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Cancer incidence in participants in a long-distance ski race (Vasaloppet, Sweden) compared to the background population

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Abstract ***Background:*** We studied the association between taking part in a long distance ski race and cancer incidence to address the hypothesis that a lifestyle involving a high degree of physical activity (PA) lowers cancer incidence with a pattern that is different by cancer site.
Methods: Cancer incidence was estimated in a large cohort of skiers ($n = 185{,}412$) participating in the Vasaloppet long distance ski race in Sweden 1989–2010 and non-participants in the ski race, randomly selected from the Swedish general population ($n = 184{,}617$). Data include race finishing times as a measurement of physical fitness.
Hazard ratios (HRs) and net probability of cancer over twenty years of follow-up were estimated for all invasive cancer, and separately for prostate, breast, colo-rectal and lung cancer, and groups of cancers with presumed relation to lifestyle.
Findings: Participating in Vasaloppet was associated with a relative risk reduction for all invasive cancer of 6% (95% confidence interval 2–9%) and a relative risk reduction of 32% (95% confidence interval 28–37%) of cancer sites where there is epidemiological evidence that smoking, bodyweight, regular PA and consumption of fruit and vegetables are aetiological factors. For skin cancer the risk was increased, as for prostate cancer. Skiers with shorter finishing times had lower incidence of cancer.

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Interpretation: This study indicates that it is unrealistic to reduce overall population cancer incidence drastically with life style. However, cancers that are epidemiologically associated with life style factors were significantly reduced by what presumably is a blend of non-smoking, normal body weight, sound dietary habits and PA. Our data thus provide additional support for present days' recommendations about life style prevention. Higher health awareness is associated with attendance to screening, which may explain our results for prostate cancer.
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1. Introduction

A worldwide study estimated that 35% of all invasive cancers are attributable to nine modifiable life style factors [1]. World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) issued in 2007 eight recommendations on diet, physical activity and weight management for cancer prevention [2,3]. European Code Against Cancer refers to life style factors for cancer prevention, promoted by European Partnership in Action Against Cancer [4].

The association between self-reported physical activity (PA) and cancer has been reviewed [5–7]. There is consistent evidence for a beneficial effect of PA on risk for colon cancer and a probable evidence for an effect on endometrial and breast cancers, and to a lesser extent for lung, ovary and prostate cancer and no convincing evidence for remaining sites.

We studied the association between taking part in a long distance ski race and cancer incidence and an equal number of non-participants, randomly selected from the general population. We aimed to address the hypothesis that a life style involving a high degree of physical activity lowers cancer incidence, and if so, with a pattern that is different by cancer site.

2. Methods

2.1. Participants and registers

Vasaloppet, the largest cross-country ski event in the world started in 1922. From 1989 the *Vasaloppet race register* records the Swedish national registration number (NRN) and gender for Swedish skiers together with year, race distance and finishing time. Fifty-five percent skied the classic 90 km race, the other shorter distances of 30 or 45 km. The race recruits both elite skiers and leisure skiers from 1989 to 2010. The Vasaloppet skiers entered the study and were considered exposed, independent of the race distance, when they participated in their first race at 20 years of age or older. Due to different race conditions and race distances finishing time is represented by per cent of the winners (male respective women) time in each race.

Non-participants of Vasaloppet ski-race were randomly selected from the general population register by *Statistics Sweden* as a frequency matched group of the same age (five year-intervals), gender and county of residence the same years as the Vasaloppet skiers were included. The randomly selected non-participants contribute person-years to an unexposed cohort, but are censored at the date of race-participation should they later participate in the Vasaloppet.

Using the unique Swedish NRN, the Vasaloppet skiers and the non-participants were linked to information about all hospital admissions in the National Patient Register (NPR), about incident cancers in the National Cancer Register (NCR) and about death and causes of death in the Causes of Death Register (CDR), all held at the *National Board of Health and Welfare*. The cohorts were also linked by the NRN to *Statistics Sweden* adding information about educational level, occupational and civil status.

The individuals among the Vasaloppet skiers and the non-participants with any cancer diagnosis before first race or the selection date, 1st March for the non-participants were excluded. To account for the selection of healthier individuals to the Vasaloppet skiers, we also excluded from both cohorts those with hospitalisations because of severe chronic diseases (Supplement Table 1). To control for remaining co morbidity in the cohorts, Charlson co-morbidity index [8] was calculated based on hospital admission data in the NPR from 1964 and forward.

Ethics committee approval granted for the study (Uppsala Dnr 2010/305, 2012/067, Stockholm Dnr 2011/Ö30).

2.2. Grouping of cancer diagnoses

We used the WRCF/AIRC conclusions [6] and EPIC lists [9] when we analysed the association between participation in Vasaloppet and incidence of invasive cancer by site (Table 2).

2.3. Statistical analyses

Follow-up started one year after inclusion and ended on the date of diagnosis of the cancer of interest, death, emigration, or December 31st 2010, whichever came first.

