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Ten-year mortality among older male recreational endurance athletes in the Birkebeiner Aging Study in comparison with older men from the Tromsø Study

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Background: Physical activity (PA) is associated with reduced mortality. However, whether there is an added benefit of long-term endurance training is unclear. Thus, we aimed to examine 10-year mortality in older male endurance athletes compared with an older male general population.

Method: Male athletes ($n = 503$) participating in an annual long-distance ski race (median years of participation: 14, range: 1–53) from the Norwegian Birkebeiner Aging study (BiAS), and non-athletic men ($n = 1867$) attending the sixth Tromsø Study (Tromsø6) aged ≥65 years were included. Associations with endurance sport practice and joint exposures of endurance sport practice and self-reported leisure-time PA with all-cause mortality were examined. We analyzed the data with Cox proportional hazard models and regression standardization.

See Acknowledgements for NEXAF.

Results: After 10 years (median: 10.4, range: 0.5–11.1) the mortality rate was lower in athletes (hazard ratio (HR) 0.34, 95% confidence interval (CI): 0.24–0.49) compared with non-athletes, corresponding to a 15% (95% CI: 12–19%) absolute risk reduction associated with endurance sport practice. In joint analyses categorized according to PA and endurance sport practice, we observed an inverse dose–response relationship with mortality ($p < 0.001$). Compared to inactive non-athletes, PA was associated with lower mortality in both active non-athletes and athletes. However, the observed benefit among participants reporting moderate-to-vigorous PA was larger in athletes (HR: 0.21, 95% CI: 0.14–0.32) than non-athletes (HR: 0.43, 95% CI: 0.31–0.59) ($p < 0.01$).

Conclusion: Endurance sport practice was associated with reduced 10-year mortality, beyond the effect of PA in older men. This study suggests that long-term endurance sport practice maintained into older adulthood promotes longevity.

KEYWORDS

athletes, endurance training, epidemiology, mortality, physical activity

1 | INTRODUCTION

Physical inactivity is associated with an elevated burden of multiple non-communicable diseases, estimated to account for roughly five million deaths per year.[1] Conversely, regularly partaking in leisure-time physical activity (PA) is associated with a reduced risk of at least 25 chronic medical conditions.[2] Several observational studies further indicate a strong inverse association between PA and mortality and that maintaining regular PA in older adults is crucial.[3,4]

Several studies have indicated that the dose–response association between PA, exercise and mortality is curvilinear with diminishing returns at a higher dosage of exercise.[4–6] PA likely reduces the prevalence of multiple cardiovascular and metabolic risk factors; however, vigorous PA and systematic endurance training may simultaneously have adverse effects in some individuals. Although not related to an increase in mortality, the intriguing observation that endurance athletes seem to have an increased load of coronary calcification has recently been highlighted as a potential cause for concern.[7,8] Furthermore, the risk of arrhythmias appears particularly elevated among endurance athletes,[9] and participation in strenuous endurance competition has also been linked to an increased risk of acute cardiovascular mortality.[10]

Athletic populations and especially endurance athletes, typically have reduced mortality rates compared with the general population.[11] Clarke and colleagues[12] showed that Olympic medallists on average lived 2.8 years longer than age-matched controls. Endurance sport practice has further been observed to yield considerable reductions of mortality among recreational endurance athletes when compared with the general population.[13] However, there is a lack of research addressing whether there is an added benefit of endurance sport practice compared with regular leisure time PA. Thus, to further address nuances in the association between PA, endurance sport practice and mortality, we aimed to (1) investigate the association between long-term exposure to endurance sport practice and all-cause mortality, and (2) study the joint effects of PA and endurance sport practice on mortality in a cohort of older male endurance athletes compared with men of the same age from a general population.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

The present analysis is based upon a prospective study of two separate Norwegian cohorts of men aged ≥65 years; the Birkebeiner Aging Study (BiAS) including male endurance athletes, and the sixth survey of the Tromsø Study (Tromsø6), with participants from a general population. The pooled study sample of the present study yielded 2370 participants.

