Sport as a medicine for health and health inequalities

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Chapter |3|

Chapter 3. Sport participation and health inequalities by health status

How are sport participation, and other forms of physical activity, related to mortality, diabetes and prediabetes for different Body Mass Index levels?[2]

Abstract

Objectives: Physical activity (PA) has many positive health effects. However, relatively limited research has been undertaken to explore the health effects of PA types, including sport participation. Stratifying the health effects of PA and sport on different levels of BMI may help identifying PA types as potential successful health interventions. We examined the associations of different types of PA with prediabetes type 2 diabetes mellitus (T2DM) and all-cause mortality for three BMI-level subpopulations.

Methods: We used the Lifelines cohort study with 97,212 individuals (58.4% women; mean age: 46.5 years) to research the associations between five types of leisure-time PA (sport participation, cycling, gardening, doing odd jobs and walking) and the risk of prediabetes, T2DM and all-cause mortality. We used Cox proportional hazards regression with adjustment for potential confounders to estimate the health risks, stratified for persons with a healthy weight, overweight and obesity.

Results: Sport participation was associated with lower health risks, but only significantly so for prediabetes (HR = 0.86, 95% CI: 0.81-0.92). For healthy weight persons, sport participation was associated with the largest risk reductions, with significantly lower risks of prediabetes (HR = 0.78, 95% CI: 0.68-0.90) and all-cause mortality (HR = 0.79, 95% CI 0.65-0.96). Other PA types were not associated with significantly lower health risks, with the exception of cycling, for which significantly lower health risks for persons with overweight were found.

Conclusion: Our findings show that sport participation is associated with lower health risks, especially prediabetes, but the effect varies between BMI levels, with the strongest link for persons with a healthy weight. Sport participation, together with cycling, is likely to be more effective in reducing health risks than other types of PA.

[2] Joint work with L.H. Dekker, E. Corpeleijn, J.O. Mierau and R.H. Koning. A condensed version of this chapter has been published in Scandinavian Journal of Medicine & Science in Sports as De Boer et al. (2021a).

3.1 Introduction

The prevalence of overweight and obesity has increased rapidly over the past decades throughout the world (Ng et al., 2014). This has raised serious public health concerns because of the association between overweight and obesity and increased risk of a wide range of chronic diseases, including cardiovascular diseases, type 2 diabetes mellitus (T2DM), and all-cause mortality (He & Baker, 2004; Meigs et al., 2006; PSC, 2009; Aune et al., 2016). It is well established that physical activity (PA) has many positive health benefits, including increased life expectancy and reduced chances of being diagnosed with cardiovascular diseases (CVD) (Geiss et al., 2010; Koolhaas et al., 2017; Cosentino et al., 2019). In addition, physical inactivity has large economic consequences, including health care costs and productivity loss (Ding et al., 2016; De Boer et al., 2020). Worldwide, PA guidelines and policies have been established to promote PA, but with limited effect, and physical inactivity has been identified as a 'pandemic' by the World Health Organization (Haskell., et al., 2009; Khan et al., 2012; Kohl et al., 2012).

Although the health effects of PA in general have been studied extensively, for sport participation knowledge is limited. Several observational population studies have shown that participation in specific sports increases life expectancy and reduces risk of CVD (Khan et al., 2012; Oja et al., 2015; Oja et al., 2017; Pedisic et al., 2019). In addition, Koolhaas et al. (2018) found that, for middle-aged persons, sport participation is the only PA type associated with a higher health-related quality of life. These findings suggest that sport participation can be more effective in improving health than other types of PA. However, little is known about the association of sport participation with other specific health outcomes, such as the incidence of T2DM and prediabetes.

Research (Cavill et al., 2001; Goodpaster et al., 2010; Pedisic et al., 2019) has also shown that the effects of PA on health outcomes can differ by socioeconomic background, lifestyle and initial health status. PA in general has been found to significantly contribute to reducing risks of health problems and improve health for specific risk-groups, such as overweight and obese individuals (He & Baker, 2004; Oja & Titze, 2011; Expert Panel Members et al., 2014). Gill and Cooper (2008) found that an individual's BMI level plays a major role for the risk of being diagnosed with T2DM. Consequently, a 'one size fits all' mass–population strategy may not provide the most appropriate approach (O'Hagan et al., 2013). This leads to the question to what extent sport participation is associated with lower health risks for different levels of BMI, in comparison to other types of leisure-time PA. However, to our knowledge, no study exists that investigates the relationship between sport participation and health outcomes in relation to BMI levels(Loureiro & Nayga Jr, 2006).

The objective of our study is to investigate the association of sport participation with the incidence of prediabetes, T2DM and all-cause mortality, and assess this association across individuals with healthy weight, overweight and obesity. In addition, we compared the outcomes of sport participation with those of the other types of leisure-time PA: cycling, gardening, doing odd jobs and walking.