The net probability of cancer was estimated with the Kaplan–Meier method by treating cancer diagnosis as the event of interest, while censoring for death from any cause. This approach resulted in estimates of the probability of cancer in a hypothetical world were being diagnosed with cancer is the only event that is allowed to occur. Differences in net probability were univariately tested using the log rank test, and hazard ratios with corresponding 95% confidence intervals were estimated with Cox proportional hazard models. Because skiers and non-participants of the ski-race were frequency-matched by age and sex, our crude base model approximated an 'age- and sex-adjusted' model. We additionally performed stratified analysis of categories of the year and age of inclusion, sex, educational level, employment status and Charlson co-morbidity index.

We verified the results from the analysis of net probability by comparing them to an analysis of the crude probability of cancer, which was estimated by treating cancer diagnosis and death from any cause as competing events. This approach resulted in estimates of the probability of cancer diagnosis in a real world setting where it is possible for the individuals to die before being diagnosed with cancer. The results from the two different analyses were very similar for all cancer groups.

All statistical analyses were performed with the R statistical software package [10].

3. Results

The Vasaloppet register includes 199,818 skiers who participated from 1989 to 2010. Non-participants selected from the population for the corresponding year include 199,818 individuals. Both groups without a cancer or significant disease before the selection date (Fig. 1). We aimed to observe all individuals for at least one year and thus Vasaloppet skiers and the non-participants for 2010 and all censored or with an invasive

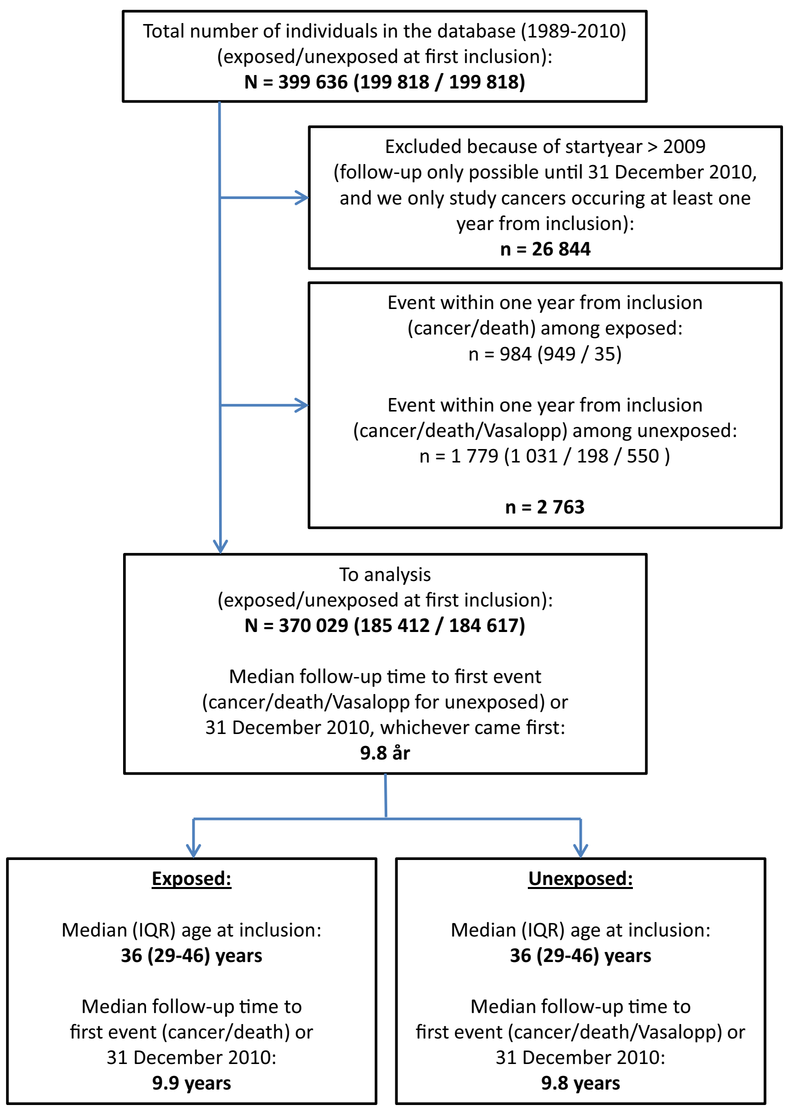

Fig. 1. Flowchart. IQR: Inter quartile range.

cancer within one year of follow up were excluded. As a result 185,412 Vasaloppet skiers and 184,617 non-participants remained eligible for the study (Fig. 1). Table 1 shows the baseline characteristics of the Vasaloppet skiers (exposed) and the non-participants (unexposed). Charlson co-morbidity index was similarly distributed between the groups. The skiers had more often a higher education and were more often gainfully employed than the non-participants; we checked all analyses with Cox models adjusted for educational level, employment status, sex and age with very similar results to the unadjusted results. We ran models excluding the first five years of follow-up with similar results to those excluding the first year (data not shown). Characteristics in different performance groups, see Supplement Table 2.

Table 2 shows the number of cancer cases after one year of follow up by exposure status and by cancer group. The total number of events was 12,822.

