Association between recorded physical activity and cancer progression or mortality in individuals diagnosed with cancer in South Africa

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bjsports-2024-108813).

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Accepted 22 November 2024

ABSTRACT

Objectives This study aimed to determine the association between progression and mortality in individuals with stage 1 cancer and their recorded physical activity before the diagnosis of the cancer.
Methods We included 28 248 members with stage 1 cancers enrolled in an oncology programme in South Africa. Physical activity was recorded using fitness devices, logged gym sessions and participation in organised fitness events. Levels of physical activity over the 12 months before cancer diagnosis were categorised as no physical activity, low physical activity (an average of <60 min/week) and moderate to high physical activity (≥60 min/week). Measured outcomes were time to progression, time to death and all cause mortality.
Results Physically active members showed lower rates of cancer progression and lower rates of death from all causes. The HR for progression to higher stages or death was 0.84 (95% CI 0.79 to 0.89), comparing low activity with no physical activity, and 0.73 (95% CI 0.70 to 0.77), comparing medium to high physical activity with no physical activity. The HR for all cause mortality was 0.67 (95% CI 0.61 to 0.74), comparing low physical activity with no activity, and 0.53 (95% CI 0.50 to 0.58), comparing medium to high physical activity with no physical activity.
Conclusions Individuals engaging in any level of recorded physical activity showed a reduced risk of cancer progression or mortality than those not physically active. There was a further reduction among individuals with moderate to high levels of physical activity compared with those with lower levels.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Physical activity plays a significant role in preventing cancer and reducing mortality.

WHAT THIS STUDY ADDS

⇒ Being physically active before the diagnosis of cancer reduced the risk of cancer progression or mortality.
⇒ Individuals who engaged in higher levels of physical activity had a lower rate of progression and death compared with individuals with lower levels of physical activity or no recorded physical activity.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Public health guidelines should encourage individuals to engage in physical activity to not only prevent cancer but to mitigate the risk of cancer progression.
⇒ Individuals diagnosed with cancer should be encouraged by health care professionals to engage in physical activity to levels tolerated by the individual.

INTRODUCTION

Cancer is a leading cause of premature mortality worldwide.[1] It is estimated that in 2019 and 2020, approximately 10 million deaths each year were attributable to cancer globally.[2] According to the International Agency for Research on Cancer, 56 802 cancer deaths were recorded in South Africa in 2020.[3] The five leading causes of cancer mortality in South Africa were lung, cervical, breast, prostate and oesophageal cancers.[3] It is estimated that 30–40% of cancers are preventable by addressing environmental and modifiable lifestyle risk factors, such as smoking, poor dietary patterns, obesity and physical inactivity.[4] In people already diagnosed with cancer, the risk of progression, recurrence and death may also be affected by similar modifiable risk factors.[5]

There is compelling evidence that moderate to vigorous levels of physical activity play a significant role in reducing cancer mortality.[6–8] High levels of physical activity compared with lower levels in pre-and/or post-diagnosed cancer patients have been associated with an 18% reduction in cancer specific mortality.[7] A systematic review by the US Physical Activity Guidelines Advisory Committee in 2018 found a 40–50% relative risk reduction in mortality from breast, colon and prostate cancers when comparing high versus low levels of physical activity.[9] Moreover, there is plausible evidence that the highest level of physical activity is associated with an 11% reduction in the incidence of cancer compared with the lowest level.[10] However, the impact of physical activity on cancer incidence, recurrence and mortality requires an expanded analysis of dose, type, duration and intensity of physical activity.[5]

Although substantial evidence suggests that physical activity is associated with a decrease in cancer incidence and mortality,[6 11 12] studies to date have

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To cite: Mabena N, Rugbeer N, Lehmann S, *et al*. *Br J Sports Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjsports-2024-108813

acknowledged several methodological limitations, including self-reported physical activity, inadequate information on duration and forms of physical activity and insufficient data pertaining to the types of cancer most responsive to physical activity.[6 11 12]