BiAS is a prospective cohort study including athletes who completed the Birkebeiner ski race in 2009 and 2010.[14] All exposure data were self-reported and collected using questionnaires distributed by post with prepaid postage along with an invitation letter to participate in October and November 2009, and November 2010. The main aim of BiAS is to examine the association between endurance sports practice and health with advancing age. The Birkebeiner ski race is arranged annually in Norway and is one of the most challenging ski races in the world, with a course of 54 km and about 1000 uphill altitude meters. Cross-country skiing is classified as an endurance sport discipline of high intensity.[15,16] Regular endurance exercise is considered mandatory to complete the race, and a high level of cardiovascular fitness ($\dot{V}O_{2max}$) has been documented in athletes participating in the race.[17] All male ($n = 607$) skiers who completed the race in 2009 or 2010 were invited to participate. Among those invited, 509 accepted the invitation to participate, out of which 503 (83%) were included into the current study (Figure 1).

The reference population includes men aged ≥65 years who participated in Tromsø6 which is a prospective study of various health conditions in a general population.[18] Seven surveys have been completed since the study was first initiated in 1974. The study population is considered representative of a Northern European Caucasian population.[18,19] The data collection in Tromsø6 was carried out between 01.10.2007 and 19.12.2008. In total 2757 men were invited and 1867 (68%) attended the study.

2.2 | Assessment of exposures and outcomes

The main exposure was whether individuals had completed the Birkebeiner ski race or not (athletes vs. non-athletes). In addition, participants reported number of races completed and medals achieved. Two athletes had missing data for number of races completed and five did not report number of medals achieved. A medal is awarded to individuals who complete the race within the average time of the top five participants of each 5-year age group +25%. Non-athletes were assumed to never have participated in the Birkebeiner ski race. Participants with the greatest number of races completed, and medals achieved, may represent athletes with the highest cardiovascular fitness level for their age.[9] Furthermore, leisure-time PA was examined through administration of the Saltin-Grimby questionnaire.[20] The questionnaire assesses PA during the last 12 months on a four-level scale: 1 = Sedentary, almost completely inactive. 2 = Light, PA at least 4 h/week such as walking and riding a bicycle. 3 = Moderate, regular PA and training at least 3 h/week such as heavy gardening, running, and swimming. 4 = Vigorous PA, such as running events, skiing, swimming several times per week. The questionnaire has been validated in several studies[21,22] and is found to positively correlate with $\dot{V}O_{2max}$.[20] In total there were 258 participants with missing data on PA (10.9%), with the majority of missing observations ($n = 245$) among non-athletes. As there were only one athlete reporting to be inactive and few non-athletes ($n = 12$) reporting vigorous PA, we examined joint associations of endurance sport practice and PA on mortality with a 5-category scale (1 = Inactive non-athletes, 2 = Light non-athletes, 3 = Moderate-to-vigorous non-athletes, 4 = Light athletes, 5 = Moderate-to-vigorous athletes).

All-cause mortality was available through linkage to the Norwegian Cause of Death Registry for participants in Tromsø6. The registry covers individuals registered as residents of Norway at the time of their death, including deaths that took place in Norway and abroad. Information regarding