3.2. Methods

3.2.1 Data

The Lifelines cohort study (Scholtens et al., 2015) is a large population-based cohort study and biobank of 167,729 persons living in the Northern part of the Netherlands. Participants are screened through physical examination, including anthropometry. In addition, they fill in questionnaires on, amongst others, demographics, health status, lifestyle and psychosocial matters. The Lifelines study is constructed conform the Declaration of Helsinki (Scholtens et al., 2015). All participants of Lifelines signed a declaration, where he/she approved of the use of the (anonymized) data and material for scientific purposes. Baseline measurements (1A) took place from 2006 until 2013. A full-population follow-up measurement (2A) was conducted between 2014 and 2017, with new physical examinations and questionnaires for the full (surviving) population. Intermediate questionnaire surveys (1B and 1C) were conducted with an interval of around 1.5 years. From the 167,729 participants of the Lifelines study, we excluded persons under age 25, a BMI below 18.5 or with missing or implausible data for any of the variables included in our analysis. In total, 97,212 participants were eligible for our study on all-cause mortality (see flow chart Fig. A3.1 in the Appendix). Due to a limited response to the follow-up questionnaires and glucose measurement and exclusion of persons with prediabetes at baseline (for the analysis of the incidence of prediabetes at follow-up), the remaining sample size was 76,141 for T2DM and 54,452 for prediabetes.

Sport participation, as well as the other types of PA (cycling, gardening, doing odd jobs and walking), were assessed using the short questionnaire to assess health-enhancing physical activity questionnaire (SQUASH). SQUASH is a validated questionnaire that inquires participants about the frequency and duration of participation in several types of PA, including sport participation (Wendel-Vos et al., 2003). Respondents were asked about their amount of PA in minutes per week, for a normal week in the preceding months. In SQUASH, cycling and walking are only considered part of sport participation if they were done as a leisure time sport discipline (i.e. leisure time cycling with a racing bike or a mountain bike), while for all other purposes (such as commuting or shopping) they are categorized as the separate 'cycling' and 'walking' PA types. An individual can thus take part in both cycling as a sport and cycling for other purposes, but the amount of time spend participating in one or the other must be allocated to each specific PA type (in order to avoid double counting). For BMI, height and weight were measured using standard anthropometry procedures at baseline (Scholtens et al., 2015). Persons with a BMI of 18.5 to 24.9 kg/m² were classified as 'healthy weight', those with a BMI of 25.0 to 29.9 kg/m² as 'overweight' and 30.0 kg/m² and higher as 'obese'.

Outcome variables in our analysis were dummy variables for the incidence of prediabetes, T2DM and all-cause mortality, measured at any time beyond baseline. Following the 2003 American Diabetes Association diagnostic criteria (ADA), participants who registered a fasting glucose from 5.6 to 6.9 mmol/L at follow-up were identified as incident cases for prediabetes (WHO, 2006). Following Dêschenes et al. (2018), participants were identified as having T2DM at a follow-up period (1B, 1C or 2A), if they (1) self-reported a newly developed doctor-diagnosed T2DM; (2) were measured to have a fasting glucose value of 7.0 mmol/L or higher; or (3) had a hemoglobin A1c (HbA1c, the hemoglobin type that is bound to glucose) value of 6.5%. Mortality is registered in Lifelines on a monthly basis and we used data to the end of 2019.

To adjust for confounding, we followed the model of Pedicic et al. (2019), which uses directed acyclic graphs to show the relation between possible confounders on sport participation and all-cause mortality risk. We believe this model is also applicable to other PA types and health outcomes. The model includes sociodemographic factors, unhealthy lifestyle, adiposity, health status and amount of PA as confounders. For socioeconomic determinants we included age, sex, education and net household income in the analysis. Lifestyle variables included alcohol consumption, smoking status and diet quality (i.e. the Lifelines Diet Score, see Dekker et al., 2017). For health status, the presence of depression and burn-out for mental health was included as well as doctor-diagnosed cardiovascular diseases and cancer. In addition, the amount of leisure time was included as a covariate as well as subjective well-being (following the RAND-36 questionnaire) to account for general health status (Hays & Morales, 2001). Finally, the PA type categories are not exclusive, i.e. one person can be a participant in more than one PA type. To account for physical activities other than the one that is investigated we calculated an physical activity score (PA Score) for each individual, based on the amount of participation in these other physical activities. Here this covariate is calculated by multiplying the number of hours being physically active in a given PA type by the metabolic equivalent (MET), summed over all PA types except the PA type for which the health effect was being estimated (Ainsworth et al., 2011). This PA Score is therefore different for every PA type.

3.2.2 Analysis

In this study we assessed the associations between sport participation (any versus none) and the incidence of prediabetes, T2DM and all-cause mortality, for three BMI types. For this analysis, we estimated several Cox proportional hazard regression models. The Cox proportional hazard model was chosen because it can take into account the time-to-event, i.e. the time between baseline measurement (1A) and the first moment of incidence; as well as time-at-risk, i.e. the time between baseline and the last measurement (2A for prediabetes and T2DM, or the end of 2019 for morbidity). For each model, the hazard ratio was measured for participating in a certain type of PA, compared with not participating in that type of PA (with a set hazard ratio of 1). In addition, the data for each type of PA differed on one covariate: the amount of PA done on other PA types (PA Score).