Also, there are limited epidemiological data on modifiable risk factors influencing cancer progression in an African context. Countries in sub-Saharan Africa have been undergoing a major economic, demographic and epidemiological transition, resulting in a rising incidence of non-communicable chronic diseases, including cancer.[13] This rise in non-communicable chronic diseases is adding to the already heavy burden of infectious diseases, malnutrition and perinatal diseases. Based on data from Global Burden Disease, it is estimated that neoplasms contributed 11.2% (approximately 16·9 million) to disability life years in sub-Saharan Africa in 2017, with cervical and breast cancer the leading causes. The recorded incidence of cancer in sub-Saharan Africa has doubled in the past 30 years.[14]

We conducted a retrospective longitudinal cohort analysis of the association between recorded physical activity levels before the diagnosis of cancer and progression of cancer and mortality among members of a South African health plan who had been diagnosed with stage 1 cancers and were registered with the plan's oncology programme.

METHODS

Data source

Permission for use of anonymised medical and physical activity data from the Discovery Health Medical Scheme (DHMS) was obtained from the research governance committee of DHMS.

Setting

This study was conducted with anonymised client data from Discovery Health and Vitality. DHMS is the largest open medical plan in South Africa, covering approximately 2.8 million beneficiaries.[15] All members diagnosed with cancer receive comprehensive treatment cover on the oncology care programme of DHMS.

Vitality is a voluntary health promotion and behavioural change programme linked to DHMS that encourages and rewards members for engaging in healthy lifestyle behaviours.[16 17] Specifically, Vitality members earn points for engaging in physical activity. A summary of point allocations is listed in online supplemental file 1. Points are awarded for physical activity recorded via wearable fitness devices, clocked gym attendance or registered mass sports event participation. The Vitality programme allows for the measurement of activity type, frequency, duration and intensity for most recorded activities. Vitality activity points are awarded for both duration and intensity of exercise (see online supplemental file 1) and reflected as equivalent weekly minutes of exercise in table 1. For activities recorded by wearable devices such as Apple or Garmin watches, actual duration and intensity of activities are obtained from the device and transferred by a systems link to the Vitality Active Rewards App.[16] Distance and duration are also recorded by organised fitness events. For gym visits, the minimum duration of activity is based on swiping a Vitality linked membership card on entering and leaving the gym.

Table 1 Distribution of members by recorded physical activity

Physical activity group	No (%) of members	Recorded physical activity (min/week)
None	17 457 (61.80)	0
Low	3722 (13.18)	1–59
Moderate to high	7069 (25.02)	≥60

Study cohort

The study cohort included purposively sampled members who were enrolled in the Discovery Health Oncology Programme during the period from January 2008 to October 2022 and who were also members of Vitality. Members had to have been diagnosed with stage 1 cancer. Individuals who were initially diagnosed with stage 2 or higher cancers were excluded because of concerns regarding the influence of the greater burden of illness on physical activity (ie, reverse causality) at these higher stages. Only individuals on the Vitality programme for a minimum of 12 months before the diagnosis of cancer were included in the study. A 12 month period before diagnosis was chosen to eliminate any bias related to the variable physical and psychological effects of cancer, or its treatment, on physical activity levels after diagnosis.

Even though the analysis considered only stage 1 diagnoses, there remained a concern that some individuals may have reduced their physical activity before diagnosis because of the disease process. To address this concern we performed a subanalysis of the cohort excluding those cancers, such as haematological cancers, where there was a greater risk of the disease affecting physical activity before diagnosis. This subset is referred to as the reduced subset cohort and is included in the addendum. A separate analysis excluded individuals with these cancers from the sample to control for this risk. A further examination of this concern, also presented in the appendix, considered physical activity levels in the period from 13 to 24 months before the initial diagnosis. Separate analyses were also performed on the three largest cancer diagnosis groups (prostate, breast and skin) as the sample sizes were sufficient to perform the analysis.