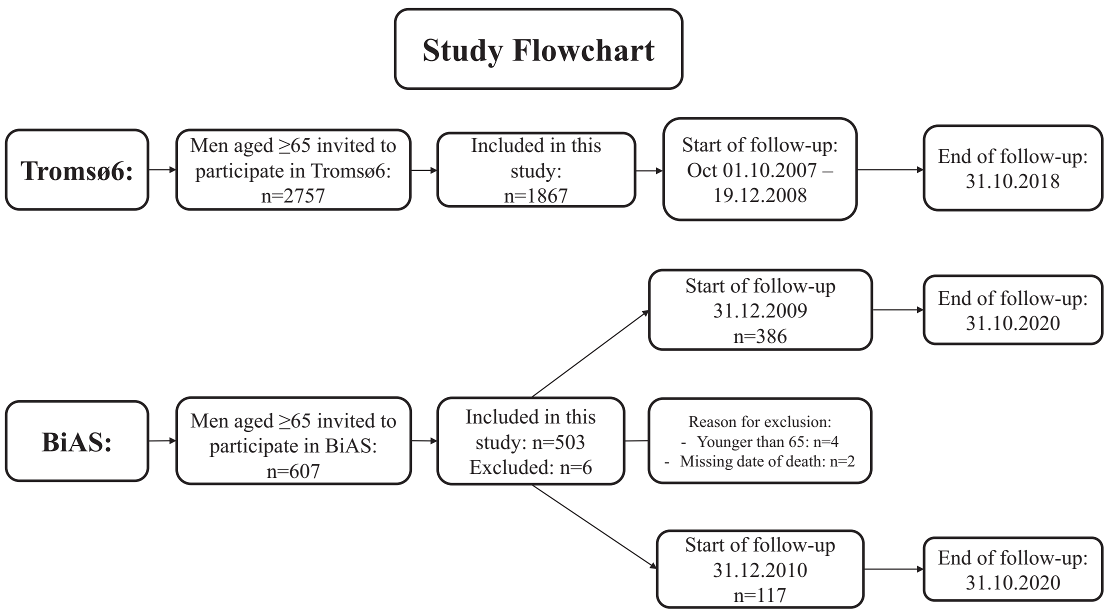

FIGURE 1 Flow chart providing an overview over study inclusion, start of follow-up and end of follow-up. The Birkebeiner Aging Study and the Tromsø Study.

mortality in athletes was collected at Diakonhjemmet hospital by retrieval of electronical patient journals linked with the Norwegian Population Registry. Non-athletes were followed from date of examination in Tromsø6 to the date of death or until end of follow-up (31.10.2018), whichever came first. Athletes were followed from date of registration (31.12.2009 or 31.12.2010) until death or end of follow-up which was 31.10.2020.

2.3 | Covariates

Height (cm) and weight (kg) were self-reported in BiAS, while in Tromsø6, height and weight were measured to the nearest decimal, wearing light clothing and no shoes. Body mass index was calculated as weight divided by the square of height in meters. All other data were recorded by questionnaires for both study cohorts. Coronary heart disease, diabetes, atrial fibrillation and stroke status were assessed by the question "Do you have, or have you had (disease)?". Use of lipid lowering and antihypertensive medication was assessed with the question "Do you use, or have you used cholesterol/blood pressure lowering drugs?" (1 = No, 2 = Yes, previously, 3 = Yes, currently). Questions regarding education (1 = Primary school, 2 = High school, 3 = University <4 years, 4 = University >4 years), smoking habits (1 = Never, 2 = Previous, 3 = Current), and frequency of alcohol consumption (1 = Never, 2 = Monthly or less, 3 = 2–4 times per month, 4 = 2–3 times per week, 5 = 4 or more per week) differed slightly as there were more alternatives available in the BiAS questionnaire[23] compared to the Tromsø6 questionnaire.[24] Thus, the answers were recoded and amalgamated to match the Tromsø6 questionnaire.

2.4 | Statistical analysis

Descriptive characteristics were presented as median (range or 1st and 3rd quartile) for continuous variables, and as percentages for categorical variables. Crude mortality rates per 100 000 person-years and Kaplan–Meier survival curves are presented. Furthermore, we estimated adjusted hazard ratios (HRs) and corresponding 95% confidence intervals (CI) with Cox proportional hazard regression for athletes with non-athletes as the reference group. The proportional hazards assumption was examined by Schoenfeld's test of residuals and by inspection of log minus log plots. Covariates for adjustment was identified by a directed acyclic graph drawn with the web application DAGitty (www.daggity.net) (Figure S1). We present age-adjusted models and multivariable models further adjusted for education, smoking status and frequency of alcohol consumption. Furthermore, we applied flexible parametric survival models with the Stata package "stpm2"[25] in order to calculate survival probabilities and obtain standardized survival curves for athletes and non-athletes using the postestimation command "standsurv".[26] In joint association analyses with endurance sport practice and PA we used inactive non-athletes as the reference group. Furthermore, to examine differences between the highest level of PA for athletes compared to non-athletes, we repeated the same analysis with moderate-to-vigorously active non-athletes as the reference group. The significance level was set to 5%. Statistical analyses were performed with Stata version 17 (StataCorp).