First, we estimated the association of sport participation with prediabetes and T2DM incidence and all-cause mortality, with only age and sex as covariates (Model 1). This model was estimated for sport participation as well as the other PA types. The hazard function of Model 1 is:

$$h(t)=h_0(t) \times exp\ (\beta_{sport}\ Sport + \beta_1\ age + \beta_2\ sex) \tag{3.1}$$

where t represents the time between baseline measurement and the time of observation of the event (incidence of prediabetes, T2DM or mortality) or end of final observation in the case of no event. The hazard function $h(t)$ is determined by sport participation (*Sport*) and a set of covariates (age and sex), with h_0(t) the hazard when covariates and sport participation are equal to zero. The hazard varies over time (t), but equals one at baseline measurement (h(0) = 1). The quantity exp(β_{sport} *Sport*) is the hazard ratio (HR) for participating in sport. A hazard ratio below one (HR <1) indicates that participating in sport leads to a smaller chance of incidence of the health outcome (such as being diagnosed with prediabetes) and thus an increased length of survival. Similarly the coefficients (β_1, β_2) measured the effect sizes of covariates. Similar models were analyzed for the other four PA types.

Next, a model with all covariates (as mentioned above) including BMI-level dummy variables (for overweight and obesity) was estimated (Model 2). This second Cox proportional hazard model included all relevant covariates (j) that were available (see Table 3.1), including dummy variables for the BMI levels 'overweight' and 'obese':

$$h(t)=h_0(t) \times exp\ (\beta_{sport}\ Sport + \textstyle\sum_{j=1}^{J} \beta_j\ covariate_j). \tag{3.2}$$

Next, we estimated the association of sport participation stratified by BMI level subpopulations (Models 3). In this model, BMI level variables were excluded, as well as non-relevant covariates. To determine the relevant covariates for the final models, we used the log-rank test of equality (together with Kaplan-Meier survival plots) to examine the proportional hazards association of sport participation, PA types and potential confounders with the outcome measures. Only potential confounders (j=1,..., n) with a p-value below 0.2 were included in the full Model 3. This model can be written as an expanded version of equation (3.2):

$$h_j(t) = h_{0,k}(t) \times exp\,(\beta_{sport,k}\ Sport + \sum_{j=1,}^{n} \beta_{j,k}\ covariate_{j,k}) \tag{3.3}$$

where k represents the population with a healthy BMI (k=1), overweight (k=2) or obesity (k=3). For comparison reasons, we also analyzed similar models for the other four PA types in place of sport participation.

So, the 3 types of Models mentioned above were estimated for 5 different PA types. Since our main focus was on sport participation as an explanatory variable, we additionally investigated the interaction of sport participation and BMI-type in a Cox proportional hazards regression (Model 4):

$$h(t) = h_0(t) \times exp\,(\beta_{sport}\ Sport + \beta_1\ Overweight + \beta_2\ Obese + \beta_3\ Overweight * Sport + \beta_4\ Obese * Sport) \tag{3.4}$$

For each of the models, we present the hazard ratio (HR) for participating in a given PA type with a 95% confidence interval (CI) and p-values, with HRs with a p-value below 0.05 identified as statistically significant. Analysis was carried out with Stata 13 (Stata Corp. LLC, College Station, Texas, USA).

3.3. Results

Population characteristics at baseline measurement of the full dataset (for all-cause mortality) are presented in Table 3.1. Follow-up was on average 4.8 ± 2.1 years for both prediabetes and diabetes, corresponding to 258,147 and 357,913 person years of survival, respectively. For all-cause mortality, follow-up was 7.7 ± 1.6 years, corresponding to 753,197 person years. Incidence was 3,547 for prediabetes, 1,086 for diabetes and 1,379 for all-cause mortality (see also Table A3.1 in the Appendix). For all three health outcomes, the incidence rate was lowest for the healthy weight category and highest for obesity.

The all-cause mortality study group was predominantly female (58.4%) with an average age of 46.5 years at baseline. Females and middle-aged persons are over-represented compared with the general population of the Northern part of the Netherlands, but this is in line with the total population of Lifelines.(Ainsworth et al., 2011) Of the population, 43.3% was of a healthy weight (median BMI 22.9 kg/m^2), 41.0% was overweight (median BMI 26.9 kg/m^2) and 15.7% was obese (median BMI 32.4 kg/m^2). Persons with a healthy weight participated more in sport (61.9%) than overweight persons (55.3%), while less than half (46.0%) of the obese persons participated in sport.

