

Addendum to “The association between recorded physical activity and cancer progression or mortality in individuals diagnosed with cancer in South Africa”

Due to space limitations in the paper, we have added an addendum to further contextualise and support the main text and tables. The first section supplies the demographic data broken down by the dependent variable (cancer progression and death), as opposed to the independent variable (levels of physical activity).(1,2) The second section shows the analyses of the three most common forms of cancer. The third section analysis the subset with available BMI data, and the subset with a lower possibility of impact on physical activity before diagnosis. Section four is an analysis of the primary dataset, using the data on physical activity in the period 13-24 months prior to diagnosis.

Finally, the last section is a re-analysis of the primary dataset, using interval scales for age and SES.(3)

Extended Demographics Tables.

Table 1. Demographics of members across cancer progression outcomes

	No progression	Progression to higher stages	Total
No. of Members	18 503	9 745	28 248
Female	9 333 (50.44%)	4 275 (43.87%)	13 608
Male	9 170 (49.56%)	5 470 (56.13%)	14 640
Age < 36 years	1 839 (9.94%)	689 (7.07%)	2 528
Age [36, 45] years	2 439 (13.18%)	1 049 (10.76%)	3 488
Age [46, 55] years	4 056 (21.92%)	1 653 (16.96%)	5 709
Age [56, 65] years	5 227 (28.25%)	2 664 (27.34%)	7 891
Age > 65 years	4 942 (26.71%)	3 690 (37.87%)	8 632
RUB [0-2]	2 318 (12.53%)	1 105 (11.34%)	3 423
RUB 3	9 095 (49.15%)	3 877 (39.78%)	12 972
RUB 4	5 360 (28.97%)	3 195 (32.79%)	8 555
RUB 5	1 730 (9.35%)	1 568 (16.09%)	3 298
Low SES	969 (5.24%)	652 (6.69%)	1 621
Moderate SES	9 964 (53.85%)	5 420 (55.62%)	15 384
High SES	7 570 (40.91%)	3 673 (37.69%)	11 243
Low BMI	57 (0.31%)	25 (0.26%)	82
Normal BMI	1 381 (7.46%)	437 (4.48%)	1 818

High BMI	1 344 (7.26%)	598 (6.14%)	1 942
Obese BMI	766 (4.14%)	361 (3.7%)	1 127
Missing BMI	14 955 (80.82%)	8 324 (85.42%)	23 279
No PA	10 796 (58.35%)	6 661 (68.35%)	17 457
Low PA	2 609 (14.1%)	1 113 (11.42%)	3 722
Moderate/High PA	5 098 (27.55%)	1 971 (20.23%)	7 069

Table 2. Demographics of members across all-cause death outcomes

	Alive	Death from all causes	Total
No. of Members	22 937	5 311	28 248
Female	11 440 (49.88%)	2 168 (40.82%)	13 608
Male	11 497 (50.12%)	3 143 (59.18%)	14 640
Age < 36	2 156 (9.4%)	372 (7%)	2 528
Age [36, 45]	3 021 (13.17%)	467 (8.79%)	3 488
Age [46, 55]	4 998 (21.79%)	711 (13.39%)	5 709
Age [56, 65]	6 539 (28.51%)	1 352 (25.46%)	7 891
Age > 65	6 223 (27.13%)	2 409 (45.36%)	8 632
RUB [0-2]	2 896 (12.63%)	527 (9.92%)	3 423
RUB 3	11 224 (48.93%)	1 748 (32.91%)	12 972
RUB 4	6 660 (29.04%)	1 895 (35.68%)	8 555
RUB 5	2 157 (9.4%)	1 141 (21.48%)	3 298
Low SES	1 234 (5.38%)	387 (7.29%)	1 621
Moderate SES	12 388 (54.01%)	2 996 (56.41%)	15 384
High SES	9 315 (40.61%)	1 928 (36.3%)	11 243
Low BMI	73 (0.32%)	9 (0.17%)	82
Normal BMI	1 623 (7.08%)	195 (3.67%)	1 818
High BMI	1 680 (7.32%)	262 (4.93%)	1 942
Obese BMI	965 (4.21%)	162 (3.05%)	1 127
Missing BMI	18 596 (81.07%)	4 683 (88.18%)	23 279
No PA	13 459 (58.68%)	3 998 (75.28%)	17 457
Low PA	3 232 (14.09%)	490 (9.23%)	3 722
Moderate/High PA	6 246 (27.23%)	823 (15.5%)	7 069

Analyses for the three most frequent cancer diagnoses.