Study design

The study adopted a retrospective longitudinal observational design that used historical Discovery Health (from January 2008 to October 2022) and Vitality data (from January 2007 to October 2022) of members who were registered with the Discovery Health Oncology Programme and who were also members of Vitality. The mean duration of Vitality membership of those included in the study was 114 months. Discovery Health receives information and claims from providers for approval of payments for consultations, investigations and treatment. Engagement with physical activity in the Vitality programme is recorded as described above.

The study cohort was divided into three groups based on levels of physical activity: no physical activity, low physical activity and moderate to high physical activity (table 1). The no physical activity cohort was comprised of members who did not record any physical activity points over the 12 months before diagnosis (ie, those engaging in no recorded physical activity per week). Members who recorded an average of 1–400 physical activity points/week over the 12 months before diagnosis were categorised as low physical activity (these members were assessed as engaging in <60 min of at least moderate intensity physical activity per week), while members who had an average of >400 physical activity points/week were categorised as moderate to high levels of physical activity (ie, those engaging in ≥60 min of at least moderate intensity physical activity per week). Note that 400 points/week is equivalent to two 30 min sessions of moderate intensity activity per week. These categories are based on the distribution of recorded physical activity data for the cohort under study rather than specific international guidelines, such as the American College of Sports Medicine,[18] which recommends at least 150–300 min of moderate and vigorous activity to reduce the incidence or mortality from cancer.[19]

The covariates included in the analysis were age (in years) at diagnosis (age groups <36, 36–45, 46–55, 56–65 and >65 years), sex and socioeconomic status (SES). Covariates were selected based on a theoretical relationship to both the main exposure variable and study outcome. The decision to categorise the age variable was based on previous experience which indicated a complex non-linear relationship between age and cancer risk. In general, categorising data reduces the level of information and can unnecessarily reduce the quality of the covariate.[20 21] To evaluate the potential impact, a separate analysis considered a combination of a linear and exponential curve (which mapped closely to the risk relationship identified in the data) for the age relationship. Included in the addendum, the results for physical activity are almost identical to the results using age in categories.

SES was based on a combination of factors, including residential address, Discovery Health plan type, Discovery Life plan type and other forms of insurance held with Discovery. Based on these factors, members were categorised into low, medium and high SES. The analysis was further adjusted for comorbidities and patient complexity, as measured by the Johns Hopkins Adjusted Clinical Groups Systems software.[22] The Adjusted Clinical Groups software assigns a six level (low to high) simplified morbidity category, termed resource utilisation band (RUB), to each patient. The RUB value of a member was defined as the average RUB value calculated over the 12 months before the member was diagnosed with cancer. Members who had an average RUB value of 0–2 were grouped to create one category to offset exposure concerns (ie, to avoid bias and to achieve statistical significance, which may not have been possible had we considered RUB 0, RUB 1 and RUB 2 separately due to the small sizes of these groups). Thus the analysis included four RUB categories: RUB (0–2), RUB 3, RUB 4 and RUB 5.

Body mass index (BMI) was initially considered as a predictor variable to be included in the model; however, due to the availability of BMI measurements for only a minority of members (17.5%), this variable was not included in the primary analysis. A secondary analysis considered only the 17.5% of respondents for whom a BMI measurement was available. While race and ethnicity may influence cancer incidence and, possibly progression, it was not included in this analysis as the DHMS does not ask members to identify by race.

Outcomes were defined by stage of cancer of members in the measured period following their initial diagnosis, and the time to a progression in stage if it occurred. If a member progressed to a higher stage or died during the study period, the number of months that had passed since the initial diagnosis was recorded and the member was included in the progressed group. If a member progressed to a higher stage and then later died, both dates were recorded and they appeared as a case in both analyses. If the end of the investigation period arrived or the member left the scheme before progression occurred, then the number of months since the initial stage 1 diagnosis was recorded and the member was treated as censored. The period between diagnosis and change in status or end of/exit from the study ranged from 1 to 154 months (12 years and 10 months). The study did not differentiate between causes of death in every case. For the 80.2% of the sample where the cause of death was available, 81.8% were directly related to cancer and a further 17.0% were related to other disease processes. The remainder, except for a one known accidental death, were due to complications associated with cancer treatment.

