Association between life-course leisure-time physical activity and prostate cancer

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Abstract

Objective. To evaluate the association between life-course leisure-time physical activity (PA) and prostate cancer (PC) among males living in Mexico City. **Materials and methods.** Information from 394 incident PC cases and 794 population controls matched by age (± 5 years), was analyzed. Using leisure-time PA information at different life stages, life-course PA patterns were constructed. The association between PA and PC was estimated using an unconditional logistic regression model. **Results.** Three life-course PA patterns were identified: low PA (71.0%), moderate PA (22.0%), and high PA (7.0%); this last pattern was characterized by higher levels and consistent PA practice. Compared with inactive males, those in the high PA pattern (OR: 0.50; 95%CI: 0.26-0.93) had significantly lower PC odds. **Conclusion.** Intense and regular PA could reduce the possibility of PC. These results are in accordance with PA World Health Organization recommendations.

Keywords: life-course; METS; Mexico; physical activity; prostate cancer

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Resumen

Objetivo. Evaluar la asociación entre la actividad física (AF) en la vida y el cáncer de próstata (CP) en hombres. **Material y métodos.** Se analizó la AF de 394 casos incidentes de CP y 794 controles poblacionales pareados por edad (± 5 años). Se utilizó la información de AF en diferentes etapas para generar los patrones de AF a lo largo de la vida. La asociación entre AF y CP se estimó mediante regresión logística no condicionada. **Resultados.** Se identificaron tres patrones de AF: baja (71.0%), moderada (22.0%) y alta (7.0%); este último patrón se caracterizó por una AF consistentemente mayor a lo largo de la vida. Comparado con los hombres inactivos, aquéllos en el patrón de alta AF (RM= 0.50; IC95% = 0.26-0.93) presentaron menos posibilidades de tener CP. **Conclusión.** El papel protector de la AF parece estar en función de la intensidad y regularidad de su práctica y apoyan las recomendaciones de la OMS.

Palabras clave: patrones; METs; México; actividad física; cáncer de próstata

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Prostate cancer (PC) is the second most common cancer and the fifth cause of death among men worldwide, mainly in low-and-middle-income countries.[1] Several risk factors for PC have been identified, such as age, PC family history, and African American ethnicity;[2] however, the link between PC and lifestyle factors such as physical activity (PA) is inconclusive.[3] PA is an important, modifiable, and preventive factor associated with a lower risk of colon, endometrium, and post-menopausal breast cancer.[3]

Overall, PA is associated with a 10% decrease in the risk of developing PC,[4] with differences by type of PA. Occupational PA has been consistently associated with lower PC risk,[4] while a mixed association with leisure-time PA has been observed.[5] These mixed results could be a consequence of the inability to capture the intra-individual variability in leisure-time PA that occurs across the lifespan. PA is a behavior that does not develop uniformly between individuals and its practice depends on motivation, age, sex, health, and socioeconomic status.[6,7] Longitudinal studies using finite mixture modeling confirm the existence of at least three or four different PA trajectories across the lifespan, which seem to be mainly determined during childhood and adolescence, remaining more stable during adulthood.[6]

To date, most studies have focused on the accumulated PA throughout life or in specific life stages. For instance, longitudinal studies using self-reported PA have measured it at baseline (follow-up time 3-24.8 years),[8-16] and/or accumulated as the sum of leisure-time PA over different periods.[15] In case-control studies, leisure-time PA has been evaluated at interview considering information from childhood until diagnosis/interview, generating lifetime accumulated PA,[17,18] or from adult life only.[19] Some of these studies considered the frequency, time, and/or intensity of the PA; however, none of these approaches measured the variability of PA throughout life.

Therefore, we aimed to evaluate the association between leisure-time PA and PC among males living in Mexico City, using a life-course PA approach and compare these results with those obtained through a lifetime accumulated PA approach.