Table 3.1: Population characteristics at baseline, for the all-cause mortality sample, by BMI category

Variable	Healthy weight (BMI 18.5-24.9 kg/m²)	Overweight (BMI 25.0-29.9 kg/m²)	Obese (BMI >= 30.0 kg/m²)	All
Observations	42,139	39,819	15,254	97,212
Sex (% female)	65.9	49.2	61.6	58.4
Age	44.3	48.2	48.0	46.5
Education				
Low (%)	22.2	32.3	39.0	29.0
High (%)	40.5	29.5	21.4	33.0
Income				
Low (< 2000 Euro, %)	23.5	22.5	28.5	23.9
High (> 3000 Euro, %)	34.8	32.9	24.3	32.3
Smoking				
Current (%)	20.1	18.9	17.7	19.2
Former, excl. current (%)	30.0	38.1	38.8	34.7
Alcohol				
No/little (< 1 glass/week, %)	15.3	15.7	25.8	17.1
Heavy (>= 5 days/week, %)	13.1	13.5	8.8	12.6
Nutrition (Lifelines Diet Score)	24.7	24.3	23.9	24.4
Leisure time (avg. min./week)	535.2	582.3	517.8	551.8
PA score per week (median)	115.6	117.5	109.4	115.4
Leisure-time PA score (median)	30.5	33.0	27.0	31.0
CVD at baseline (%)	7.9	9.5	11.3	9.1
Cancer at baseline (%)	4.6	5.3	5.2	5.0
BMI (median)	22.9	26.9	32.4	25.5
Explanatory variables				
Sport participation (any, %)	61.9	55.3	46.0	56.7
Other types of physical activity				
Cycling, not in sport (any, %)	66.3	64.5	59.8	64.5
Gardening (any, %)	56.3	58.3	51.1	56.3
Odd jobs (any, %)	40.8	48.8	40.4	44.0
Walking, not in sport (any, %)	78.2	76.7	73.4	76.8
Dependent variables				
Prediabetes (ADA) at follow-up (%)	3.4	8.1	13.3	6.5
T2DM at follow-up (ex. baseline; %)	0.5	1.6	3.9	1.4
All-cause mortality (until 2019, %)	1.0	1.7	1.8	1.4

Notes: BMI = Body Mass Index; PA = physical activity, CVD = Cardiovascular Disease; T2DM =Type 2 Diabetes Mellitus

The all-cause mortality study group was somewhat older and included relatively more higher educated and high income individuals than the full Lifelines dataset (see Table A3.2 for a more detailed breakdown of the datasets). The main reason for this is the exclusion of persons below 25 years old. For the T2DM and prediabetes study groups, the sample was to a large extent similar to the mortality study group, albeit with more females and fewer low income individuals. This is fully the result of selection based on exclusion of persons who had, at baseline, incidence or incomplete data for T2DM (exclusion of 21,071 individuals) or prediabetes (another 21,689 persons excluded). Males and low income groups are known to be more at risk for these diseases (Kavanagh et al., 2010). As with the whole Lifelines population (Klijs et al., 2015), the risks of selection bias for the subpopulations appear to be relatively small.

Table 3.2 shows the outcomes of Cox proportional hazard ratio regressions models for sport participation, as well as the other PA types, with age and sex as confounders (Model 1). In this simple model, sport participation was associated with significant reduced risks for all health outcomes, with the largest reduced risk (HR = 0.68, 95% CI 0.60 to 0.77) for T2DM. Of the other PA types, only cycling was associated with significantly lower risk for all three health outcomes.

Table 3.2 Associations between doing physical activity (PA) at baseline and prediabetes, diabetes type 2 and all-cause mortality in adults at follow-up (Model 1).

	Prediabetes	**T2DM**	**Mortality**
PA type	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Sport participation	0.74 (0.69 -0.79)**	0.68 (0.60-0.77)**	0.78 (0.70-0.87)**
Cycling	0.83 (0.77-0.89)**	0.64 (0.56-0.73)**	0.69 (0.61-0.77)**
Gardening	0.94 (0.88-1.01)	0.88 (0.77-0.99)*	0.80 (0.72-0.89)**
Odd jobs	0.95 (0.88-1.02)	1.00 (0.88-1.15)	0.91 (0.81-1.03)
Walking	0.96(0.89-1.04)	0.82 (0.71-0.94)**	0.89 (0.79-1.01)

Notes: HR = hazard ratio; CI = confidence interval. H hazard ratios for separate univariate model outcomes, adjusted for age and sex (Models 1), for 5 types of PA.
*p < 0.05, ** p < 0.01, hazard ratios compared not participating in that kind of PA.

Table 3.3 shows the outcomes of full model Cox hazards ratio regressions, including BMI type as a confounder (Model 2), for sport participation on all three health outcomes. Sport participation was associated with a significantly lower risk for prediabetes (HR=0.86, 95% CI 0.81 to 0.92). For T2DM (HR=0.88, 95% CI 0.78 to 1.00) and all-cause mortality (HR=0.91, 95% CI 0.81 to 1.01), the associated risks of sport participation were also lower, but insignificant. For prediabetes and T2DM, but not mortality, overweight and obesity were significantly associated with a much higher risk of incidence, when compared to healthy weight persons.