Table 3 shows incidence rates and Hazard ratios (HRs) in univariate Cox models comparing the Vasaloppet skiers and non-participants. The relative reduction associated with participation in the Vasaloppet was six percent (HR 0.94 (95% confidence interval (CI) 0.91–0.98)) for cancers of all sites, rising to 14% when prostate cancer was excluded. Prostate cancer was more common among Vasaloppet skiers, as was skin cancer and malignant melanomas. There was 18% relative reduction of cancers related to PA, diet and bodyweight and a marked reduction in cancers related to smoking, e.g. 70% relative reduction in the incidence of lung cancer. When cancers related to smoking and other lifestyle factors were combined, there was a 32% relative risk reduction (HR 0.68 (95% CI 0.63–0.72)) (Table 3).

3.1. Net probability of death and invasive cancer (Figs. 2–4)

We estimated net probability for death and for invasive cancer and show them graphically to illustrate the absolute risks and the pattern over time. The probability

Table 1
Baseline characteristics of study participants.

	Skiers $N = 185,412$	Non-participants $N = 184,617$	Total $N = 370,029$
Follow-up, yr			
Median (IQR)	9.9 (5.8–14.9)	9.8 (5.8–14.8)	9.8 (5.8–14.9)
Year of inclusion (%)			
1989–2000	95,218 (51.4)	94,770 (51.3)	189,988 (51.3)
2001–2005	52,006 (28.0)	51,780 (28.0)	103,786 (28.0)
2006–2009	38,188 (20.6)	38,067 (20.6)	76,255 (20.6)
Sex (%)			
Male	116,000 (62.6)	115,456 (62.5)	231,456 (62.6)
Female	69,412 (37.4)	69,161 (37.5)	138,573 (37.4)
Age at inclusion			
Median (IQR)	36 (29–46)	36 (29–46)	36 (29–46)
Age at inclusion (%)			
20–29	52,268 (28.2)	52,152 (28.2)	104,420 (28.2)
30–39	56,304 (30.4)	56,253 (30.5)	112,557 (30.4)
40–49	44,584 (24.0)	44,157 (23.9)	88,741 (24.0)
50+	32,256 (17.4)	32,055 (17.4)	64,311 (17.4)
Highest level of education (%)			
Primary school	14,213 (7.7)	33,845 (18.3)	48,058 (13.0)
Secondary school	72,811 (39.3)	93,287 (50.5)	166,098 (44.9)
University	98,039 (52.9)	54,802 (29.7)	152,841 (41.3)
Missing	349 (0.2)	2683 (1.5)	3032 (0.8)
Employment (%)			
Employed	154,316 (83.2)	133,039 (72.1)	287,355 (77.7)
Not employed	22,826 (12.3)	41,793 (22.6)	64,619 (17.5)
Retired	1971 (1.1)	2102 (1.1)	4073 (1.1)
Missing	6299 (3.4)	7683 (4.2)	13,982 (3.8)
Charlson comorbidity index (%)			
0	178,089 (96.1)	174,454 (94.5)	352,543 (95.3)
1	6908 (3.7)	8913 (4.8)	15,821 (4.3)
2+	415 (0.2)	1250 (0.7)	1665 (0.4)

Exposed: Vasaloppet skier. Unexposed: Non-participants, matched individuals from the Swedish population of same gender, age and county of residence as the skiers. Numbers represent frequencies with percent in brackets. IQR: Inter quartile range. Charlson co-morbidity index is extracted from Swedish National Patient Register (NPR) from 1964 to inclusion. Characteristics in different performance groups, see Supplement Table 2.

Table 2
Number of cancer cases by cancer site and cancer groups defined by epidemiological evidence for aetiology.

Cancer site and cancer groups	Skiers	Non-participants	Total
All invasive cancers	6342	6480	12,822
Prostate cancer	1827	1435	3262
Breast cancer, age ⩽50/age >50	349/508	341/506	690/1014
Colorectal cancer	520	594	1114
Lung cancer	125	403	528
Cancers related to tobacco smoking (lung-, ear-nose-throat-, larynx-, oesophagus-, urine bladder cancer)	411	897	1308
Cancer with relation to lifestyle with physical activity, normal weight, diet with fruits and vegetables (colon cancer, postmenopausal breast cancer (>50 years of age), kidney cancer, endometrial cancer, cancer I gallbladder, pancreas and oesophagus)	1138	1322	2460
Cancers where *expose to sunlight* (out-door activities) is important (skin cancer including, malignant melanoma, but not basal cell cancer)	840	584	1424

Exposed: Vasaloppet skier. Unexposed: Non-participants, matched individuals from the Swedish population of same gender, age and county of residence. The International classification of diseases (ICD), versions 7, 8, 9 and 10 were used to identify the cancers in the registers. Only tumours classified as invasive cancer in the National Cancer Register (NCR) were considered.

Table 3
Events of cancer per 1000 person years and hazard ratios (HR) for Vasaloppet skiers compared to non-participants derived from Cox proportional hazards models at a median of 9.8 years follow up.