Materials and methods

From November 2011 to August 2014, we conducted a population-based case-control study on males who were 42 to 94 years old and living in Mexico City for at least one year. Study details have been previously described.[20] Briefly, information was obtained from 402 incident PC cases (participation rate 85.9%), histologically confirmed, without a history of any other type of cancer, who were identified and interviewed in two secondary- and four tertiary-level hospitals in Mexico City. The PC cases were categorized according to Gleason score at diagnosis, into well-differentiated (Gleason ≤6), moderately-differentiated (Gleason =7), or poorly-differentiated (Gleason ≥8) PC.[21]

Controls (n=805) were males who were age-matched (±5 years) to cases, without a history of previous cancer or prostate diseases. Subjects reporting urological symptoms such as dysuria, hematuria, or those under clinical prostatic evaluation or who reported a prostate-specific antigen ≥4 ng/mL, were not considered as potential controls. For control selection and based on the 2005 National Households Count and Population survey, we chose 33 basic geostatistical areas in Mexico City considering the probability of finding one male ≥40 years old at these households. Ten blocks were randomly selected and starting from the northeast corner of each block all consecutive households were visited. In each home, we verified the presence of a male who met the eligibility criteria; if more than one male was found, a random selection was made to obtain just one. If the potential control was not present, we made up to three attempts to find him before searching for another control. All the interviews of controls were conducted at their homes with a participation rate of 87.5%. All subjects declining participation provided information regarding age, birthplace, marital status, and educational level.

The study was conducted according to the Helsinki Declaration and was also approved by the Ethics Committee of the National Public Health Institute (CI: 980), as well as the ethics committees of all participating hospitals.

Interview

Trained staff who were unaware of the specific study hypothesis conducted face-to-face interviews. Using a structured questionnaire, we obtained information regarding sociodemographic features, PC family history in first-degree relatives, personal history of chronic diseases as well as sexual history, PA, diet, and smoking history.

Leisure-time PA

Through a modified version of a PA questionnaire which was previously validated in Spanish speaking population[22] and used in a Mexican urban cohort,[23] we obtained information about selected leisure-time activities in four life stages: 15–18, 19–29, >30 years old, and last three years before the interview. For each stage, we requested the number of hours per day, days per week, and months per year spent carrying out the

following activities: volleyball, weightlifting, cycling, brisk walking for at least 20 minutes, dancing, aerobics, boxing, basketball, doubles tennis, cycling at a moderate speed, swimming, soccer, skating, tennis, climbing, running, and other activities (figure 1a). These activities were identified in a pilot study as the ones that are most frequently performed by Mexican males.

At each life stage, we estimated time invested in each activity separately (hour/week/year) and considering the energy expenditure stated for each activity in the PA compendium,[24] we calculated Metabolic Equivalent of Task (METs) hour/week/year for each activity. Afterward, the lifetime accumulated leisure-time PA was estimated as the sum of total METs hour/week/year across the first three (15-18, 19-29, and >30 years old) or four (previous stages plus last three years) life stages. For subjects performing any activity, the lifetime accumulated leisure-time PA was categorized into tertiles according to the controls' distribution.

Taking the total METs hour/week/year for each life stage among those males who performed at least one activity during one life stage and using KmL packages (k-means+ method) for longitudinal data in R software,[25] the individual leisure-time life-course PA patterns were constructed considering the first three or four life stages. These patterns were verified using Calinski and Harabasz's quality criteria[25] as well as using K-means++ method[26] and we obtained similar results.