All of the log-rank tests of equality for the health effects sport participation had a p-value of below 0.2, indicating a potential relationship between sport participation and the health outcomes. In addition, Kaplan-Meier curves also showed lower survival rates for doing no sport than participating in sport. Of the potential covariates, being diagnosed with burn-out, total amount of PA (using the PA Score) and the amount of leisure time the log-rank tests showed p-values that were (much) higher than 0.2. It was therefore highly unlikely that these variables would contribute anything to a full model which includes other predictors. These variables were therefore excluded from these final full model (Model 3). All the other potential confounders had low p-values in the log-rank tests and therefore were included these models.

Table 3.3 Model outcomes (hazard ratios) for the associations between sport participation and prediabetes. diabetes type 2 and all-cause mortality (Model 2)

Variable	Prediabetes HR (95%CI)	T2DM HR (95%CI)	All-cause mortality HR (95%CI)
Sport participation	0.86 (0.81-0.92)**	0.88 (0.78-1.00)*	0.91 (0.81-1.01)
Sex (female)	0.52 (0.49-0.56)**	0.85 (0.75-0.97)*	0.73 (0.65-0.82)**
Age	1.03 (1.03-1.03)**	1.05 (1.04-1.05)**	1.10 (1.10-1.11)**
Current smoker	1.28 (1.17-1.41)	1.32 (1.12-1.57)**	1.94 (1.65-2.27)**
Former smoker	1.05 (0.97-1.13)	1.16 (1.01-1.33)*	1.24 (1.09-1.41)**
No/little alchohol	1.05 (0.95-1.16)	1.22 (1.05-1.43)*	1.19 (1.03-1.37)*
High alcohol	1.02 (0.93-1.12)	0.99 (0.83-1.18)	1.12 (0.98-1.28)
Lifelines Diet Score	1.00 (0.99-1.00)	0.98 (0.97-0.99)**	0.97 (0.96-0.98)**
CVD	1.21 (1.09-1.35)**	1.36 (1.15-1.92)**	1.36 (1.19-1.56)**
Cancer	1.03 (0.89-1.20)	0.81 (0.62-1.06)	2.25 (1.96-2.57)**
Subjective well-being	1.05 (1.00-1.10)*	1.35 (1.23-1.47)**	1.24 (1.15-1.34)**
Depression	1.25 (1.08-1.43)**	1.17 (0.92-1.49)	1.38 (1.11-1.71)**
Education low	1.02 (0.94-1.10)	1.13 (0.98-1.30)	0.81 (0.72-0.93)**
Education high	0.81 (0.74-0.89)**	0.98 (0.83-1.16)	0.90 (0.78-1.05)
Low income	1.04 (0.95-1.13)	1.08 (0.94-1.25)	1.17 (1.03-1.33)*
High income	1.05 (0.97-1.14)	1.06 (0.91-1.24)	0.93 (0.81-1.08)
Overweight (BMI type)	1.90 (1.81-1.99)**	2.49 (2.28-2.72) **	1.04 (0.97-1.13)
Obese (BMI type)	3.60 (3.22-4.01)**	3.89 (3.26-4.71)**	1.09 (1.01-1.19)*

*p < 0.05, ** p < 0.01

Table 3.4 shows the results of the final model (Model 3) multivariate analyses of the association with prediabetes, T2DM and all-cause mortality for sport participation, as well as other PA types, by BMI type. For *prediabetes*, sport participation was associated with risk reductions for all three BMI types. For healthy weight (HR=0.78, 95% CI 0.68 to 0.90) and overweight (HR=0.88, 95% CI 0.80 to 0.97) this reduction is significant, but not for obese persons (HR=0.90, 95% CI 0.79 to 1.03). Moreover, the difference in reduction of the prediabetes risk associated with sport participation, between persons on a healthy weight and those with obesity, was significant. Most other PA types had hazard ratios around 1, indicating no association with lower prediabetes risks. However, for persons with overweight, cycling was associated with a significantly lower risk of prediabetes.

The full model analysis of the associated risks of *T2DM* shows that sport participation is associated with lower, but not significant, T2DM risks for person with a healthy weight (HR=0.86, 95% CI 0.63 to 1.19) and overweight (HR=0.86, 95% CI 0.71 to 1.03). The HR for obesity was somewhat higher but also below 1.00 (HR=0.93, 95% CI 0.78 to 1.13). In comparison, cycling is associated with a significant lower T2DM risk for overweight persons (HR = 0.72, 95% CI 0.59 to 0.87), while also having lower hazard ratios than sport participation for the other BMI types. By contrast, the other PA types had higher HRs and were not significantly associated with lower T2DM risks for any of the BMI types.

For *all-cause mortality*, sport participation was found to be significantly associated with lower all-cause mortality risks only for persons on a healthy weight (HR=0.79, 95% CI 0.65 to

0.96). For obesity, the association of sport participation with all-cause mortality risks was even somewhat higher than for non-participants (HR=1.06, 95% CI 0.83 to 1.36). Of the other PA types, cycling was significantly associated with lower all-cause mortality risks for all BMI types and gardening for persons on a healthy weight. The largest risk reduction associated with cycling was for obese persons (HR=0.73, 95% CI 0.57 to 0.93). For persons with obesity, all other PA types are associated with non-significant, but lower all-cause mortality risks.