Statistical analysis

The data were analysed using R (V.4.3.2). Two extended Cox proportional hazards models[23] were used to estimate the association between physical activity and time-to-event outcomes: (a) time to progression to a higher stage or death and (b) time to death. Each subject had the 0 month start set at the date of the first diagnosis at stage 1 cancer. The end time was determined by the date of death/progression (measured in months since diagnosis) or the end of the study or the date (in rare instances) when the subject resigned from DHMS.

We examined the proportional hazards assumption using the Schoenfield residuals from the standard Cox model.[23] To handle non-proportionality, we divided the time post-diagnosis into groups and included the time group as a stratifying variable for affected covariates in the modified Cox model.[23] The primary variable of concern (physical activity level) did not show any substantive deviations from the proportional hazards assumption. The same tests, applied to the reduced subset cohort, did not show substantive deviations from the proportional hazards assumption.

We examined the direction and magnitude of the association between physical activity levels and outcomes. Using the parameter estimates of the model, a set of predicted survival curves for each of the three physical activity levels was derived. The sample size of 28 248, including all individuals who met the relevant criteria, appeared sufficient to provide reliable estimates of the effects. A simplified power calculation (ignoring covariates) indicated that the sample would have a 96% chance of giving a significant effect for no exercise versus some exercise in the time-to-death model, and a 99.8% chance in the time-to-progression to higher stage or death model.

Equity, diversity and inclusion statement

Our author group consisted of five women and six men of different ethnicities, from five institutions across three countries. The investigators included both senior and junior researchers with a range of research experience, integrating different disciplines (sport and exercise medicine, exercise physiology, epidemiology and biostatistics, actuarial science, public health

Table 2 Cancer types accounting for 80% of all cancers included in the study

Cancer type	Members (%)	Included in reduced subset cohort
Breast in women	22.5	Yes
Prostate	21.4	Yes
Skin cancers	11.5	Yes
Lymphatic and haematopoietic	3.7	No
Colon and rectum	3.6	Yes
Urinary	3.2	Yes
Thyroid	2.6	No
Central nervous system	2.4	Yes
Malignant multiple myeloma	2.0	No
Lungs, bronchi or mediastinum	2.0	Yes
Leukaemia	1.6	No
Ovarian	1.4	Yes
Cervix and uterine	1.3	Yes
Hodgkin's lymphoma	1.3	No

Table 3 Demographic profile of members across physical activity categories

	Physical activity			
	No	Low	Moderate to high	Total
Women	8605 (49.29)	1891 (50.81)	3112 (44.02)	13 608
Men	8852 (50.71)	1831 (49.19)	3957 (55.98)	14 640
Age <36 years	1532 (8.78)	413 (11.1)	583 (8.25)	2528
Age 36–45 years	1692 (9.69)	702 (18.86)	1094 (15.48)	3488
Age 46–55 years	3100 (17.76)	939 (25.23)	1670 (23.62)	5709
Age 56–65 years	4931 (28.25)	927 (24.91)	2033 (28.76)	7891
Age >65 years	6202 (35.53)	741 (19.91)	1689 (23.89)	8632
RUB (0–2)	2005 (11.49)	488 (13.11)	930 (13.16)	3423
RUB 3	7630 (43.71)	1 741 (46.78)	3601 (50.94)	12 972
RUB 4	5477 (31.37)	1124 (30.2)	1954 (27.64)	8555
RUB 5	2345 (13.43)	369 (9.91)	584 (8.26)	3298
Low SES	1258 (7.21)	150 (4.03)	213 (3.01)	1621
Moderate SES	10 312 (59.07)	1809 (48.6)	3263 (46.16)	15 384
High SES	5887 (33.72)	1763 (47.37)	3593 (50.83)	11 243
Missing BMI	15 919 (91.19)	3004 (80.71)	4356 (61.62)	23 279
Low BMI	30 (0.17)	11 (0.3)	41 (0.58)	82
Normal BMI	456 (2.61)	264 (7.09)	1098 (15.53)	1818
High BMI	591 (3.39)	248 (6.66)	1103 (15.6)	1942
Obese BMI	461 (2.64)	195 (5.24)	471 (6.66)	1127
No progression	10 796 (61.84)	2609 (70.1)	5098 (72.12)	18 503
Progression	6661 (38.16)	1113 (29.9)	1971 (27.88)	9745
Survived	13 459 (77.1)	3232 (86.84)	6246 (88.36)	22 937
Died	3998 (22.9)	490 (13.16)	823 (11.64)	5311