The tables below describe the results for the 3 most common cancers examined in the study, namely Prostate Cancer, Breast Cancer, and Skin Cancer (Including Malignant Melanoma). Gender was excluded for the Prostate Cancer group (as all subjects were male) and the Breast Cancer group as the proportion of males was too small to identify effects reliably. Some of the categories were reduced (e.g., age as there are very small numbers of young men in the prostate group.)

Table 3. Significance of model parameters for the cancer progression and all-cause mortality models for the prostate cancer group

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	p	χ^2	df	p
Age Group (Stratified)	118.37	18	<0.0001	152.48	18	<0.0001
RUB Grp (Stratified)	42.47	18	0.001	61.67	18	<0.0001
SES	1.56	2	0.4585	7.98	2	0.0185
PA	8.20	2	0.0166	50.41	2	<0.0001

Table 4. Significance of model parameters for the cancer progression and all-cause mortality models for the breast cancer group

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	p	χ^2	df	p
Age Group (Stratified)	134.06	18	<0.0001	106.53	18	<0.0001
RUB Grp (Stratified)	22.19	18	0.2235	53.47	18	<0.0001
SES	33.45	2	<0.0001	8.94	2	0.0115
PA	30.07	2	<0.0001	40.11	2	<0.0001

Table 5. Significance of model parameters for the cancer progression and all-cause mortality models for the skin cancer group

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	p	χ^2	df	p
Age Group (Stratified)	80.51	18	<0.0001	94.97	24	<0.0001
RUB Grp (Stratified)	72.87	18	<0.0001	91.06	24	<0.0001
Gender (Stratified)	17.99	6	0.0063	11.20	8	0.1906
SES ^s	2.55	2	0.2799	0.42	2	0.8113
PA	20.82	2	<0.0001	27.77	2	<0.0001

Table 6. Comparison of physical activity levels for the prostate cancer progression model

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.86 (0.75-1.00)	1.95	0.0517
Moderate/High PA Level vs No PA	0.88 (0.79-0.97)	2.46	0.0138
Moderate/High PA Level vs Low PA	1.02 (0.87-1.20)	0.21	0.8331

Table 7. Comparison of physical activity levels for the prostate cancer all-cause mortality model

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.64 (0.48-0.86)	2.98	0.0028
Moderate/High PA Level vs No PA	0.49 (0.40-0.60)	6.78	<0.0001
Moderate/High PA Level vs Low PA	0.76 (0.54-1.06)	1.63	0.1023

Table 8. Comparison of physical activity levels for the breast cancer progression model

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.84 (0.73-0.97)	2.38	<0.0174
Moderate/High PA Level vs No PA	0.72 (0.64-0.81)	5.37	<0.0001
Moderate/High PA Level vs Low PA	0.85 (0.73-1.00)	1.92	0.0545

Table 9. Comparison of physical activity levels for the breast cancer all-cause mortality model

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.58 (0.42-0.79)	3.36	<0.0008
Moderate/High PA Level vs No PA	0.45 (0.35-0.59)	5.81	<0.0001
Moderate/High PA Level vs Low PA	0.79 (0.53-1.16)	1.23	0.2196

Table 10. Comparison of physical activity levels for the skin cancer progression model

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.68 (0.53-0.88)	2.95	<0.0031
Moderate/High PA Level vs No PA	0.68 (0.56-0.82)	4.04	<0.0001
Moderate/High PA Level vs Low PA	1.00 (0.76-1.33)	0.02	0.9847

Table 11. Comparison of physical activity levels for the skin cancer all-cause mortality Model

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.46 (0.30-0.70)	3.63	<0.0003
Moderate/High PA Level vs No PA	0.55 (0.42-0.72)	4.32	<0.0001