Finally, the outcomes of these interaction models (Model 4) for sport participation can be seen in Table 3.5 below. Compared with persons with obesity (the baseline), sport participation is associated with significant lower prediabetes risks for persons with a healthy weight. Similarly, for all-cause mortality, sport participation is associated with significant lower risks for both persons on a healthy weight and overweight. For T2DM no significant interaction effects were measured.

Table 3.4 Outcomes of the Cox proportional hazard regression models for the association of sport participation, and other types of PA, with prediabetes, T2DM and all-cause mortality (Model 3).

PA type	Healthy weight (BMI 18.5-24.9)	Overweight (BMI 25.0-29.9)	Obese (BMI[a] 30.0 and higher)
	HR (95%CI)	HR (95%CI)	HR (95%CI)
Prediabetes			
Sport participation	0.78 (0.68-0.90) **	0.88 (0.80-0.97) **	0.90 (0.79-1.03)
Cycling	1.05 (0.89–1.23)	0.89 (0.81-0.99) *	0.90 (0.78-1.04)
Gardening	0.89 (0.77-1.02)	1.06 (0.97-1.17)	0.99 (0.86-1.13)
Odd jobs	1.00 (0.86-1.16)	0.92 (0.83-1.02)	1.00 (0.87-1.16)
Walking	1.06 (0.89-1.25)	1.05 (0.94-1.17)	1.00 (0.86.1.16)
T2DM[c]			
Sport participation	0.86 (0.63-1.19)	0.86 (0.71-1.03)	0.93 (0.76-1.13)
Cycling	0.73 (0.52-1.04)	0.72 (0.59-0.87) **	0.87 (0.71-1.07)
Gardening	1.12 (0.81-1.54)	0.92 (0.76-1.10)	1.06 (0.87-1.28)
Odd jobs	0.98 (0.69-1.38)	0.89 (0.73-1.09)	1.37 (1.11-1.70) **
Walking	0.98 (0.66-1.44)	1.01 (0.82-1.25)	0.90 (0.73-1.11)
All-cause mortality			
Sport participation	0.79 (0.65-0.96)*	0.94 (0.80-1.10)	1.06 (0.83-1.36)
Cycling	0.78 (0.63-0.98)*	0.82 (0.70-0.98) *	0.73 (0.57-0.93) *
Gardening	0.77 (0.63-0.94)**	0.94 (0.80-1.10)	0.83 (0.65-1.06)
Odd jobs	0.89 (0.72-1.10)	1.00 (0.85-1.19)	0.81 (0.62-1.07)
Walking	1.00 (0.79-1.27)	1.00 (0.84-1.20)	0.83 (0.64-1.07)

Note: : hazard ratios for separate univariate models, stratified by BMI type (Models 3), for 5 types of PA. *p < 0.05, ** p < 0.01, hazard ratios compared not participating in that kind of PA.

Table 3.5: Outcomes of cox proportional interaction hazard model (Model 4) on the association of sport participation and BMI types at baseline and incidence prediabetes, T2DM and all-cause mortality in adults at follow-up.

Variable	Prediabetes		Diabetes		Mortality	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Sport participation	0.84 (0.73-0.95)	0.008	0.79 (0.65-0.96)	0.018	0.87 (0.68-1.11)	0.254
BMI type						
Overweight	2.20 (1.96-2.48)	< 0.001	3.30 (2.55-4.27)	< 0.001	1.44 (1.23-1.70)	< 0.001
Obese	3.63 (3.18-4.15)	< 0.001	7.86 (6.06-10.20)	< 0.001	1.30 (1.06-1.59)	0.011
Interaction Sport participation * BMI type						
Sport participation * healthy weight	0.78 (0.65-0.94)	0.009	0.86 (0.60-1.24)	0.433	0.60 (0.44-0.81)	0.001
Sport participation * overweight	0.92 (0.78-1.08)	0.312	0.86 (0.67-1.12)	0.267	0.75 (0.56-0.99)	0.046
Sport participation * obese	1 (reference)		1 (reference)		1 (reference)	

Note: Table shows separate univariate (i.e. no other covariates included) model outcomes with interactions between sport participation and BMI type.

3.4 Discussion

In this study, we examined the association of sport participation with prediabetes, T2DM and all-cause mortality. Our study contributes to the small, but growing, literature on the relation between sport participation and health outcomes. By including prediabetes and T2DM, our study ventured into new but interesting territory.

Our study is the first to stratify the relation of sport participation with health outcomes by BMI types. Direct comparisons with similar stratifying strategies are thus limited.

