016–2018) in Lapland was 80.45 years and in the whole of Finland 81.46 years [3].

The strengths of the study

The main strengths of the present study are the long follow-up (31 years) and good participation rate. Our

study cohort included 69.9% of the people born between 1915 and 1958 and living in the Muonio–Enontekiö district, and they had long-term exposure to cold. In 1984, there were 5,300 inhabitants (0.5 inhabitants/km²) living in the area [3,23].

Study limitations

The main limitation of the present study is that nearly every diagnosis concerning cause of death was based on clinical examinations at Muonio–Enontekiö Health Centre. According to contemporary clinical practice, only a few autopsies were conducted at Lapland Central Hospital or University Hospital of Oulu. Regarding cholesterol panel investigations, it is worth saying that, in 1984, it was possible to analyse only serum total cholesterol levels. Finally, we had to exclude 54 subjects because we could not identify them, and the total variable information was not available from all participants.

Conclusion

One in 10 of the target population of this study were ethnically and culturally different from the main Finnish population. They lived in the subarctic area with many unique features. Despite those differences, their most common causes of death, and the main risk factors predicting death were the same as those of the main Finnish population. Cardiovascular diseases were the leading cause of death also in the Muonio–Enontekiö district. Not only diseases but also lifestyle factors related to mortality, including social status, were similar as those of the main Finnish population. The most common causes of death did not differ between men and women, but men were more likely than women to die from cardiovascular causes, injuries and accidents. Dementia and respiratory diseases were more often

diagnosed among women than men. Cerebrovascular and pulmonary deaths were more common during winter than summer. Our study confirms the seasonal variation, possibly a cold effect in cerebrovascular and pulmonary reasons of death. Our results did not differ from the national data on causes of death, in spite of the uniqueness of our study population. That finding can encourage those in subarctic regions to apply the results of clinical and epidemiological studies carried out elsewhere, and practice evidence-based medicine.

Acknowledgments

We would like to thank the field study team and study nurses who performed all of the clinical examinations and helped in the data collection.

Ethical approval

The Ethics Committee of the Northern Ostrobothnia Hospital District approved the research protocol on 21 January 2013.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by Center for Life Course Health Research, University of Oulu [1]; Cultural Foundation of Finland [4]; Health Centre of Muonio–Enontekiö [3]; and Northern Finland Health Care Foundation [2].

References

- [1] The top 10 causes of death. *World Health Organization* 24 May 2018.
- [2] Global, regional and national age-sex-specific mortality for 282 causes of death in 195 countries and territories 1980–2017: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017 Sept 16; DOI: [10.1016/S0140-6736\(17\)32152-9](https://doi.org/10.1016/S0140-6736(17)32152-9).
- [3] Statistics Finland (SVT): Mortal diagnosis: years 2000–2019. *Helsinki: statistics Centre of Finland*. Web:<http://www.stat.fi/til/ksyyt/ksyyt/index.html>. Finnish Meteorological Institute. *Annual Statistics 1981–2010*.
- [4] Finnish Meteorological Institute. *Annual Statistics 1981–2014*.
- [5] World Health Organization. *Follow-up Report 2008–2014*.
- [6] Finnish Current Care Guidelines 2020.
- [7] Nousiainen T. Anemiapotilaan tutkiminen. Kirjassa. In: Porkka K, Lassila R, Remes K, et al., editors. Veritaudit. Kustannus Oy Duodecim. 2015. p. 162–168.
- [8] Fogelholm M, Vuori I, Taimela S, et al. Assessment of physical activity and exercise. *Medicine of Physical Activity*. 3 ed. ed. Helsinki: Duodecim; 2005. p. 77–91.
- [9] Strandberg TE, Salomaa VV, Vanhanen HT, et al. Blood pressure and mortality during an up to 32-year follow-up. *J Hypertens*. 2001;19(1):35–39.
- [10] Carter BD, Abnet CC, Feskanich D, et al. Smoking and Mortality – beyond Established Causes. *N Engl J Med*. 2015 Feb 12;372(7):631–640.
- [11] Stokes A, Preston S Smoking and reverse causation create an obesity paradox on cardiovascular disease. *Obesity (Silver Spring)*. 2015 Dec; 231:2485–2490. *Published online* 2015 Sep 30. .
- [12] Okamura T, Tanaka H, Miyamatsu N, et al. for the NIPPON DA80 research group. The relationship between serum total cholesterol and all-cause or cause-specific mortality in a 17.3-year study of Japanese cohort. *Atherosclerosis*. 2007 Jan;190(1):216–223. *Issue*.
- [13] Hämäläinen P, Saltevo J, Kautiainen H, et al. Erythropoietin, ferritin, haptoglobin, haemoglobin and transferrin receptor in metabolic syndrome: a case control study. *Cardiovasc Diabetol*. 2012 Sep 27;11(1):116.
- [14] Lakka H-M, Laaksonen DE, Lakka T, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002;288((21)):2709–2716.
- [15] Crimmins EM, Shim H, Zhang YS and Kim JK. Differences between Men and Women in Mortality and the Health Dimensions of the Morbidity Process. *Clin Chem*. 2019 Jan;65(1):135–145.
- [16] Manzoli L, Villari PM, Pirone G, et al. Marital status and mortality in the elderly: a systematic review and meta-analysis. *Soc Sci Med*. 1982 [2006 Sep 29];64((1)):77–94.
- [17] Byhoff E, Hamati MC, Power R, et al. Increasing educational attainment and mortality reduction: a systematic review and taxonomy. *BMC Public Health*. 2017;17(719). [10.1186/s12889-017-4754-1](https://doi.org/10.1186/s12889-017-4754-1)
- [18] Nocon M, Hiemann T, Myller-Riemenschneider F, et al. Association of physical activity with all-cause and cardiovascular mortality: a systemic review and meta-analysis. *European Journal of Preventive Cardiology* 1 June 2008 2047-4873. *Online* 2047-4881. 15 3 239–246
- [19] Ikäheimo TM, Jaakkola JJ. The effects of environmental temperature on health preparedness. 2019;135((22)):2159–2166. *Finnish Duodecim*.
- [20] Ryti NR, Mäkikyrö EM, Antikainen H, et al. Risk of sudden cardiac death in relation to season-specific cold spells: a case-crossover study in Finland. *BMJ*. 2017. DOI:[10.1136/bmjopen-2017-017398](https://doi.org/10.1136/bmjopen-2017-017398)
- [21] Näyhä S. Cold and the risk of cardiovascular diseases: a review. *Int J Circumpolar Health*. 2002;61(4):373–380.
- [22] Life expectancy in the Arctic: Nordregio at www.nordregio.org, 19 March 2019.
- [23] Report of the Regional Council of Lapland: the development of the municipal population in Lapland 1970–2008. http://www.lappi.fi/lapinliitto/c/document_library/get_file?folderId=52584&name=DLFE-3123.pdf