Values are number (%).
BMI, body mass index; RUB, resource utilisation band; SES, socioeconomic status.

and primary care). The study cohort spanned different socioeconomic groups and both sexes.

RESULTS

A total of 28 248 Discovery Health members on the oncology programme were considered eligible for inclusion. Most members had no recorded physical activity (61.80%); however, more members performed moderate to high physical activity (25.02%) compared with low physical activity (13.18%) (table 1). Table 2 shows the percentages of cancers that accounted for 80% of all cancers included in the study. Breast cancer in women and prostate cancer were the most common cancers, together accounting for 44% of all cancers. In the reduced subset cohort, to control for the risk of reverse causality, 22 676 members were included; table 2 highlights which members were excluded.

Table 3 shows the demographic profile of members by level of physical activity. Of the total population considered in the study, 65.5% did not progress to higher TNM (tumour, node, metastases) stages after being diagnosed at stage 1, while 34.5% progressed to higher TNM stages. In addition, 81.2% of the sample survived and 18.8% died within the period of the study.

Median time to death was 20 (IQR 7–45) months and median time to progression or death was 7 (IQR 2–25) months. For members who did not die, median time to censoring was 54 (IQR 27–89) months and, for those who did not progress to higher stages, median time to censoring was 54 (IQR 26–89) months. Of the 28 248 subjects, 70.7% were censored because they survived until the end of the study, while 10.5% were censored because they left the scheme before the end of the period, and 18.8% died.

Table 4 shows the statistical significance of the covariate effects for the models. All outcomes were statistically significant and, in particular, the level of physical activity was a significant predictor after accounting for the other covariates for both cancer progression (χ^2=149.6, df=2, p<0.0001) and all cause mortality model (χ^2=290.9, df=2, p<0.0001). In equivalent models fitted using the subset of the sample that had a BMI measurement and adjusting for BMI (see addendum), physical activity association was significant for both cancer progression (χ^2=20.1, df=2, p<0.0001) and all cause mortality (χ^2=49.2, df=2, p<0.0001). In addition, the model fitted on the reduced subset cohort (addendum) also showed a significant physical activity benefit for both cancer progression (χ^2=126.2, df=2, p<0.0001) and all cause mortality models (χ^2=245.66, df=2, p<0.0001). Analysis of the three most common cancers (detailed in the addendum) indicated statistical significance for the effect of physical activity. All p values were <0.0001 except for the cancer progression model for the prostate cancer group (χ^2=8.20, df=2, p=0.0166).

Table 4 Significance of model parameters for cancer progression and all cause mortality models

	Cancer progression			All cause mortality		
Effect	χ^2	df	P value	χ^2	df	P value
Age group (stratified)	511.42	32	<0.0001	595.33	32	<0.0001
RUB group (stratified)	322.90	24	<0.0001	720.21	24	<0.0001
Sex (stratified)	105.81	8	<0.0001	70.95	8	<0.0001
SES*	63.49	2	<0.0001	102.82	16	<0.0001
Physical activity	149.60	2	<0.0001	290.92	2	<0.0001

*Socioeconomic status included a time stratification for the all cause mortality model.
RUB, resource utilisation band; SES, socioeconomic status.