Moderate/High PA Level vs Low PA	1.21 (0.76-1.93)	0.81	0.4175
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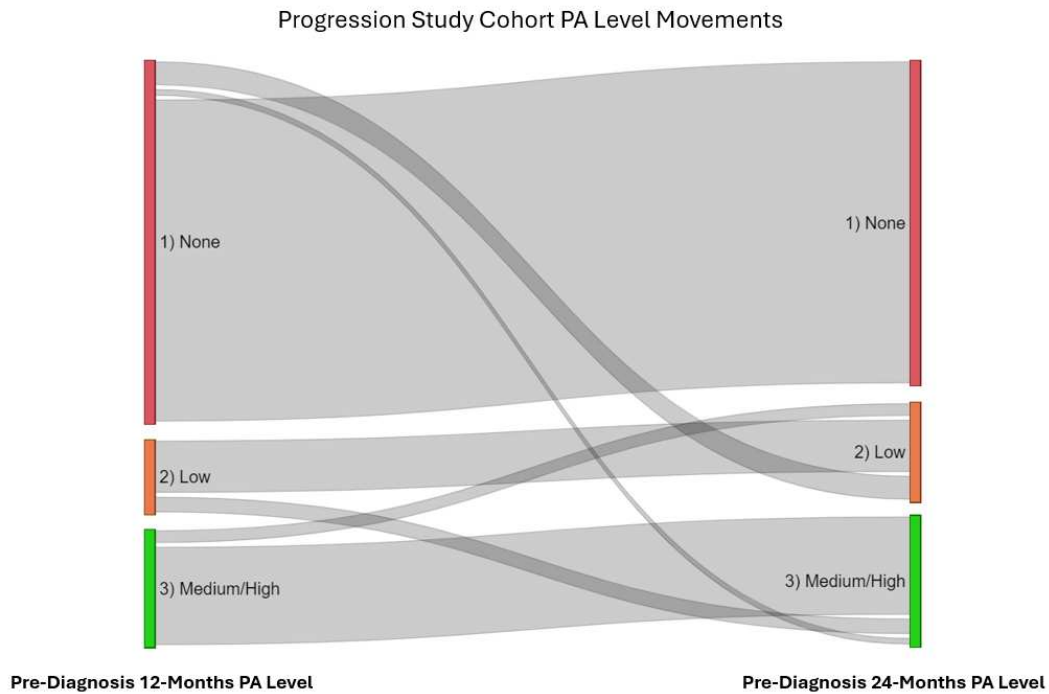


Figure 1. Progression study cohort physical activity level movements

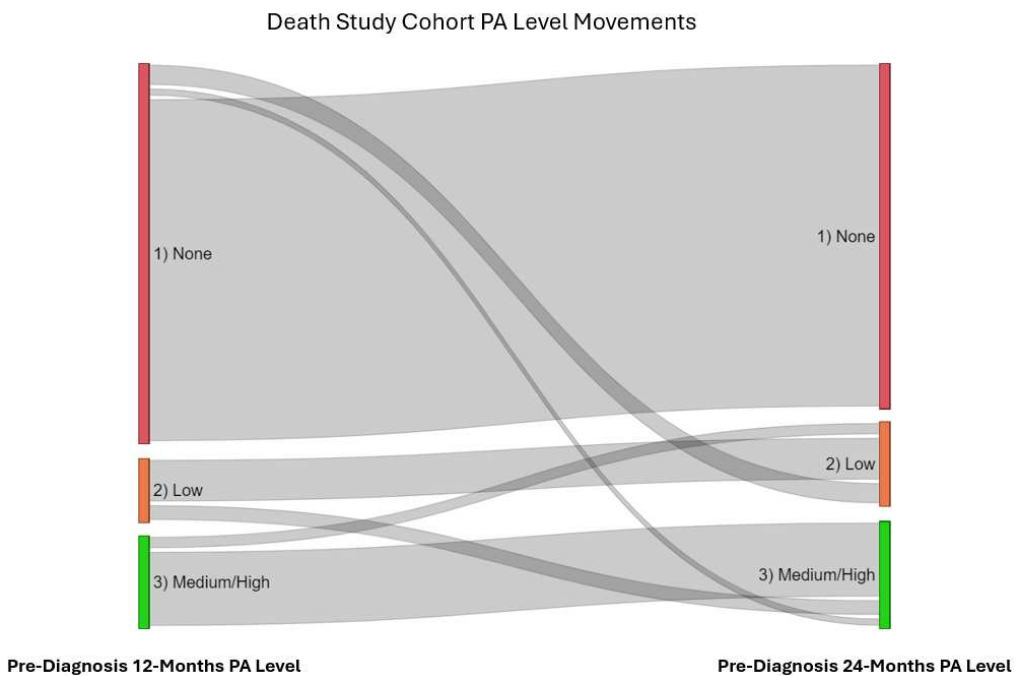


Figure 2. Death study cohort physical activity level movements

Analyses of the subset with available BMI data and the subset with a lower possibility of impact on physical activity before diagnosis

The tables below describe the results for the sub-sets of the data considered but only summarised briefly in the paper.