2.5 | Sensitivity analysis

We performed several sensitivity analyses to examine the robustness of our results. We evaluated the potential for reverse causation bias by (1) removing the initial 2 years of follow-up (Table S1), and (2) excluding baseline coronary heart disease cases (Table S2). The potential for residual confounding by age was further examined by restricting our analysis to participants aged 65–74 only. (3) As several mediating pathways might also be affected by other unmeasured variables, residual confounding was further assessed by multivariable adjustment for model 2 + body mass index, lipid lowering and antihypertensive medication, diabetes and coronary heart disease (Table S3). Furthermore, in exploratory analyses we obtained standardized survival curves conditional on the non-athletic populations covariate distribution to further examine the potential effect of endurance sport practice in non-athletes (Figure S2).

2.6 | Ethics

The present study was approved by the Regional Committee for Medical and Health Research Ethics (REK: 2020-175586) and is performed in compliance with the declaration of Helsinki. Participants signed a written informed consent form before participation.

3 | RESULTS

Baseline characteristics of study participants are presented in Table 1. Athletes reported a median 36 (range: 0–67) years of systematic endurance training, and 14 (range: 1–53) years of annual participation in the Birkebeiner

TABLE 1 Baseline characteristics of BiAS (athletes) and Tromsø6 (non-athletes) participants.

Baseline characteristics	Athletes ($n=503$)	Non-athletes ($n=1867$)
Age (years)	68 (66–71)	70 (67–75)
Height (cm)	178.0 (175.0–182.0)	174.5 (170.1–178.8)
Weight (kg)	75.0 (70.0–80.0)	81.2 (73.4–89.9)
BMI ($kg \cdot m^{-2}$)	23.5 (22.2–24.8)	26.8 (24.4–29.1)
Education		
Primary/Secondary school	16.7 (83)	35.6 (646)
High school	42.2 (210)	35.8 (649)
College/University	41.2 (205)	28.6 (518)
Smoking status		
Current	0.8 (4)	15.4 (281)
Former	37.9 (190)	60.6 (1103)
Never	61.4 (308)	24.0 (436)
Frequency of alcohol consumption		
Never	9.5 (46)	14.2 (259)
1–4 times per month	72.8 (354)	64.1 (1169)
2–3 times a week	14.6 (71)	15.6 (284)
4 times or more per week	3.1 (15)	6.2 (113)
Self-reported leisure time physical activity		
Sedentary	0.2 (1)	19.4 (314)
Light activity	9.8 (48)	58.0 (941)
Moderate	51.0 (250)	21.9 (355)
Vigorous	39.0 (191)	0.7 (12)
Disease status		
Coronary heart disease	3.6 (18)	24.3 (444)
Previous stroke	1.6 (8)	7.0 (126)
Atrial fibrillation	13.8 (69)	12.3 (217)
Diabetes	0.8 (4)	8.5 (154)
Currently or previously taking antihypertensive medication	15.8 (76)	40.5 (729)
Currently or previously taking lipid lowering medication	15.1 (73)	34.3 (617)
Overweight participants	21.1 (105)	50.6 (943)
Obese participants	0.4 (2)	18.9 (352)

Note: Athletes are BiAS participants, non-athletes are Tromsø6 participants. Values are presented as median (1st and 3rd quartile) for continuous variables and as percentage (numeric) for categorical variables.

race. Nearly one fifth of the athletes had been competing in the race for ≥30 years. Athletes were 2 years younger, 3.5 cm taller and weighted 6.2 kg less than non-athletes. More athletes than non-athletes were university educated (41.2% vs. 28.6%) while fewer smoked regularly (0.8% vs. 15.4%). Furthermore, the prevalence of hypertension and cardiometabolic disease was lower among athletes.