Table 5 Comparison of physical activity (PA) levels for cancer progression and all cause mortality models

	Low PA level vs no PA	Moderate to high vs no PA	Moderate to high vs low PA
Cancer progression	0.84 (0.79 to 0.89)*	0.73 (0.70 to 0.77)*	0.88 (0.81 to 0.94)*
Mortality	0.67 (0.61 to 0.74)*	0.53 (0.50 to 0.58)*	0.79 (0.71 to 0.89)*
Prostate cancer progression	0.86 (0.75 to 1.00)†	0.88 (0.79 to 0.97)‡	1.02 (0.87 to 1.20)†
Breast cancer progression	0.84 (0.73 to 0.97)‡	0.72 (0.64 to 0.81)*	0.85 (0.73 to 1.00)†
Skin cancer progression	0.68 (0.53 to 0.88)§	0.68 (0.56 to 0.82)*	1.00 (0.76 to 1.33)†
Prostate cancer mortality	0.64 (0.48 to 0.86)§	0.49 (0.40 to 0.60)*	0.76 (0.54 to 1.06)†
Breast cancer mortality	0.58 (0.42 to 0.79)*	0.45 (0.35 to 0.59)*	0.79 (0.53 to 1.16)†
Skin cancer mortality	0.46 (0.30 to 0.70)*	0.55 (0.42 to 0.72)*	1.21 (0.76 to 1.93)†

Values are hazard ratios (95% CI).
*p<0.001.
†p>0.05.
‡p<0.05.
§p<0.01.

Post hoc analyses were performed on the three physical activity levels to confirm which levels of physical activity showed a difference. Using a Bonferroni adjustment on the significance level to reflect the multiple comparisons (ie, reducing the level of significance from 5% to 1.67%) showed that all groups were statistically significantly different from each other in the cancer progression and all cause mortality models (table 5).

The HRs showed that the risk of progression was lower for higher levels of physical activity. HR was 0.84 (95% CI 0.79 to 0.89) when comparing low physical activity with no activity, 0.73 (95% CI 0.70 to 0.77) when comparing high physical level with no activity and 0.88 (95% CI 0.81 to 0.94) when comparing high physical activity with low physical activity.

In the cancer progression model using members with a BMI score (addendum), there was no significant difference between the low physical activity level and the no physical activity level (p=0.55), but significant differences for the other two comparisons were evident. For the model fitted on the reduced subset cohort, all three comparisons were statistically significant.

The all cause death model showed that all differences were significant for the group, including those with available BMI data. The HRs showed that the risk of progression was lower for higher levels of physical activity, but the associations were stronger than what was evident in the cancer progression model. HR was 0.67 (95% CI 0.61 to 0.74) when comparing low physical activity with no activity and 0.79 (95% CI 0.71 to 0.89) when comparing high physical activity with low physical activity. For the models of the three most prevalent cancers, the patterns were similar, with HRs for higher levels of physical activity compared with no physical activity <1 in all comparisons.

We also examined the probabilities of progression (table 6) and death (table 7) for the three levels of physical activity. These were calculated using an example male individual, aged 55–65, with medium SES and a RUB of 3. The group was chosen as it was the largest single group and the median value for all categories as described in table 2.

Twenty-four months after diagnosis, individuals who were diagnosed as stage 1 had a 74.0% probability of not advancing to higher levels of progression or death when their average physical activity level 12 months before diagnosis was zero (no physical activity), versus a 78% and 80% probability of not advancing to higher levels of progression or death when their average physical activity was low and moderate to high, respectively. Similar patterns of non-progression were seen at 36 months (71%, 75% and 78% for inactive, low activity and moderate to high activity, respectively) and at 60 months (66%, 70% and 73%). Again, a similar increasing pattern was evident for the group including members with measured BMI, showing a difference of 5.1–6.2% between the estimated proportion of those who progressed when comparing the no physical activity group with the medium to high physical activity group. The same pattern was evident for the model fitted on the reduced subset cohort of members with a cancer diagnosis, with a difference of 6.8–7.2% in the estimated proportion of progression.