Cancer site and cancer groups	No. of cancers per 1000 person-years		Univariate Cox model		
	Skiers	Non-participants	HR	(95% CI)	*p*
All invasive cancers	3.31	3.48	0.94	(0.91–0.98)	0.001
All invasive cancers (excluding prostate cancer)	2.35	2.73	0.86	(0.82–0.89)	<0.001
Prostate cancer	1.51	1.22	1.22	(1.13–1.30)	<0.001
Premenopausal breast cancer	0.82	0.80	1.02	(0.88–1.19)	0.774
Postmenopausal breast cancer	2.57	2.64	0.97	(0.86–1.11)	0.688
Colon cancer	0.16	0.20	0.81	(0.69–0.94)	0.007
Lung cancer	0.07	0.23	0.30	(0.24–0.36)	<0.001
Cancers related to tobacco smoking	0.22	0.50	0.44	(0.39–0.50)	<0.001
Cancer with relation to lifestyle with physical activity, normal weight, diet with fruits and vegetables	0.60	0.72	0.82	(0.76–0.89)	<0.001
Cancers related to tobacco smoking or cancer with relation to lifestyle with physical activity, normal weight, diet with fruits and vegetables	0.81	1.18	0.68	(0.63–0.72)	<0.001
Cancers where expose to sunlight is important (out-door activities)	0.43	0.31	1.38	(1.24–1.54)	<0.001

Exposed: Vasaloppet skier. Unexposed: Non-participants, matched individuals from the Swedish population of same gender, age and county of residence. 95% CI: 95% confidence interval.

of death from any cause even after 20 years was low but about twice as high among the non-participants during the follow-up (Fig. 2a); the net probability of any invasive cancer event was also low, but similar among Vasaloppet skiers and non-participants (Fig. 2b). Due to the difference in death rates, we also compared the results of net probability against those of crude probability (data not shown) and the results were virtually equal, which was true for all cancer groups.

Fig. 3 shows the net probabilities by major cancer sites. Net probability of prostate cancer was higher in Vasaloppet skiers (4.6% at 20 years) than in non-participants (3.8% at 20 years), slowly increasing over follow-up (Fig. 3a) while for breast cancer the net probabilities were very similar in both groups (Fig. 3b). The patterns were similar for both pre- and postmenopausal breast cancer (under 50 respective over 50 year of age) (data not shown). In lung cancer the difference in net probabilities increases markedly over time and stays low among skiers (0.2% at 20 years) compared with the population-based non-participants of the race (0.6% at 20 years) (Fig. 3c). For colorectal cancer, the net probabilities begin to differ at 5 years of follow-up, but the development in the Vasaloppet skiers and the non-participants stays largely parallel between ten and 20 years (Fig. 3d).

Fig. 4 shows the net probabilities by aetiology group. As expected, for cancers related to tobacco smoking the pattern is similar to that of lung cancer (Fig. 4a). For cancers related to diet, overweight and physical activity the net probability begins to differ early between Vasaloppet skiers and non-participants, but increases