During a median follow-up time of 10.4 (range: 0.5–11.1) years, we observed 628 deaths during 22 401 person years, of which 7.4% ($n=37$) occurred in athletes and 31.7% ($n=591$) occurred in non-athletes (Table 2). Unadjusted Kaplan–Meier survival curves and standardized survival curves are presented in Figure 2. After 10 years of follow-up, no exposure to endurance sport practice was associated with a standardized survival probability of 0.74 (95% CI: 0.73–0.76), whereas exposure to endurance sport practice was associated with a standardized survival probability of 0.90 (95% CI: 0.87–0.93), resulting in an absolute difference of 15.4% (95% CI: 11.6%– 9.2%). Standardizing to the non-athletic covariate distribution resulted in a slightly but not significantly higher survival difference at 10 years of follow-up (16.7%, 95% CI: 12.6%–20.8%).

TABLE 2 Mortality rates and hazard ratio with 95% confidence interval. The Birkebeiner Aging Study and the Tromsø Study.

Age group	*n*	Dead *n* (%)	Observed person-years	Mortality rate (per 100 000)	HR (95% CI) Model 1	HR (95% CI) Model 2
All non-athletes	1867	591 (31.7)	17199.1	3436.2	1 Reference	1 Reference
All athletes	503	37 (7.4)	5202.0	711.3	0.27 (0.19–0.38)	0.34 (0.24–0.49)
<75						
Non-athletes	1346	282 (21.0)	13040.3	2162.5	1 Reference	1 Reference
Athletes	445	28 (6.3)	4607.2	607.7	0.30 (0.20–0.44)	0.40 (0.26–0.60)
≥75						
Non-athletes	521	309 (59.3)	4158.8	7430.0	1 Reference	1 Reference
Athletes	58	9 (15.5)	594.8	1513.1	0.21 (0.11–0.40)	0.23 (0.11–0.47)

Note: Crude mortality rates are presented per 100 000 person years. Model 1 is adjusted for age, model 2 is further adjusted for education, smoking and frequency of alcohol intake.

Abbreviations: CI, confidence interval; HR, hazard ratio.

Compared with non-athletes, the univariable age-adjusted rate of mortality in athletes was reduced by 73% (HR: 0.27, 95% CI: 0.19–0.38). After multivariable adjustment, the rate of mortality in athletes was 66% lower (HR: 0.34, 95% CI: 0.24–0.49). In joint analyses categorizing the study population according to endurance sport practice and PA levels (Figure 3), a linear, inverse dose–response relationship with mortality ($p < 0.001$) was indicated. Compared to inactive non-athletes, PA was associated with a substantially reduced mortality rate in both study cohorts. However, the observed benefit was larger for athletes (HR: 0.21, 95% CI: 0.14–0.32) than non-athletes reporting moderate-to-vigorous PA (HR: 0.43, 95% CI: 0.31–0.59). When using moderate-to-vigorously active non-athletes as the reference group, the adjusted mortality rate was 51% lower in athletes reporting the same PA level (HR: 0.49, 95% CI: 0.31–0.77). We did not observe any association between number of races or medals achieved and mortality among athletes.

Overall, sensitivity analyses did not reveal any substantial changes to our results. As a limited proportion of athletes was aged ≥75 years (11.5%) compared to non-athletes (27.9%), we restricted our analysis to participants aged <75 only; however, the relative hazards did not change substantially (HR: 0.40, 95% CI: 0.26–0.60). Further age-stratified analyses are given in Table S4.