An equivalent pattern was evident for the all cause death model. Twenty-four months after diagnosis, stage 1 patients had a 91% probability of survival when their average physical activity level 12 months before diagnosis was zero (no physical activity), versus a 94% and 95% probability of survival when their average physical activity was low and moderate to high, respectively. Similar patterns of non-progression were seen at 36 months (88%, 92% and 94%) and 60 months (84%, 89% and 91%). Again, a similar pattern was evident for those with measured BMI and with analysis of the reduced subset cohort.

Table 6 Comparison of estimated proportions of non-progression to higher stages at key time points (months)

Time (months)	Physical activity		
	No	Low	Moderate to high
24	0.74 (0.72 to 0.77)	0.78 (0.75 to 0.81)	0.80 (0.78 to 0.83)
36	0.71 (0.68 to 0.74)	0.75 (0.72 to 0.78)	0.78 (0.75 to 0.80)
60	0.66 (0.62 to 0.69)	0.71 (0.67 to 0.74)	0.73 (0.70 to 0.77)

Values are hazard ratios (95% CI).
Results are shown for men aged 56–65 years, with resource utilisation band=L3 and medium socioeconomic status.

Table 7 Comparison of estimated proportions of survival at key time points (months)

Time (months)	Physical activity		
	No	Low	Moderate to high
24	0.91 (0.90–0.93)	0.94 (0.93–0.95)	0.95 (0.94–0.96)
36	0.88 (0.86–0.90)	0.92 (0.90–0.94)	0.94 (0.92–0.95)
60	0.84 (0.81–0.87)	0.90 (0.87–0.91)	0.91 (0.89–0.93)

Values are hazard ratios (95% CI).
Results are shown for men aged 56–65 years, with resource utilisation band=L3 and medium socioeconomic status.

DISCUSSION

Our results provide compelling evidence of the inverse association between pre-diagnosis physical activity and cancer progression and overall mortality among people diagnosed with stage 1 cancers in a sample of members enrolled in a South African health plan. This association was significantly greater for individuals doing more than an average of 60 min of moderate to vigorous physical activity per week compared with those doing <60 min of recorded activity per week and those with no recorded physical activity. A notable finding of our study was that even members who had engaged in low levels of physical activity had a significantly lower likelihood of progression of cancer or death compared with individuals who had no recorded physical activity. This suggests that greater levels of physical activity are associated with a lower relative risk of cancer progression and mortality and concurs with similar findings regarding the protective effect of measured physical activity against COVID-19, as previously reported by our team.[17] These findings were robust when the subset of subjects with a BMI score was considered and when the subset of cancers that could potentially affect physical activity before a stage 1 diagnosis were removed.

Our results are in alignment with the findings of Friedenreich *et al* who showed in a systematic review and meta-analysis of 136 studies that higher levels of physical activity compared with lower levels provided a protective effect against all cause mortality and cancer specific mortality for at least 11 cancer types, before and after the diagnosis of cancer.[7] Specifically, higher pre-diagnosis physical activity was protective against all cause mortality in individuals with colorectal, breast, prostate and haematologic cancers. The results were even more pronounced for post-diagnosis physical activity, especially for colorectal and breast cancers, where a greater reduction of 37–42% was observed for post-diagnosis physical activity compared with pre-diagnosis physical activity (14–20%) for all cause mortality and cancer specific mortality. Similar findings were reported in a meta-analysis of 31 873 colorectal cancer patients,[24] where the highest level compared with the lowest level of pre-diagnosis physical activity showed a 19% decreased total mortality risk and a 15% reduction of cancer specific mortality. A previous meta-analysis of people diagnosed with colorectal cancer found similar outcomes.[25] Another meta-analysis of 42 602 patients showed that individuals who performed high levels of physical activity before diagnosis had a 19% reduced risk of breast cancer specific mortality compared with individuals who participated in moderate levels of physical activity, which resulted in a 17% reduction of breast cancer specific mortality.[26] Furthermore, the study showed an inverse association between all cause mortality and pre-diagnosed physical activity.