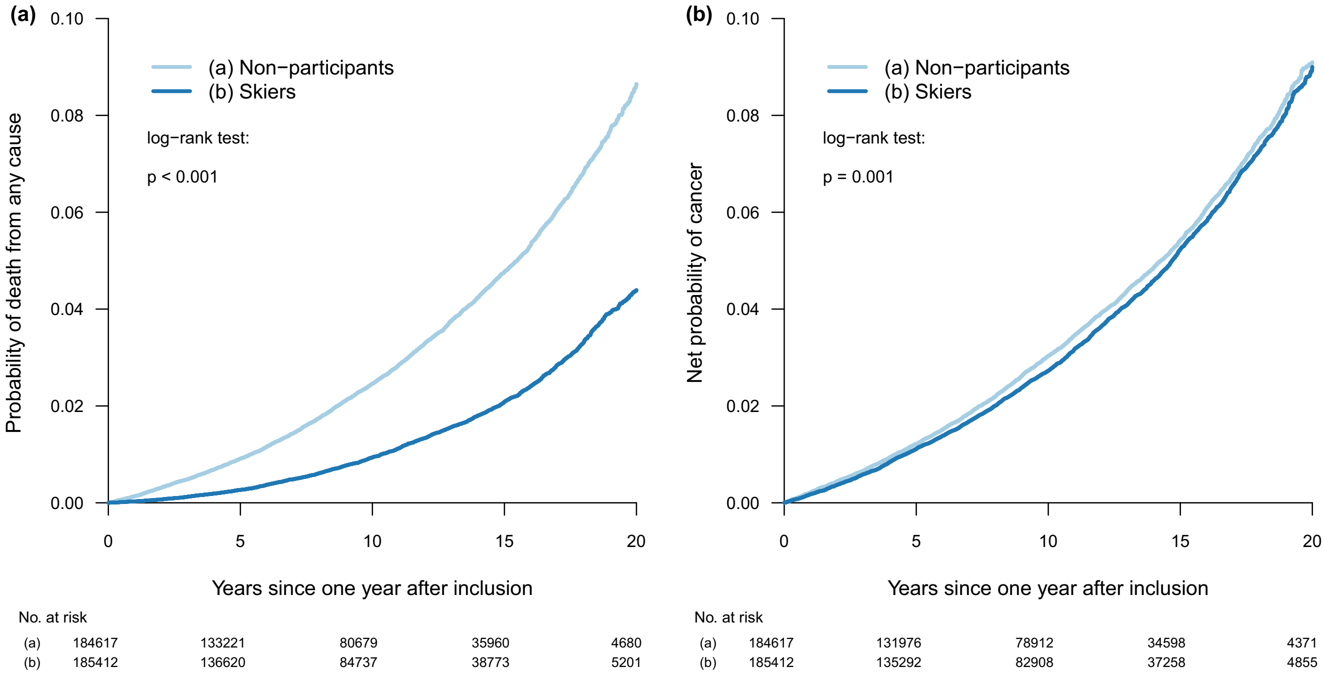

Fig. 2. (a) Probability of death from any cause. (b) Net probability of invasive cancer, all sites. Exposed: Skiers in the Vasaloppet, Unexposed: Non-participants matched from population.

modestly over time to 1.6% and 1.8% respectively at 20 years (Fig. 4b). When this analysis was repeated by finishing time dividing the skiers into three performance groups (from very high performance with 100–150% of the winner's finishing time to performance groups of 151–200% and more than 200% of the winner's finishing time), a dose–response pattern was seen. The net probability for the lowest performance group was similar for that of the non-participants (1.6% at 20 years), while the highest performance group had a considerably lower (0.9% at 20 years) net probability (Fig. 4c). This result prompted an analysis by performance status of all invasive cancer where the non-participants and the two lower performance groups had similar net probabilities of cancer at 20 years, varying between 9.0% and 9.8%, while the highest performance group had 7.0% probability (data not shown). These results were verified in an age-adjusted Cox model (HR = 0.84 for the high performance group versus non-participants) (Data not shown).

Cancers related to out-door activities had a higher net probability of occurring among the Vasaloppet skiers (Fig. 4d).

3.2. Stratified analyses (Table 4)

As mentioned, all adjusted Cox models yielded similar results to the unadjusted results, but we also explored if the association between participation in Vasaloppet and cancer risk was modified by year of first participation, gender, age at first participation, educational level, employment status or Charlson co-morbidity index. The only indication of an interaction that was not random was for gender in cancers related to PA and weight/diet: the group as such has a HR of 0.82 in comparison between Vasaloppet skiers and non-participants but for men HR was 0.70 (95% CI 0.61–0.80) and for women HR was 0.91 (95% CI 0.82–1.01) with a statistically significant test of interaction ($p = 0{,}002.$). After exclusion of breast cancer, the HR was lowered to 0.80 for women and a test of interaction no longer remained statistically significant ($p = 0.218$) (Table 4).

4. Discussion

In our 350,000 study subjects with more than 12,800 cancers during median ten years follow-up, we found a small overall reduction of cancer incidence following participation in a challenging long distance cross-country ski-race. However, the relative reduction of cancer incidence was 32% for cancers where life style is presumed to have a protective effect which includes 29% of all cancer events in the cohort. Interestingly, we found a dose–response relationship: skiers with higher performance had a lower cancer incidence than skiers with lower fitness. Male skiers had a clearer inverse association with occurrence of life style cancers than women, a difference that was not as clear when breast cancer as an event was excluded.

Participating in Vasaloppet is a marker of a lifestyle that involves a high degree of PA, but which also is associated with factors such as a healthier diet, lower body