Dietary, weight, and smoking information

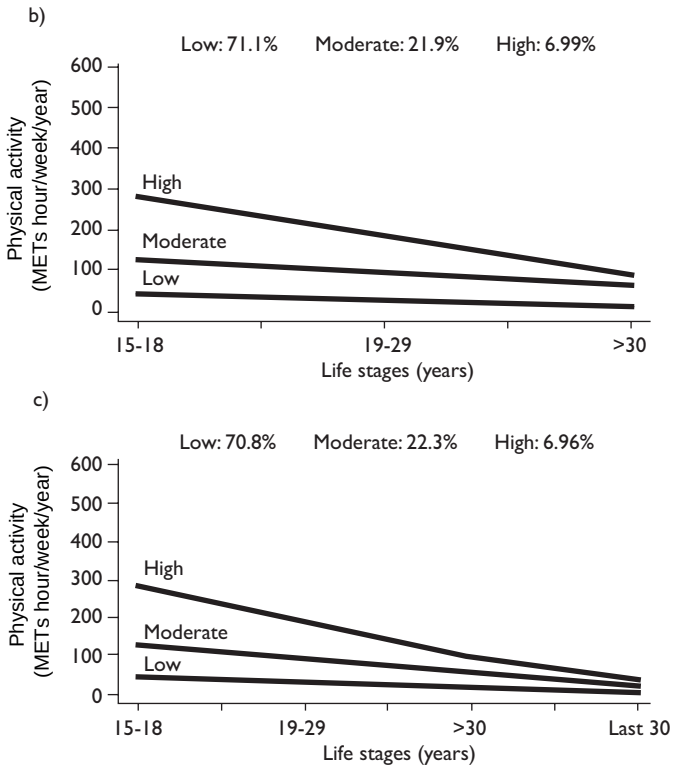
Dietary information was obtained from a validated, semi-quantitative food frequency questionnaire[27] which retrieved information on a 3-year time frame before diagnosis, for cases, or before the interview, for controls. For each food-item, reported intake frequency ranged from "never" to "up to six times per day". Using the dietary information, and the energy density approach, we calculated the Energy Dietary Inflammatory Index (E-DII).[28]

Since PC could affect weight at diagnosis, we constructed the life-course weight patterns considering the perceived body silhouette at different life stages[29] (from

a)

Intensity	Mets	Activity
Moderate	3	Volleyball
	3	Lifting
	4	Cycling
	4.3	Walking*
	5	Dancing
	5.5	Aerobics
	5.5	Boxing
Vigorous	6	Basketball
	6	Doubles tennis
	6.8	Cycling‡
	7	Swimming
	7	Football soccer
	7.3	Tennis
	8	Climbing
	8	Running

* Brisk walking for at least 20 minutes
‡ Cycling at moderate velocity



a: Physical activity according to the intensity
b: Considering three life stages 15-18 years old, 19-29 years old, and >30 years old
c: Considering four life stages 15-18 years old, 19-29 years old, >30 years old, and the last three years before the interview
Low: showed a consistently low physical activity; Moderate, presented a moderated physical activity throughout life, and High showed a higher and consistently physical activity practice
METs: Metabolic Equivalent of Task

FIGURE 1. PHYSICAL ACTIVITIES ACCORDING TO THE INTENSITY AND LEISURE-TIME LIFE-COURSE PHYSICAL ACTIVITY PATTERNS. MEXICO CITY, 2011-2014

5-50 years old): Pattern A was characterized by males who showed a weight increment throughout adolescence and held normal weight (silhouette I and II) until they were 50 years old; pattern B males had heavy weight since childhood and a small weight increase during adulthood; meanwhile, pattern C included males that had a greater weight increase throughout life and reached a state of overweight between ages 40 and 50.

Two life-course smoking patterns among ever smokers were identified: Pattern A was characterized by males who reported low and constant smoking intensity and Pattern B, which referred to males with an initial period of low smoking intensity, followed by an increase during the second stage of life.[30]

The final study population included 394 cases and 794 controls due to the exclusion of cases (n=8) and controls (n=11) with extremely low (<800 calories) or high (>4 500 calories) total energy intakes.

Statistical analysis

PA and other selected characteristics were compared between cases and controls, using Student's *t* or chi-squared test as appropriate. Unconditional logistic regression models were used to estimate the association between leisure-time life-course PA patterns or lifetime accumulated PA and PC. Males who did not perform PA were considered as the reference category. For the lifetime accumulated approach, we tested a potential monotonic trend to evaluate if increasing levels of PA were associated with lower PC.

Age was included as a covariate in all analyses. A directed acyclic graph was used to select additional variables included in the model as confounders: educational level, history of chronic diseases, life-course smoking patterns, life-course weight patterns, and E-DII. PC family history in first-degree relatives is an established risk factor for PC but not necessarily associated with PA, and thus should not be included in the model; however, we decided to adjust by this variable. Finally, among controls, we evaluated the possibility and magnitude of an exposure measurement error comparing the proportion of males categorized by lifetime accumulated PA versus the observed life-course PA patterns. All analyses were performed using Stata 15.0* and R Studio 3.6.‡

* StataCorp. Stata Stadistical Software 15.0. Collage Station, TX: Stata-Corp LLC, 2017.