4 | DISCUSSION

In this cohort of older men, long-term endurance sport practice was associated with a substantial reduction in mortality during 10-years of follow-up. Although moderate-to-vigorous PA was associated with substantial benefits on mortality in both athletes and non-athletes, the observed benefit was greater in athletes, suggesting that exposure to long-term endurance sport practice may yield additional health benefits compared to regular PA corresponding to current recommendations.

4.1 | Mortality in endurance athletes

After 10 years of follow-up, we documented a 15% reduced absolute risk of mortality associated with endurance sport practice. The survival benefit associated with long-term exposure to endurance sport practice may be attributed to an increased $\dot{V}O_{2max}$ level.[27,28] In line with this notion, Grimsmo et al.[17] showed that male skiers who were still active and competing at a mean age of 75 years on average had a $\dot{V}O_{2max}$ value of 38.3 mL·kg^{-1}·min^{-1}, which is 22% higher than men at a mean age of 73 years according to national reference standards.[29]

Overall, we observed that the adjusted mortality rate was 66% lower among athletes compared with the general population. Our findings are in line with previous research documenting that athletes live longer than the general population.[11–13,30] Kettunen et al.[30] observed that endurance athletes who previously represented the Finnish national team had a 30% lower rate of mortality compared with healthy controls. Since athletes who were active in the period 1920–1960 was included, the differences compared to our estimates may in part be attributed to a birth cohort effect and due to their lengthy follow-up period. Another study conducted on American runners aged >50 years observed a reduced mortality rate of almost 40%.[31] The survival advantage associated with endurance sport practice observed in the present study is also somewhat larger than what was observed in a younger cohort of male Swedish skiers participating in the long-distance ski race Vasaloppet.[13] Thus, it appears that our estimates are in the upper range

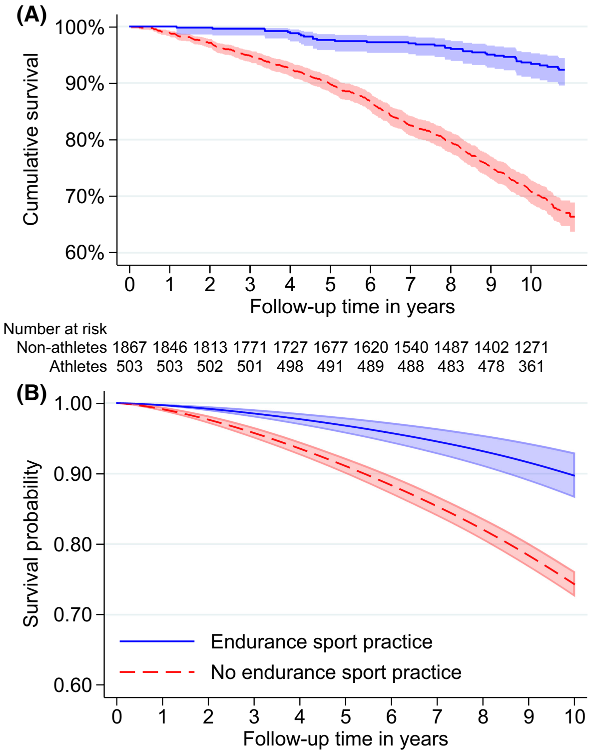

FIGURE 2 (A) Kaplan–Meier cumulative survival curves for athletes and non-athletes during the study period. The solid blue curve illustrates cumulative survival for athletes while the dashed red curve illustrates cumulative survival in non-athletes. Athletes: Participants from the Birkebeiner Aging Study; Non-Athletes: Participants from Tromsø6. (B) Standardized survival curves with endurance sport practice as the exposure. The solid curve illustrates the estimated survival probability with everyone exposed, while the dashed curve illustrates the survival probability with no one exposed. The standardized effect of endurance sport practice has been adjusted for age, education, smoking and frequency of alcohol consumption.

of studies examining mortality in athletes compared with non-athletes.[11] Although this discrepancy may in part be explained by differences in follow-up length and choice of analytical procedure, it is also possible that the health benefits of endurance sport practice is magnified in older athletes.[13]