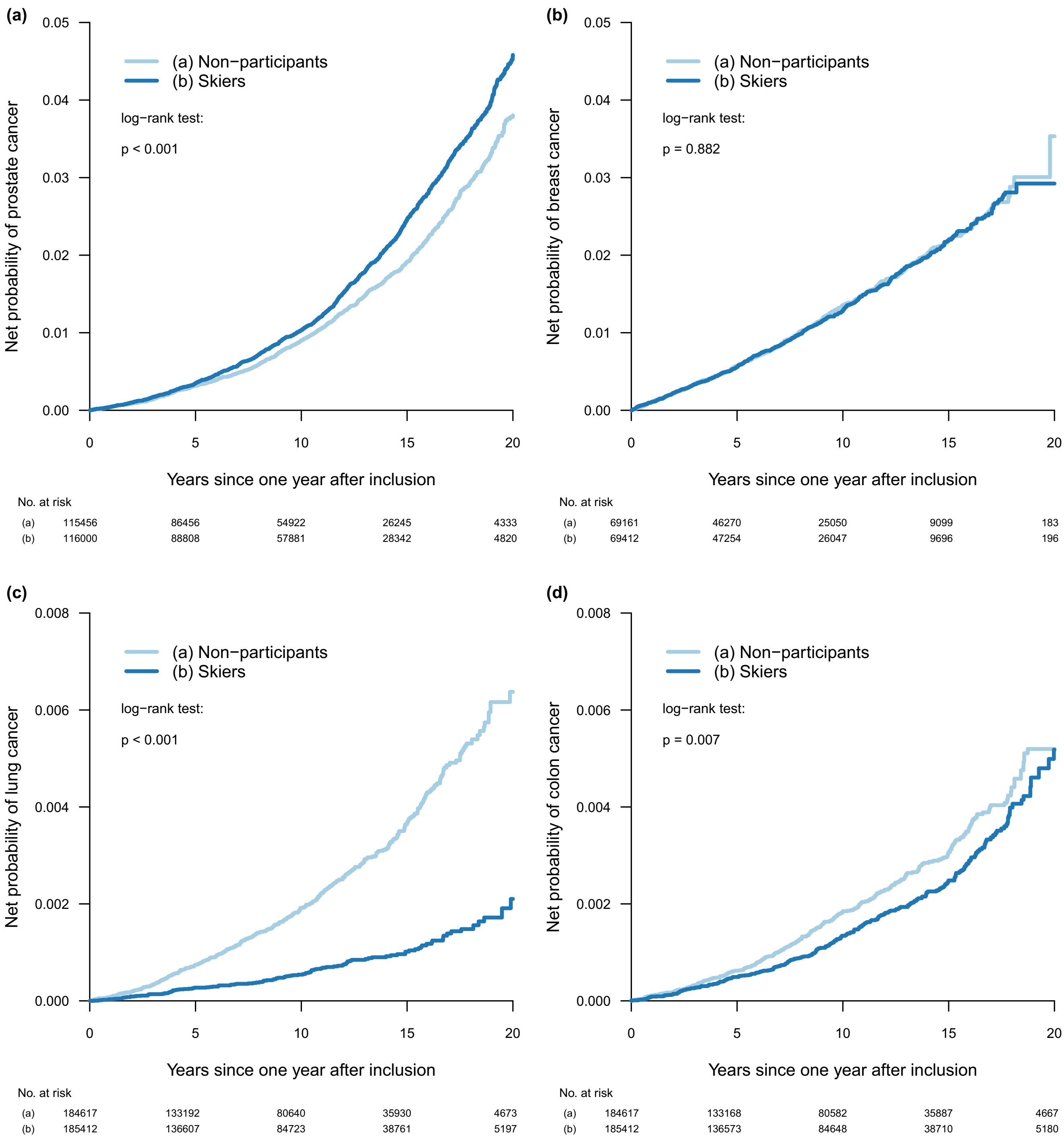

Fig. 3. (a) Net probability prostate cancer. (b) Net probability of breast cancer. (c) Net probability lung cancer. (d) Net probability colo-rectal cancer. Exposed: Skiers in the Vasaloppet, Unexposed: Non-participants matched from population.

weight and a low prevalence of smoking. The oxygen uptake (fitness), VO_2-max, for the skiers is 45–80 ml kg^{-1} min^{-1} compared with the background population VO_2-max 35 ml kg^{-1} min^{-1} [11]. Surveys to Vasaloppet skiers [12] (Supplement Table 3) show that 60% of the Vasaloppet skiers were physically active four hours or more weekly compared to 18% in the background population. This corresponds to a mean value among Vasaloppet skiers of about 20 Metabolic Equivalent hours per week (MET-h $week^{-1}$). The prevalence of BMI >25 among the skiers is 31% for men, 16% for women compared with 52% respective 39% in the background population. Fruit and vegetable consumption is higher among Vasaloppet skiers compared with the background population [12] and only 1–2% are daily smokers among the Vasaloppet skiers and about 13–15% in the background population. As other studies have shown, participation in sports activities or being