‡ RStudio. RStudio 3.6.0. Boston, MA: RStudio, 2019.

Results

Mean age was similar among cases and controls (67.69±8.39 vs. 66.94±8.94); however, a higher proportion of cases reported college education (20.6 vs. 11.7%), history of chronic diseases (58.1 vs. 41.2%), PC family history (10.4 vs. 2.5%), as well as weight patterns consistent with a history of obesity or overweight (83.0 vs. 76.4%) (table I).

The most frequent activities practiced throughout life were soccer (~28%), running (~12%), and brisk walking for at least 20 minutes (~12%). Of all participants, 11.0% reported not been engaged in PA throughout their lifetime. Regardless of the number of life stages considered among males who reported any leisure-time PA in at least one life stage (89.0%), three PA patterns throughout life were identified (figure 1b-1c): low PA (71.0%), moderate PA (22.0%), and high PA (7.0%) patterns. Independently of case and control condition, the highest activity level was observed between ages 15-18 years (table II).

Table III shows the adjusted association between PA approaches and PC. Compared to non-active males, those physically active (Low – High patterns) have a decrease in PC odds ($OR_{Pattern\ low\text{-}high\ vs.\ inactive} = 0.60$; 95%CI = 0.41-0.89). However, the main decrease was observed among males who performed higher and consistent PA levels throughout life (OR = 0.50; 95%CI = 0.26-0.93). Using the lifetime accumulated approach of three or four life stages, PA was inversely associated with PC in the first and second tertile, but not in the highest accumulated PA tertile (table III). We did not observe a monotonic trend of accumulated PA and PC.

Comparison between PA approaches among controls (table IV) highlights the fact that the highest category of lifetime accumulated PA, considering three or four life stages, is a mixture of the three PA patterns, where the highest proportion corresponds to moderate PA pattern. Meanwhile, the low PA pattern has a different proportion of subjects classified across the three categories of lifetime accumulated leisure-time PA.

Discussion

We aimed to evaluate the association between leisure-time PA and PC among males living in Mexico City. Using a life-course PA approach, we identified three different PA patterns and those males who performed higher and had consistent PA levels throughout their life had lower PC odds. Meanwhile, the lifetime accumulated PA approach did not show a clear inverse dose-response relationship because the highest category was a mixture of the three different life-course PA patterns.

Table I
SELECTED CHARACTERISTICS OF THE STUDY POPULATION ACCORDING TO CASE AND CONTROL STATUS. MEXICO CITY, 2011-2014

Characteristics	*Cases (n=394)*	*Controls (n=794)*	*p value**
Age (years old)			
Mean ± SD	67.69 ± 8.39	66.94 ± 8.94	0.17
Marital status (%)			
Not united	90 (22.8)	158 (19.9)	0.24
United‡	304 (77.2)	636 (80.1)	
Education level (%)			
Elementary school or lower	177 (44.9)	358 (45.1)	<0.001
Junior high school	66 (16.7)	199 (25.1)	
High school	70 (17.8)	144 (18.1)	
College education or higher	81 (20.6)	93 (11.7)	
Life-course smoking (%)§			
Never	128 (32.5)	261 (32.9)	<0.42
A	228 (57.9)	474 (59.7)	
B	38 (9.6)	59 (7.4)	
History of chronic diseases (%)#			
No	165 (41.9)	467 (58.8)	<0.001
Yes	229 (58.1)	327 (41.2)	
Family history of prostate cancer (%)&			
No	353 (89.6)	774 (97.5)	<0.001
Yes	41 (10.4)	20 (2.5)	
Life-course weight (%)≠			
A	67 (17.0)	187 (23.6)	0.02
B	200 (50.8)	352 (44.4)	
C	127 (32.2)	254 (32.0)	
Energy adjusted dietary inflammatory index			
Mean ± SD	0.43 ± 1.60	0.52 ± 1.53	0.35