4.2 | Joint effects of endurance sport and physical activity

The health benefits of PA on physical health is well documented in observational studies.[2] Recent findings from a general population indicate that a highly active lifestyle is associated with approximately a 70% reduced rate of all-cause mortality.[4] Interestingly, we observed that relative to inactive non-athletes, athletes reporting moderate-to-vigorous PA had a rate reduction corresponding to 79%, which is similar to what was observed in the most active individuals in the meta-analysis by Ekelund and colleagues.[4] Furthermore, as the relative rate of mortality was lower in athletes reporting the same level of PA as non-athletes, this may indicate that prolonged exposure to endurance sport practice yields additional health benefits. However, whether this benefit is related to exercise dosage (i.e., intensity, frequency, and volume), duration (years of exposure) of exercise, or other unmeasured factors remains unclear. Regardless, our study substantiates the notion that a highly active lifestyle throughout the adult lifespan that is maintained into older age coincides with monumental health benefits.

4.3 | Dose–response associations

Although systematic endurance training appears largely beneficial, other investigators examining dose–response relationships with mortality have observed a curvilinear[6] or even a U-shaped[5] association, potentially as a result of adverse effects associated with higher doses of endurance training. Our results do not support a U-shaped association as we observed additional benefits of exposure to endurance sport practice compared with individuals exposed to moderate-to-vigorous PA only. However, as we did not observe a dose–response association between number of races completed, medals achieved and mortality among athletes, our data support the notion that there may be a point of no further benefit.

Our findings are partially in agreement with Farahmand and colleagues,[13] who did not observe an association with race-time performance albeit with number of races completed and mortality. The authors postulated that the $\dot{V}O_{2max}$ level was likely adequate to level off on the mortality risk curve even in the slowest athletes.[27] As the Birkebeiner race is one of the world's most challenging cross country ski races, our findings corroborate this notion and further suggest that the ability to complete even a single race when aged ≥65 is adequate to promote cardiovascular fitness levels sufficient to obtain a considerable survival advantage compared with the general population.

4.4 | Strengths and limitations

The main strength of the present study is the unique cohort of endurance athletes regularly participating in the Birkebeiner ski race and reporting a median 36 years of systematic endurance training and 14 years of annual participation in the race. All skiers from different regions in Norway who participated in the race in 2009