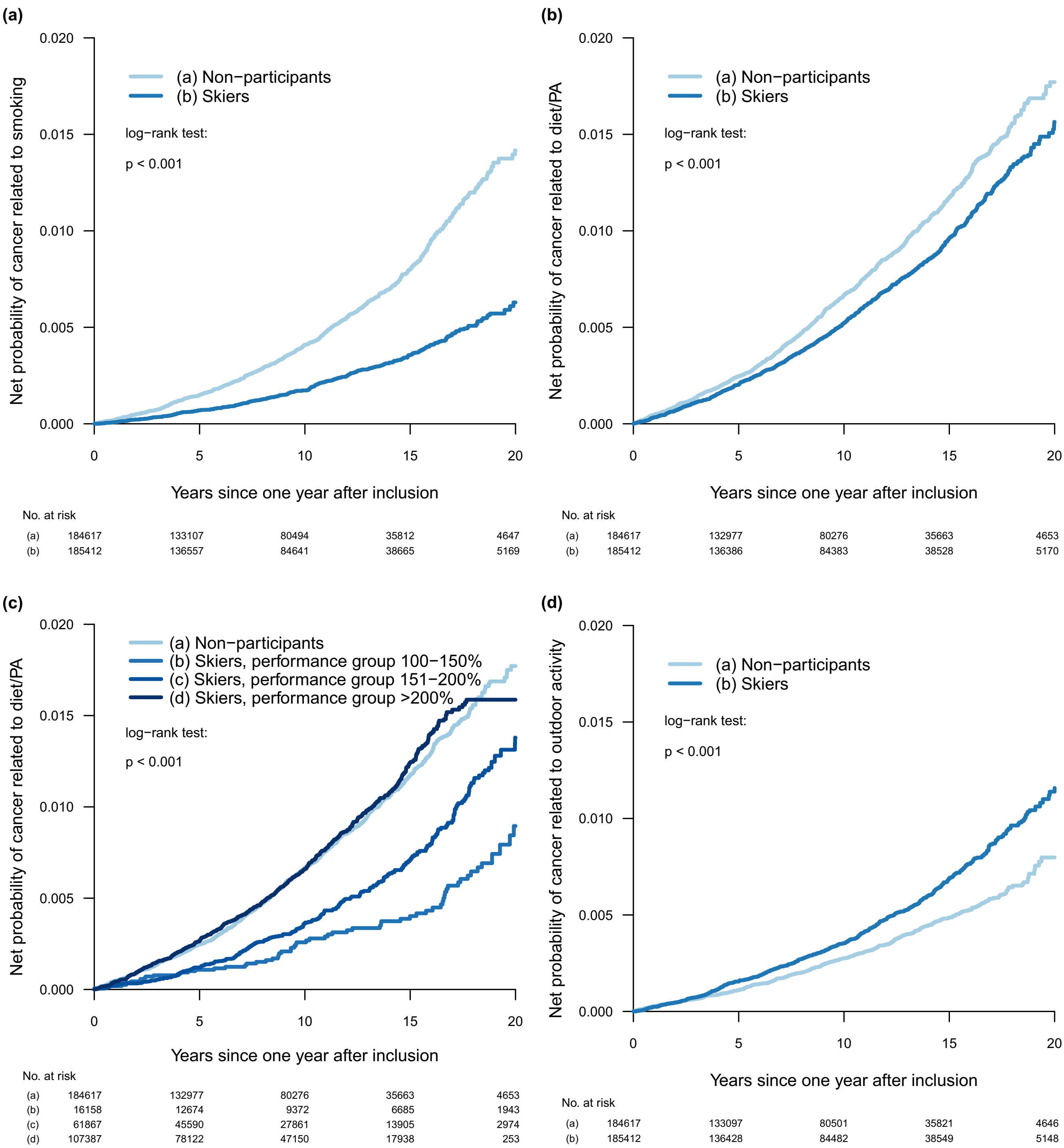

Fig. 4. (a) Net probability of cancers related to smoking. (b) Net probability of cancers related to diet, weight and physical activity. (c) Net probability for cancer in 4b with comparison between different performance groups. (d) Net probability to cancers related to out-door activity. Exposed: Skiers in the Vasaloppet, Unexposed: Non-participants matched from population.

more physical active is associated with reduced mortality, including cancer probably coupled to a plethora of life style factors [13–15].

The result that just a reduction of 6% in relative terms of *all invasive cancers* was associated with participation in Vasaloppet was disappointing in the light of expectations of preventive effects of life style changes [1]. E.g. life style was estimated to account for 26% of all cancers in a European study (skin and melanoma excluded) [16]. However, our study does not compare a life style compatible with a high degree of PA and fitness to a completely sedentary one. The randomly selected non-participants represent an average Swedish population after exclusions of persons with major co-morbidities

Table 4
Stratified analysis with hazard ratios derived from Cox proportional hazards models.

	All cancers HR[1] (95% CI)	Cancers related to tobacco smoking HR[1] (95% CI)	Cancer with relation to lifestyle with physical activity, normal weight, diet with fruits and vegetables HR[1] (95% CI)
All	0.94 (0.91–0.98)	0.44 (0.39–0.50)	0.82 (0.76–0.89)
Year of inclusion			
1989–2000	0.94 (0.90–0.98)	0.44 (0.38–0.50)	0.82 (0.75–0.90)
2001–2005	1.00 (0.92–1.10)	0.53 (0.38–0.74)	0.86 (0.70–1.06)
2006–2009	0.82 (0.68–0.99)	0.21 (0.09–0.48)	0.74 (0.48–1.15)
Sex			
Men	0.99 (0.94–1.03)	0.47 (0.41–0.53)	0.70 (0.61–0.80)
Women	0.87 (0.81–0.92)	0.36 (0.28–0.46)	0.91 (0.82–1.01)
Age at inclusion			
20–29	1.05 (0.90–1.21)	1.07 (0.55–2.10)	0.74 (0.39–1.39)
30–39	0.95 (0.85–1.05)	0.54 (0.37–0.78)	0.95 (0.69–1.29)
40–49	0.93 (0.87–1.00)	0.39 (0.32–0.49)	0.86 (0.74–0.99)
50+	0.92 (0.87–0.97)	0.42 (0.36–0.49)	0.78 (0.70–0.87)
Highest level of education[2]			
Primary school	0.88 (0.82–0.95)	0.42 (0.33–0.53)	0.73 (0.62–0.87)
Secondary school	0.94 (0.89–1.00)	0.44 (0.36–0.53)	0.76 (0.67–0.87)
University	0.94 (0.88–1.00)	0.55 (0.43–0.69)	0.88 (0.76–1.01)
Employment[2]			
Employed	0.96 (0.92–1.00)	0.47 (0.40–0.54)	0.84 (0.76–0.92)
Not employed	0.92 (0.82–1.03)	0.37 (0.25–0.54)	0.68 (0.52–0.88)
Retired	0.87 (0.76–1.00)	0.39 (0.27–0.58)	0.73 (0.51–1.04)
Charlson comorbidity index[2]			
0	0.95 (0.91–0.98)	0.44 (0.39–0.50)	0.83 (0.76–0.90)
1	0.87 (0.74–1.02)	0.38 (0.23–0.63)	0.72 (0.49–1.07)
2+	0.70 (0.42–1.17)	0.73 (0.16–3.35)	0.33 (0.08–1.43)