We found that sport participation is associated with significantly reduced risks for prediabetes for the healthy weight and overweight categories; and for T2DM for overweight persons. Our study also shows that sport participation improves life expectancy and the odds for prediabetes incidence significantly more for persons with a healthy weight than those with obesity. These results, as well as additional analysis with the interaction model (Model 4), demonstrate that the association between sport participation and health outcomes can differ significantly between BMI types. This somewhat contradicts the findings of Lee et al. (2014), who report HRs on the association of running with all-cause mortality for persons with a BMI below 25.0 to be similar to those with a higher BMI. However, the type of sport activity may be a factor that could explain differences in the BMI-level specific associations with health outcomes. Further analysis for sport disciplines should clarify this.

The population size and design (including actual health outcome measurements) of Lifelines and the amount of information on PA types and covariates were important strengths of our study. Although our research followed the concepts of other studies, we added several new covariates in our analysis, including a diet quality score, subjective well-being (both significant) and the amount of leisure time (not significant).

In our study, sport participation was associated with lower all-cause mortality, which is in agreement with the findings of several other studies (Andersen et al., 2000; Samitz et al., 2011). However, this finding was not statistically significant. We also compared sport participation with other PA types. Our findings suggest that sport participation may be more effective in reducing health risks than other PAs, with the exception of cycling. Cycling was associated with significant and large reductions of between 18% and 27% in all-cause mortality risk. This is somewhat higher than the 10% found in the systematic review of Kelly et al. (2014). In contrast to other research (Kelly et al., 2014), we found no evidence for a health impact of walking.

Our research has several limitations. First of all, the relatively low number of incidence, especially when stratifying for BMI types, leads to a somewhat weak statistical power of the outcomes. With more observations or a longer follow-up period, outcomes are likely to include more significant results. Second, we must take into account that BMI, sport participation and health are not independent. For instance, a high BMI can lead to reduce the possibilities to participate in (specific) sports, but also be the result of (previous) sport behavior. Therefore, sport participation is not independent from the health outcomes, and – although we control for various health indicators at baseline - conclusions about causality cannot be drawn. In addition, although BMI is a frequently used measure for assessing overweight and obesity, it does not distinguish between lean and fat mass, which is also relevant for studies examining the effect of PA. Third, the cross-sectional nature of baseline and follow-up measurement cannot account for changes in sport behavior between measurements. Given the data, we are only able to estimate the effects of doing PA at baseline and cannot estimate the effects of changes in sport or PA status. The estimated health effects may in part be affected by changes in PA. Gabrys et al. (2021) find that becoming active in sport reduces risks of cardio-metabolic diseases, while stopping increases those risks. Since decreases in PA may lead to increased risks for all-cause mortality (Huang et al., 2020) and sport participation generally declines with age (Eime et al., 2016), it is plausible that our findings are likely to be an underestimation of the health effects of sport participation for persons that keep participating, but may overestimate the health effects for 'quiters'. Fourth, we do not take the number of hours or intensity of sport participation into account, which may lead to over- or underestimation of its association with health risks. However, regarding the dose-effect relationship of sport participation, research has been ambiguous (Warburton, 2006). While some studies (Gill & Cooper, 2008; Byabasukh et al., 2019) find positive dose-response associations for PA in general, others show no dose effects (Oja et al., 2017) or even negative effects for very high volumes of PA (Pedisic et al., 2019). Fifth, we do not control for several unavailable potential confounding variables, such as DNA or diseases that may influence the health outcomes (mortality in particular). This may lead to research outcomes that are an over- or underestimation the actual association between PA and health outcomes. However, the findings presented here do seem to be robust. Models for several age-specific subgroups (such as 30+, 40+ and 50-75 year-olds) showed very similar outcomes. This is also true for when replacing the current time-specific hazard model with an age-specific hazard model (following the approach of e.g. Lamarca et al., 1998). Finally, we are aware that sport participation is very heterogenous concept, in terms of volume, intensity, type and context, and many other aspects. For BMI types there could be a selection bias, i.e. persons with a low BMI participate differently in sport and other types of sport (or PA) than obese persons (Kujala et al., 2003). Moreover, since low BMI sport participants have, for instance, a large metabolic capacity, this can both directly and indirectly (through sports) influence an individual's health risks (Karvinen et al., 2015). Further investigation of the diverse aspects of participating in sport (i.e. type, volume, intensity, etc.) is necessary to get a better understanding of the mechanisms at work between sport participation and health outcomes.

Future research, e.g. using an instrumental variables approach, should also look at the causal relationship of sport participation on health effects, especially for specific (risk-related) subpopulations. This enhances the knowledge on the health effects of sport participation for specific groups and may lead to improved, more personalized, advice on health behaviors.

3.5 Conclusion

Our research showed that sport participation is associated with reductions in the risks of prediabetes in particular , as well as T2DM and morbidity. By stratifying by BMI type, we found that the effects of sport participation on health outcomes were not similar across the population. Sport participation was associated with a significantly higher life expectation and significantly lower risks of prediabetes for persons with a healthy weight, especially compared with obese persons. Hence, sport participation seems to be most beneficial for persons on a healthy weight. Sport participation is more associated with larger reductions in health risks than all other PA types, with the exception of cycling, which seems to be especially beneficial in relation to all-cause mortality as well as for overweight persons.