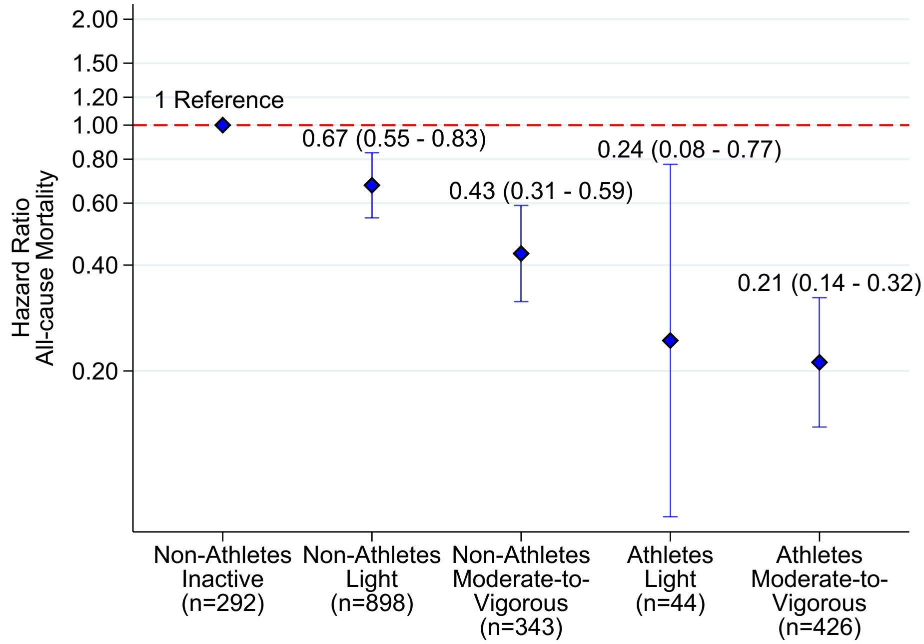

FIGURE 3 Adjusted hazard ratio and 95% confidence interval by joint associations of leisure-time physical activity and endurance sport practice. Non-athletes: Participants from Tromsø6; Athletes: Participants from the Birkebeiner Aging Study. Adjusted for age, education, smoking status and frequency of alcohol consumption. *Y*-axis is given on a logarithmic scale.

or 2010 were invited, and the high attendance of 84% further improves the external validity of the results. Another strength of the study is the reference group with a relatively high attendance proportion, enabling us to recruit older adults who are considered representative of the Norwegian population.[18] Furthermore, the limitations of only reporting HRs have previously been highlighted.[32] Therefore, we supplemented the analysis with standardized survival curves, which represents an adjusted absolute risk and may be easier to interpret.[33] Another strength compared to other studies is that we have information regarding commonly characterized confounding variables such as education, smoking status, and alcohol consumption. Furthermore, the participants provided information regarding use of blood pressure and lipid-lowering medication and reported whether they had diabetes and/or cardiovascular disease. However, as information was obtained by questionnaires, we cannot exclude the possibility of incomplete adjustment and consequently residual confounding. Moreover, as the athletes of the present study may constitute a somewhat selected cohort, bias due to unobserved factors such as differences in genotype, diet, and attained health care may potentially have caused overestimation of the observed effect size. Another element to consider is whether there is a healthy exerciser effect at play, meaning that individuals prone to illness are more likely to stop exercising.[13] This may in part explain why the observed effect among older adults appears larger than what is observed among younger individuals. In addition, as PA is limited by recall- and social desirability bias, our secondary analysis was likely affected by differential- and non-differential missclassification.[34]

4.5 | Perspective

Endurance sport practice was associated with a 66% reduced rate of mortality which corresponded with a 15% absolute risk reduction after 10 years. Thus, our findings suggest that endurance athletes experience substantial health benefits which extends into older adulthood. Considering that we observed a more pronounced risk reduction in athletes reporting similar PA levels as non-athletes, our results also indicate that recreational endurance athletes gain larger health benefits than the portion of the general population which participates in regular leisure time PA. Taken together, our study corroborates previous investigations and further emphasize that long-term endurance sport practice that is maintained with older age yields remarkable benefits to longevity.

AUTHOR CONTRIBUTIONS

KRJ drafted the manuscript and performed all statistical analyses. KRJ, MM, AHR and BM conceived the idea and design of the study. MM and AHR are responsible for data collection and management in BiAS. MLL, AHR, ES and MM contributed to acquisition and interpretation of the data. TW provided expert consultation on all statistical analyses. All authors contributed to the work and made critical revision of the manuscript for key intellectual content.

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CONFLICT OF INTEREST STATEMENT

Maja-Lisa Løchen has received lecture fees from Bayer, Sanofi and BMS/Pfizer not related to this study. Marius Myrstad has received lecture fees from Bayer, Boehringer-Ingelheim, Bristol Myers Squibb, mSD and Pfizer not related to this work. Dag S Thelle has received lecture fees from Boehringer-Ingelheim not related to this work.

DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared publicly due to GDPR regulations but are available upon reasonable request. The legal restrictions on data availability are set by the *Tromsø Study Data and Publication Committee* for privacy reasons. The data can however be made available upon application to the Tromsø Study

Data and Publication Committee. Contact information: The Tromsø Study, Department of Community Medicine, Faculty of Health Sciences, UiT The Arctic University of Norway; e-mail: tromsous@uit.no. The datasets generated in BiAS are not publicly available as the study is not yet complete, but may be available upon reasonable request. The Stata code used for the main analyses is available upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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