Table 12. Significance of model parameters for the cancer progression and all-cause mortality models for subjects with accessible BMI data

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	P	χ^2	df	p
Age Group (Stratified)	88.90	32	<0.0001	83.66	28	<0.0001
Gender (Stratified) §	27.61	8	0.0006	20.50	1	<0.0001
RUB	50.36	3	<0.0001	107.69	3	<0.0001
SES	5.40	2	0.0673	3.35	2	0.1871
BMI	7.55	2	0.0229	0.03	2	0.9862
PA	20.12	2	<0.0001	49.21	2	<0.0001

Sex was not stratified for the all-cause mortality model.

Table 13. Significance of model parameters for the cancer progression and all-cause mortality models for the subset of the diagnoses where there was low risk of physical impact before diagnosis

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	P	χ^2	df	p
Age Group (Stratified)	319.21	32	<0.0001	421.35	32	<0.0001
RUB Grp (Stratified)	238.22	24	<0.0001	511.38	24	<0.0001
Gender (Stratified)	74.41	8	<0.0001	34.07	8	<0.0001
SES §	45.55	2	<0.0001	60.30	16	<0.0001
PA	126.22	2	<0.0001	245.66	2	<0.0001

The SES model was stratified for the all-cause mortality model

Table 14. Comparison of physical activity levels for the progression model for subjects with accessible BMI data

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.95 (0.81-1.12)	0.60	0.5498
Moderate/High PA Level vs No PA	0.77 (0.68-0.87)	4.28	0.0000
Moderate/High PA Level vs Low PA	0.81 (0.69-0.95)	2.64	0.0082

Table 15. Comparison of physical activity levels for the all-cause mortality model for subjects with accessible BMI data

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.75 (0.58-0.96)	2.28	0.0223
Moderate/High PA Level vs No PA	0.53 (0.45-0.64)	7.01	<0.0001
Moderate/High PA Level vs Low PA	0.71 (0.55-0.92)	2.65	0.0081

Table 16. Comparison of physical activity levels for the progression model for the subset of the diagnoses where there was low risk of physical impact prior to diagnosis.

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.82 (0.76-0.88)	5.50	<0.0001
Moderate/High PA Level vs No PA	0.73 (0.69-0.78)	10.73	<0.0001
Moderate/High PA Level vs Low PA	0.90 (0.83-0.97)	2.58	0.0099

Table 17. Comparison of physical activity levels for the all-cause mortality model for the subset of the diagnoses where there was low risk of physical impact prior to diagnosis.

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.63 (0.56-0.70)	7.98	<0.0001
Moderate/High PA Level vs No PA	0.52 (0.47-0.56)	14.55	<0.0001
Moderate/High PA Level vs Low PA	0.82 (0.72-0.94)	2.90	0.0037

Cancers that were excluded.

Cancer Diagnosis	Exclude	N	PCT
94-Neoplasm, Malignant: Lymphatic and Haematopoietic, Other Types	YES	1055	3.7%
17-Neoplasm, Malignant: Thyroid	YES	740	2.6%
96-Neoplasm, Malignant: Multiple Myeloma	YES	573	2.0%
78-Neoplasm, Malignant: Leukaemia, Other Types	YES	461	1.6%
83-Neoplasm, Malignant: Hodgkin's Lymphoma	YES	364	1.3%
409-Other Disorders of Blood and Blood-Forming Organs	YES	358	1.3%
85-Neoplasm, Malignant: Lymphoma, Diffuse Large Cell	YES	357	1.3%
64-Neoplasm, Benign: Lymphatic or Haematopoietic	YES	352	1.2%