* t test and chi^2
‡ United: Married and common law
§ Life-course smoking patterns among ever smokers: Pattern A characterized by males who reported low and constanst smoking intensity and Pattern B, males with an initial period of low smoking intensity, followed by an increase during the second life stage
# Hypertension, diabetes or dyslipidemia
& Family history of prostate cancer in first degree relatives
≠ Life-course weight: Pattern A characterized by males that showed a weight increment throughout adolescent and held normal weight (silhouette I and II) until 50 years old; pattern B males that showed high weight from childhood and small weight increase since adulthood; meanwhile pattern C included males that had the greater weight increase throughout life and reached overweight between 40 and 50 years old. Patterns B or C are considered as an indicator of obesity

Comparing our results to other studies is difficult because, to our knowledge, this is the first study that used a life-course approach to evaluate the association between PA and PC. However, our findings are partially congruent with those from other studies. In a prospective study in which three groups of PA patterns were identified (maintainers, increasers, and decreasers), a significant decrease in cancer-related mortality was observed among males classified as PA maintainers.[31] A prospective cohort study that evaluated PA using lifetime accumulated PA at different ages (current, 30, and 50 years), found a significant PC risk reduction associated only with the fourth quartile of accumulated PA.[15] Meanwhile, results from two population-based case-control studies carried out in Canada[17] and Australia[18] that evaluated different life stages and kinds of PA, suggest that the major protective association between PA and PC occurs in early life stages and mainly in individuals who carried out vigorous PA; moderate-intensity PA was not associated with PC odds reduction.

Our life-course PA patterns suggest the importance of regular PA practice throughout life and the reported anti-carcinogenic mechanisms seem to support this finding. For example, a single bout of PA has shown to

Table II

Average physical activity at life stages considering leisure-time life-course physical activity pattern among cases and controls. Mexico City, 2011-2014

Life stages	Physical activity patterns throughout life* (METs/hour/week/year)					
	Low PA		Moderate PA		High PA	
	Cases Mean ± SD (n=215)	Controls Mean ± SD (n=524)	Cases Mean ± SD (n=96)	Controls Mean ± SD (n=139)	Cases Mean ± SD (n=25)	Controls Mean ± SD (n=57)
Considering three life stages (years old)						
15-18	43.76 ± 30.44	44.10 ± 28.87	127.72 ± 45.60	120.72 ± 53.86	253.78 ± 70.41	287.43 ± 85.07
19-29	31.29 ± 27.78	26.98 ± 24.43	104.32 ± 49.35	90.56 ± 44.34	177.97 ± 95.20	187.79 ± 94.14
>30	19.06 ± 24.31	11.60 ± 20.71	74.31 ± 58.64	54.21 ± 61.52	85.01 ± 90.22	85.44 ± 99.59
% change‡	56.44	73.70	41.82	55.09	66.50	70.27
Considering four life stages (years old)	(n=214)	(n=523)	(n=97)	(n=142)	(n=27)	(n=57)
15-18	42.67 ± 30.08	43.83 ± 28.77	126.12 ± 45.80	119.49 ± 54.38	246.23 ± 73.12	287.43 ± 85.07
19-29	31.16 ± 27.90	26.75 ± 24.28	99.81 ± 49.33	89.71 ± 44.59	179.33 ± 91.84	187.79 ± 94.14
>30	18.27 ± 23.44	11.18 ± 19.28	72.50 ± 57.76	54.71 ± 61.95	89.36 ± 88.39	85.44 ± 99.59
Last three years before the interview	9.98 ± 19.03	5.12 ± 16.15	28.30 ± 34.45	23.75 ± 45.43	35.19 ± 50.94	35.43 ± 42.02
% change‡	76.61	88.32	77.56	80.12	85.71	87.67

* Pattern low showed a consistently low physical activity; Pattern moderate presented a moderated physical activity throughout life, and Pattern high showed a higher and consistently physical activity practice

‡ Physical activity at >30 years old vs. at 15-18 years old or physical activity at last three years vs. at 15-18 years old. All changes were significant $p<0.01$