Exposed: Vasaloppet skier. Unexposed: Non-participants, matched individuals from the Swedish population of same gender, age and county of residence. HR (Hazard ratio), 95% CI (95% Confidence interval).
[1] Hazard ratio for skiers compared to non-participants for given end-point.
[2] Adjusted for age at inclusion.

and e.g. 18% in that group has been estimated to be physically active four hours or more per week. Our findings in relation to finishing times may better reflect the difference between high and a low exposure to a life style compatible with a high degree of PA. However, this interpretation depends on that a higher performance in the race is associated with a quantitatively higher exposure of PA and related life style factors and not an essentially qualitatively different life style needed for a high degree of PA.

Access to health care and participation in screening may also contribute to a low overall estimate of cancer risk reduction. A healthier lifestyle is associated with higher participation in prostate specific antigen (PSA) testing [17] and mammography screening [18] where long lead times and over-diagnosis - especially for prostate cancer – introduce a diagnostic bias. Prostate cancer increased dramatically during 1988–2002 in Sweden largely because of screening with PSA in men without symptoms. A review [19] suggests only a weak inverse association between PA and prostate cancer which is not likely to annihilate the increased incidence by screening. For breast cancer the call is closer: current estimates of over-diagnosis in overview of all breast cancer screening trials of 10–15% [18] which may partly cancel out the effects of PA, e.g. a 25% risk reduction comparing the most physically active to the least active women in a review [20]. The Swedish population-based and nation-wide mammography programme and a higher participation rate among the health consciousness may be the explanation why our results for breast cancer differ from other studies, further supported by the disappearance of the interaction for gender and a similar result in men and women when breast cancer was excluded.

The overall cancer reduction is also hampered by the increased incidence of cancers related to sunlight exposure among Vasaloppet skiers, probably due to that the physically most active groups are more often engaged in out-doors activities.

Notably, we see a substantial reduction in incidence of cancers associated with exposure to the group of life style factors, which prevalence we assume to be linked to participation in Vasaloppet. There is limited evidence that PA protects against lung cancer [2]. One deviating study estimates a reduction in lung cancer incidence with 20–50% as an effect of PA, however without an effect in never-smokers [21]. Our data indicate that abstaining from smoking is an important component of the preventive effect of a life style associated with high degree of PA. The evidence that PA is protective is convincing for colon but less for rectal cancer. PA has been associated with up to 30% reduction in risk [22–24] with a dose–response relationship [23]. Our data show a temporal pattern for colo-rectal cancer that differs from the overall pattern. The explanation is not clear and may be an interesting field for further exploration.

4.1. Limitations

We lack individual information on daily PA, smoking, dietary habits and BMI. We thus assume that participation in Vasaloppet is a marker of a healthier life style in terms of PA, smoking, diet and body weight and even more so for the highest performance group. This is supported by previous surveys, but these surveys give little information on alcohol use. The study design entails that the non-participants considered unexposed in our analysis to a degree also contain 'exposed' individuals meaning that this study reflects the effects of adding more of this assumed healthier life style over and above the average prevalence of it in Sweden as of 1989–2010.

We excluded all study subjects with indicators of serious co-morbidity that would have precluded taking part in Vasaloppet. The NPR has a high coverage, but we do not have information on serious co-morbidity treated in out-patient settings only, which may lead to residual confounding.

The time pattern seen in the analyses of net probability and our current understanding of the very long natural history of many cancers indicate that a longer follow-up of these relatively young cohorts may show larger reductions in risk. A large proportion of the participants have not reached the ages when cancer is common. Cancer heritability that may override cancer prevention by life style modifications is probably more common in younger cohorts, which in this study may mask some of the potentially protective effect of physical activity.

5. Conclusions

Our data indicate that it is unrealistic to reduce overall population cancer incidence drastically with life styles that are associated with a high degree of PA. However, cancers that are epidemiologically associated with life style factors were significantly reduced by what we presume to be a blend of non-smoking, normal body weight, sound dietary habits and PA. Furthermore and importantly, several of the cancers for which the incidence was reduced have a high mortality. Our results thus indicate that present days' recommendations about life style and cancer hold, but the overall population impact in countries already promoting these life style changes may be lower than previously thought. Our findings related to degree of fitness - and possibly to gender - raise questions about biological mechanisms that need to be further researched to answer if we need more specific advice about the preventive actions of PA. Furthermore, this study adds to the insights of how complex epidemiological studies of cancers that are subject to screening programmes have become.

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Conflict of interest statement

None declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ejca.2014.12.009.

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