76-Neoplasm, Malignant: Leukaemia, Chronic Lymphocytic	YES	295	1.0%
92-Neoplasm, Malignant: Lymphoma, Lymphoblastic	YES	245	0.9%
77-Neoplasm, Malignant: Leukaemia, Chronic Myelogenous	YES	179	0.6%
82-Neoplasm, Malignant: Hodgkin's Disease with Nodular Sclerosis	YES	106	0.4%
90-Neoplasm, Malignant: Lymphoma, Follicular, Predominantly Small Cleaved Cel	YES	64	0.2%
88-Neoplasm, Malignant: Lymphoma, Follicular Mixed Small Cleaved and Large Ce	YES	59	0.2%
399-Anemia: Aplastic, Acquired	YES	59	0.2%
97-Neoplasm, Malignant: Waldenstrom's Macroglobulinemia	YES	48	0.2%
93-Neoplasm, Malignant: Lymphoma, Small Non-cleaved Cell or Burkitt's	YES	40	0.1%
81-Neoplasm, Malignant: Hodgkin's Disease with Mixed Cellularity	YES	38	0.1%
86-Neoplasm, Malignant: Lymphoma, Diffuse Mixed Small and Large Cell	YES	35	0.1%
87-Neoplasm, Malignant: Lymphoma, Diffuse Small Cleaved Cell	YES	29	0.1%
84-Neoplasm, Malignant: Lymphoma, Cutaneous T Cell (Mycosis Fungoides)	YES	28	0.1%
89-Neoplasm, Malignant: Lymphoma, Follicular Predominantly Large Cell	YES	23	0.1%
401-Anemia: Other	YES	21	0.1%
80-Neoplasm, Malignant: Hodgkin's Disease with Lymphocytic Predominance	YES	20	0.1%
397-Anemia: Thalassemia	YES	19	0.1%
79-Neoplasm, Malignant: Hodgkin's Disease with Lymphocytic Depletion	YES	3	0.0%
338-Osteoarthritis	YES	1	0.0%
3-Neoplasm, Malignant: Breast, Female	NO	6356	22.5%
10-Neoplasm, Malignant: Prostate	NO	6056	21.4%
38-Neoplasm, Malignant: Other Skin and Soft Tissue	NO	1946	6.9%
16-Neoplasm, Malignant: Melanoma	NO	1292	4.6%
29-Neoplasm, Malignant: Colon and Rectum	NO	1016	3.6%
14-Neoplasm, Malignant: Bladder, Urinary	NO	915	3.2%
36-Neoplasm: Central Nervous System	NO	668	2.4%
18-Neoplasm, Malignant: Lungs, Bronchi, or Mediastinum	NO	552	2.0%
7-Neoplasm, Malignant: Ovaries	NO	391	1.4%
4-Neoplasm, Malignant: Cervix Uteri	NO	372	1.3%
12-Neoplasm, Malignant: Testicular	NO	363	1.3%
15-Neoplasm, Malignant: Kidneys	NO	344	1.2%
8-Neoplasm, Malignant: Endometrium	NO	332	1.2%
34-Neoplasm, Malignant: Pancreas	NO	231	0.8%
32-Neoplasm, Malignant: Stomach	NO	169	0.6%
406-Polycythemia Vera	NO	162	0.6%
33-Neoplasm, Malignant: Other Hepatobiliary Tract	NO	156	0.6%
25-Neoplasm, Malignant: Oral Cavity	NO	152	0.5%
39-Neoplasm, Malignant: Primary Bone	NO	129	0.5%

30-Neoplasm, Malignant: Esophagus	NO	122	0.4%
42-Neoplasm, Malignant: Kaposi's	NO	106	0.4%
37-Neoplasm: Eye	NO	101	0.4%
21-Neoplasm, Malignant: Larynx, Supraglottic	NO	77	0.3%
44-Neoplasm, Malignant: Other Endocrine System	NO	70	0.2%
31-Neoplasm, Malignant: Small Bowel	NO	70	0.2%
45-Neoplasm, Malignant: Unspecified Primary Site	NO	64	0.2%
41-Neoplasm, Malignant: Non-specific Sites	NO	59	0.2%
35-Neoplasm, Malignant: Other Gastrointestinal System	NO	57	0.2%
26-Neoplasm, Malignant: Salivary Glands and Mandible	NO	55	0.2%
28-Neoplasm, Malignant: Oropharynx	NO	48	0.2%
320-Other Endocrine Disorders	NO	33	0.1%
396-Anemia: Sickle Cell	NO	31	0.1%
6-Neoplasm, Malignant: Vulva	NO	26	0.1%
5-Neoplasm, Malignant: Vagina	NO	25	0.1%
9-Neoplasm, Malignant: Female Genitourinary System	NO	24	0.1%
19-Neoplasm, Malignant: Larynx, Glottis	NO	20	0.1%
22-Neoplasm, Malignant: Nasopharyngeal	NO	15	0.1%
11-Neoplasm, Malignant: Penile	NO	15	0.1%
359-Other Disorders of Female Genital System	NO	13	0.0%
23-Neoplasm, Malignant: Sinuses	NO	8	0.0%
13-Neoplasm, Malignant: Male Genitourinary System	NO	7	0.0%
63-Neoplasm, Benign: Skin or Subcutaneous Tissue	NO	5	0.0%
407-Other Immunodeficient Disorders	NO	4	0.0%
405-Agranulocytosis	NO	4	0.0%
69-Neoplasm, Benign: Brain	NO	4	0.0%
318-Primary Amyloidosis	NO	2	0.0%
27-Neoplasm, Malignant: Hypopharynx	NO	2	0.0%
369-Ante- and Postpartum Complications	NO	2	0.0%
71-Neoplasm, Benign: Other Endocrine System	NO	1	0.0%
20-Neoplasm, Malignant: Larynx, Subglottic	NO	1	0.0%
450-Other Inflammations and Infections of Skin and Subcutaneous Tissue	NO	1	0.0%
70-Neoplasm, Benign: Other Sites	NO	1	0.0%
91-Neoplasm, Malignant: Lymphoma, Histiocytic Cell	NO	1	0.0%