METs: Metabolic Equivalent of Task

PA: physical activity

increase insulin sensitivity for about 60 hours.[5] Consistent PA practice decreases serum insulin-like growth factor I (IGF-I),[5] and as a result, the liver production of Sex Hormone Binding Globulin (SHBG) increases, reducing testosterone and estradiol serum levels.[32] Low serum IGF-I stimulates p53 activity, which could regulate cell growth and facilitate apoptosis.[32] Another anti-proliferative effect appears to be mediated by activin, inhibin, and myostatin, which are produced by skeletal muscles during PA. Activin could arrest PC cell growth by blocking the cell cycle (cells in G_0/G_1 or G_2/M), which could be further enhanced by inhibin. Myostatin facilitates tumor cell apoptosis through a metabolic change from oxidative phosphorylation to glycolysis.[33] Additionally, other PA anti-inflammatory and anti-carcinogenic mechanisms could explain this association.[33,34]

For an adequate interpretation of these results, some methodological aspects need to be considered. We do not reject the possibility that our results could be underestimated; self-report tends to underestimate PA practice and we did not consider occupational, household, or transportation activities. Nevertheless, when only moderate or high-intensity activities are considered, leisure-time PA is the main contributor to total PA[35] and there is evidence that on average, Mexican men devote less time to household activities than women (10.76 ± 10.61 vs. 38.91 ± 20.04).[36] PA practice is highly variable, and subjects could have had problems recalling it; however, we consider it unlikely that our results could be a consequence of recall bias since both participants and interviewers were not aware of the specific study hypotheses. In addition, we performed a sensitivity analysis excluding eighteen cases that considered the lack of PA as a potential PC risk and the association remained in the same direction and magnitude.

Compared to the lifetime accumulated leisure-time PA, life-course PA patterns seem to discriminate the regularity and variability of PA throughout life (table IV). Although to our knowledge this is the first study that estimated life-course PA patterns in the Mexican population, the number of PA patterns and their characteristics were similar to those reported in longitudinal studies at different life stages.[6] Finally, the third life stage has a wide age range and this could affect our results if the recent PA were the most relevant one for prostate carcinogenesis, or if PA practice significantly increases during this life stage. Nevertheless, there is evidence that stable PA trajectories

Table III

CASE-CONTROL DISTRIBUTION AND ASSOCIATION BETWEEN THE LEISURE-TIME PHYSICAL ACTIVITY APPROACHES (LIFE-COURSE PATTERNS AND LIFETIME ACCUMULATED) WITH PROSTATE CANCER. MEXICO CITY, 2011-2014

Physical activity	*Cases* *(n=394)* *(%)*	*Controls* *(n=794)* *(%)*	*All* *OR* (95%CI)*
Life-course patterns‡,§			
None	58 (14.7)	74 (9.3)	1.00
Low	215 (54.6)	524 (66.0)	0.54 (0.36-0.81)
Moderate	96 (24.4)	139 (17.5)	0.90 (0.57-1.42)
High	25 (6.4)	57 (7.2)	0.50 (0.26-0.93)
Lifetime accumulated§			
None	58 (14.7)	74 (9.3)	1.00
≤ 71.89	79 (20.1)	242 (30.5)	0.44 (0.28-0.68)
71.90-150.97	103 (26.1)	239 (30.1)	0.58 (0.37-0.89)
≥ 150.98	154 (39.1)	239 (30.1)	0.84 (0.55-1.29)
			p for trend 0.21
Life-course patterns‡,#			
None	56 (14.2)	72 (9.1)	1.00
Low	214 (54.3)	523 (65.9)	0.54 (0.36-0.81)
Moderate	97 (24.6)	142 (17.9)	0.89 (0.56-1.41)
High	27 (6.9)	57 (7.2)	0.55 (0.29-1.01)
Lifetime accumulated#			
None	56 (14.2)	72 (9.1)	1.00
≤ 76.49	79 (20.1)	242 (30.5)	0.44 (0.28-0.69)
76.50-162.95	106 (26.9)	240 (30.2)	0.59 (0.38-0.91)
≥ 162.96	153 (38.8)	240 (30.2)	0.82 (0.54-1.27)
			p for trend 0.26