These results suggest that PA advice (and guidelines) should be personalized, depending on an individual's current BMI status and health objective. For example, a person with a healthy weight may be advised to do sport for diabetes prevention, while cycling would be advisable for an overweight individual. Our findings may help to contribute to the knowledge on health effects of sport participation and PA and help to improve public health for specific subpopulations.

Appendix

Figure A3.1: Flowchart of Lifelines dataset and exclusion of study participants.

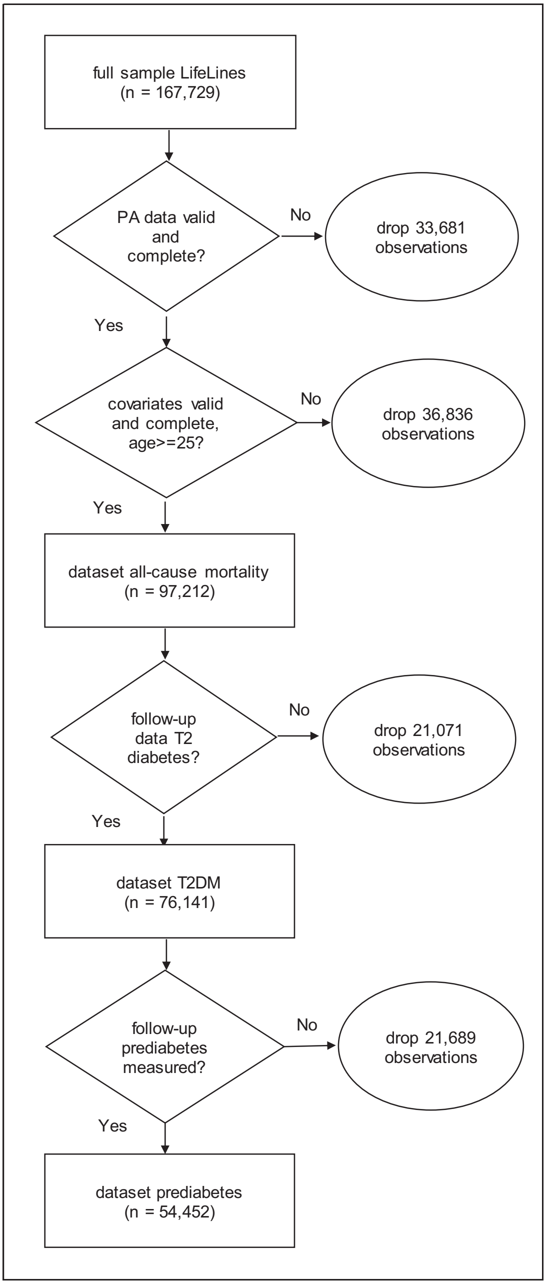

Table A3.1: Incidence of prediabetes, T2DM and all-cause mortality at follow-up, with total number of persons (cases) in datasets.

Variable	Prediabetes		T2DM		All-cause mortality	
	incidence	total cases	incidence	total cases	incidence	total cases
Full population	3,547	54,452	1,086	76,141	1,379	97,212
Sport participation	1,793	31,903	510	44,106	615	55,114
No sport participation	1,754	22,549	576	32,035	764	42,098
Other PA types (leisure time & commuting)						
Cycling	2,572	40,952	740	56,561	967	71,520
Gardening	2,113	31,424	633	43,478	798	54,740
Odd jobs	1,823	23,836	523	33,958	637	42,786
Walking	2,737	42,285	816	58,798	1,039	74,688

Table A3.2: Population characteristics at baseline, for the full Lifelines dataset and the all-cause mortality, T2DM and prediabetes subsamples, respectively

Variable	Full dataset	All-cause mortality	T2DM	Prediabetes
Observations	167,739	97,212	76,141	54,452
Sex (% female)	0.585	0.584	0.584	0.604
Age	44.6	46.5	46.3	46.2
Education				
Low (%)	0.300	0.290	0.276	0.276
High (%)	0.293	0.330	0.341	0.338
Income				
Low (< 2000 Euro, %)	0.282	0.239	0.229	0.228
High (> 3000 Euro, %)	0.288	0.323	0.333	0.330
Smoking				
Current (%)	0.214	0.192	0.184	0.180
Former, excl. current (%)	0.300	0.347	0.347	0.343
Alcohol				
No/little (< 1 glass/week, %)	0.148	0.171	0.163	0.165
Heavy (>= 5 days/week, %)	0.109	0.126	0.127	0.122
Nutrition (Lifelines Diet Score)	24.0	24.4	24.5	24.6
Leisure time (avg. min./week)	540.4	551.8	549.3	547.5
CVD at baseline (%)	0.092	0.091	0.085	0.083
Cancer at baseline (%)	0.046	0.050	0.047	0.046
BMI (median)	26.1	26.2	26.0	25.7
Sport participation (any, %)	0.565	0.567	0.579	0.586