Re-analyses of the primary dataset, using interval scales for age and SES.

Table 18. Significance of model parameters for the cancer progression and all-cause mortality models using age and SES as interval scales.

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	P	χ^2	df	p
Age Linear (Stratified)	131.99	8	<0.0001	88.80	8	<0.0001
Age Exponential	199.38	8	<0.0001	409.12	8	<0.0001

RUB Grp (Stratified)	314.63	24	<0.0001	702.02	24	<0.0001
Gender (Stratified)	116.71	8	<0.0001	88.91	8	<0.0001
SES[§]	71.72	2	<0.0001	95.27	8	<0.0001
PA	122.32	2	<0.0001	251.79	2	<0.0001

The SES model was stratified for the all-cause mortality model

Table 19. Comparison of physical activity levels for the progression model using age and SES as interval scales.

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.86 (0.81-0.92)	4.63	<0.0001
Moderate/High PA Level vs No PA	0.75 (0.72-0.79)	10.79	<0.0001
Moderate/High PA Level vs Low PA	0.87 (0.81-0.94)	3.50	<0.0001

Table 20. Comparison of physical activity levels for the all-cause mortality model using age and SES as interval scales.

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.69 (0.63 – 0.76)	7.51	<0.0001
Moderate/High PA Level vs No PA	0.56 (0.52 – 0.60)	15.00	<0.0001
Moderate/High PA Level vs Low PA	0.80 (0.72 – 0.90)	3.88	<0.0001

Re-analyses of the primary dataset, using physical activity in the period 13-24 months before diagnosis.

The analysis below examined whether a potential reverse causality explanation was supported by the data. By examining physical activity earlier there is considerably less risk of the cancer reducing physical activity. The results indicate a slight decrease in the strength of the effects, but the patterns remain the same. This suggests that reverse causality is an unlikely explanation for the results.

Table 21. Significance of model parameters for the cancer progression and all-cause mortality models using physical activity measured in the period 13-24 months before the initial diagnosis.

Effect	Cancer Progression			All-Cause Mortality		
	χ^2	Df	P	χ^2	df	P
Age Group (Stratified)	340.28	8	<0.0001	492.96	32	<0.0001
RUB Grp (Stratified)	267.42	24	<0.0001	589.62	24	<0.0001
Gender (Stratified)	101.08	8	<0.0001	57.32	8	<0.0001
SES [§]	44.06	2	<0.0001	94.83	16	<0.0001
PA	114.44	2	<0.0001	221.35	2	<0.0001

The SES model was stratified for the all-cause mortality model

Table 22. Comparison of physical activity levels for the progression model using physical activity measured in the period 13-24 months prior to the initial diagnosis.

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.86 (0.80-0.92)	4.23	<0.0001
Moderate/High PA Level vs No PA	0.74 (0.70-0.79)	10.52	<0.0001
Moderate/High PA Level vs Low PA	0.87 (0.80-0.94)	3.55	<0.0001

Table 23. Comparison of physical activity levels for the all-cause mortality model using physical activity measured in the period 13-24 months prior to the initial diagnosis.

	Hazard Ratio	Z	Pval
Low PA Level vs No PA	0.67 (0.60 - 0.75)	7.34	<0.0001
Moderate/High PA Level vs No PA	0.56 (0.52 – 0.61)	14.00	<0.0001
Moderate/High PA Level vs Low PA	0.84 (0.74 – 0.94)	2.34	<0.0001

Addendum References

1. Hosmer Jr DW, Lemeshow S, and May S. Applied survival analysis: regression modeling of time-to-event data. Vol. 618. John Wiley & Sons; 2008.
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3. Yang B. Analysing ordinal repeated measures data using SAS. In: Proceedings of the Pharmaceutical SAS Users Group 2006; May 21-24, 2006; Bonita Springs, Florida. Cary, NC: SAS Institute Inc.