Research on the inverse association between pre-diagnosis physical activity and cancer mortality complements a growing body of evidence showing the beneficial association between physical activity and the prevention of several cancers.[9 27 28] Furthermore, there is growing evidence for the benefits of physical activity post-diagnosis of cancer.[24 29] Specifically, based on a review of 11 meta-analyses, Cormie *et al* reported that higher levels of exercise compared with low or no exercise were associated with 21–35% decreased recurrence rate of cancer, 28–44% lower cancer specific mortality and 25–48% reduced risk of all-cause mortality.[29]

There are several mechanisms by which physical activity may reduce the incidence and progression of cancers. Chief among these is the strengthening of the immune system by increasing numbers of natural killer cells, lymphocytes, neutrophils and eosinophils.[30] Physical activity may also reduce the risk of progression of hormone sensitive cancers, such as breast and prostate cancers, by regulating oestrogen and testosterone levels.[31] However, more research is warranted to determine the plausible biological mechanisms by which physical activity modulates the risk and progression of certain cancers.

Strengths and limitations

Compared with most previously published studies, one of the main strengths of this study was the use of recorded physical activity data from wearable devices, gym attendance and participation in organised events. This eliminates recall bias and inaccuracies that may arise from self-reported data. We were able to capture granular data which include step counts, frequency, duration and intensity of exercise over an extended (12 month) period. The focus on stage 1 cancer patients minimised the potential for reverse causality in patients who were less physically active as a result of their higher disease burden. However, the risk of reverse causality due to the effects of even very early (undiagnosed) cancer on physical activity is acknowledged. We therefore examined physical activity earlier (13–24 months pre-diagnosis) when there is considerably less risk of the cancer reducing physical activity. Our results indicated a slight decrease in the strength of the effects, but the patterns remained the same. This suggests that reverse causality is an unlikely explanation for the results.

Limitations of the study include potential biases from not adjusting for confounding factors, such as smoking status and alcohol consumption as well as the incomplete data on BMI. We also assumed that members who did not record any physical activity points through the Vitality programme did not engage in recreational physical activity, which may not be true for all individuals. Moreover, caution should be observed in applying the findings of the study to the general South African population, as the study cohort comprised individuals who had access to private medical insurance. When comparing membership rates of private medical insurance funds in South Africa by population group, coverage by medical schemes is noticeably higher among white individuals (at 71.9%) and those of Asian descent (48.7%), than among those of mixed race (18.2%) and black Africans (9.7%).[32] DHMS does not ask members to identify by race. Of the 33% of members who chose to disclose their race, 38.4% were black/African, 32.7% white, 11.5% Asian and 9.4% of mixed race, while 7.3% choose other. Finally, it is important to emphasise that the observational study design did not allow for the establishment of causal relationships.

CONCLUSIONS

Individuals enrolled in a South African health plan who engaged in >60 min of moderate levels of physical activity per week, for at least 1 year before the diagnosis of cancer, had significantly lower rates of progression and overall mortality than those who did not engage in any physical activity. Additionally, even members who engaged in lower levels of physical activity had a favourable association with cancer outcomes compared with those who did not engage in any recorded activity. Therefore, physical activity may be considered to confer substantial benefits in terms of progression and overall mortality to those diagnosed with cancer. In a world where cancer continues to be a significant public health burden, the promotion of physical activity can yield important benefits regarding the progression of cancer as well as its prevention and management.

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Contributors NR and DP conceived the format of the paper and drafted the initial versions. NM, SL and MG conducted the actuarial and statistical analysis of the cohort data with the collaboration of Y-HC and SS. JST and GT provided expert analysis of the physical activity data. JSP coordinated the inter-institutional collaboration, oversaw the drafting of each iteration of the manuscripts and serves as the guarantor. All authors reviewed and edited each version of the manuscript and approved the final submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests NM, SL, DP and MM are employed by Discovery. MG is a consultant for Discovery. JSP is an editor of *Br J Sports Med*.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Ethics approval was obtained from the human research ethics committee of the University of the Witwatersrand, Johannesburg (clearance certificate No M230338).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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