* Adjusted by age, education level, PC family history in first degree relatives, history of chronic diseases, life-course smoking patterns among ever smokers, life-course weight patterns, and energy-adjusted dietary inflammatory index

‡ Pattern low showed a consistently low physical activity; Pattern moderate presented a moderated physical activity throughout life, and Pattern high showed a higher and consistently physical activity practice

§ METs/hour/week/year considering three life stages 15-18 years old, 19-29 years old, and >30 years old

METs/hour/week/year considering four life stages 15-18 years old, 19-29 years old, >30 years old, and the last three years before the interview

METs: Metabolic Equivalent of Task

are the most prevalent during the middle and oldest life stages[6] and we obtained similar PA patterns when we considered three or four life stages.

Participation rates between cases and controls were similar (85.9 vs. 87.5%), and we did not find differences in sociodemographic characteristics between males who agreed or did not agree to participate in the study.[20] The lack of information about PA trajectories in the Mexican population limited our ability to assess if the prevalence of life-course PA patterns among controls is representative of the population prevalence. Nevertheless, some cross-sectional studies suggest that PA decreases with increasing age[37,38] and our accumulated prevalence of physical inactivity was like that reported for Mexican males who were ≥ 15 years old (31.0 vs. 37.1 %).[37] Regarding the sample size, this limited our ability to identify a significant association between PA patterns and PC differentiation, as well as to detect the possible existence of an additional PA pattern. The moderate pattern could be a mixture of at least two different PA patterns; this limitation, could be a possible explanation for the lack of association observed between this pattern and PC. Although our final models were adjusted by the main known PC risk factors, we do not rule out the possibility of residual confounding. We did not have information about alcohol consumption, and it has been positively associated with both increasing and decreasing PA trajectories[18] as well as with PC risk.[39]

Table IV

Comparison between lifetime accumulated and leisure-time life-course physical activity among controls. Mexico City, 2011-2014

Leisure-time physical activity	Life course PA pattern					
	Low*		Moderate*		High*	
	n (%)	Median (Min-Max)	n (%)	Median (Min-Max)	n (%)	Median (Min-Max)
Lifetime accumulated‡						
≤ 71.89	242(100.0)	41.66 (3.16-71.89)	0 (0.0)	---	0 (0.0)	---
71.90-150.97	239(100.0)	108.71 (72.13-150.97)	0 (0.0)	---	0 (0.0)	---
≥ 150.98	43(18.0)	168.96 (151.93-221.39)	139 (58.2)	265.49 (164.00-520.62)	57(23.8)	560.65 (344.96-1137.38)§
Lifetime accumulated#						
≤ 76.49	242(100.0)	43.03 (3.16-76.09)	0 (0.0)	---	0 (0.0)	---
76.50-162.95	240(100.0)	113.80 (77.40-162.95)	0 (0.0)	---	0 (0.0)	---
≥ 162.96	41(17.1)	188.02 (165.35-246.11)	142(59.2)	287.66 (164.00-790.36)	57(23.7)	596.09 (355.27-1145.11)§

* Pattern low showed a consistently low physical activity; Pattern moderate presented a moderated physical activity throughout life, and Pattern high showed a higher and consistently physical activity practice
‡ METs/hour/week/year considering three life stages 15-18 years old, 19-29 years old, and >30 years old
§ Wilcoxon rank-sum test p<0.01
# METs/hour/week/year considering four life stages 15-18 years old, 19-29 years old, >30 years old, and the last three years before the interview
METs: Metabolic Equivalent of Task
PA: physical activity

Conclusion

Our results do not suggest the existence of a sensitive period; nevertheless, PA protection against PC seems to be the result of an accumulative effect throughout life. PA World Health Organization recommendations [150 minutes of moderate PA (brisk walking) or 75 minutes of vigorous PA (soccer) per week] are enough to achieve the average levels observed in the high PA pattern at different ages. However, our results highlight the importance of promoting this habit throughout life, starting from adolescence or childhood. From a research standpoint, the leisure-time life-course PA approach seems to reduce misclassification errors and our results should be validated using prospective studies with a larger sample size.

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