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Physical Activity, Muscle Strength, and Prostate Cancer Mortality: Insights from the UK Biobank Cohort

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Background and Rationale

Prostate cancer (PCa) is the **most diagnosed** male cancer worldwide, with **increasing incidence and mortality** projected.

Physical activity is widely recognized for cancer prevention and survival benefits.

Handgrip strength is a validated marker of muscular fitness and predictor of mortality.

Previous **evidence** on physical activity's effect on PCa mortality is **mixed**.

UK Biobank offers a unique opportunity to explore these associations in a large, prospective cohort.

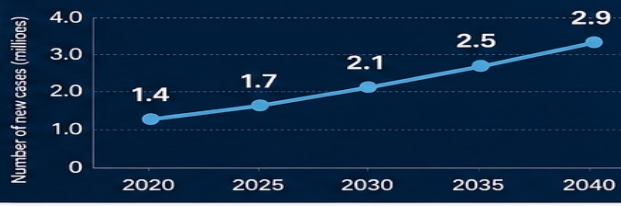
GLOBAL BURDEN OF PROSTATE CANCER (2022)

1.47 million
New cases
(7.3% of all male cancers)

397,000
Deaths
(3.8% of all male cancer deaths)

~2.9 million
New cases projected by 2040
(↑ ~85% increase)

RISING INCIDENCE OVER TIME
Estimated Number of New Cases Worldwide



Overall Rationale: Understanding the impact of lifestyle (physical activity) and physiological reserve (muscle strength) may help improve risk stratification and survival outcomes in men with prostate cancer.

Sources: Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2024;74(3):229-263.

Study Objectives and Hypotheses

OBJECTIVES

01 Investigate associations between self-reported **physical activity** and **handgrip strength** with age-adjusted prostate cancer mortality.

02 Compare mortality among **prostate cancer only**, **cancer-free controls**, and men with **multiple cancers** including prostate cancer.

HYPOTHESES

H1 Incident **prostate cancer** diagnosis does not significantly influence survival compared to **cancer-free men**.

H2 Neither **physical activity** nor **handgrip strength** would be significantly associated with prostate cancer mortality risk.

STUDY CONTEXT

Data Source: UK Biobank
Design: Prospective cohort study

Follow-up: Up to 11.9 years

Total Participants: 194,947 men

Study Design and Population

STUDY DESIGN

UK Biobank prospective cohort study
(2007–2010 recruitment; follow-up to 2020)

502,628
participants
(men and women)

194,947
eligible men included in analysis

GROUPS

Treatment Group — n = 7,278
Prostate cancer only (PCa only)

Control Group — n = 184,108
Cancer-free (no history of any cancer)

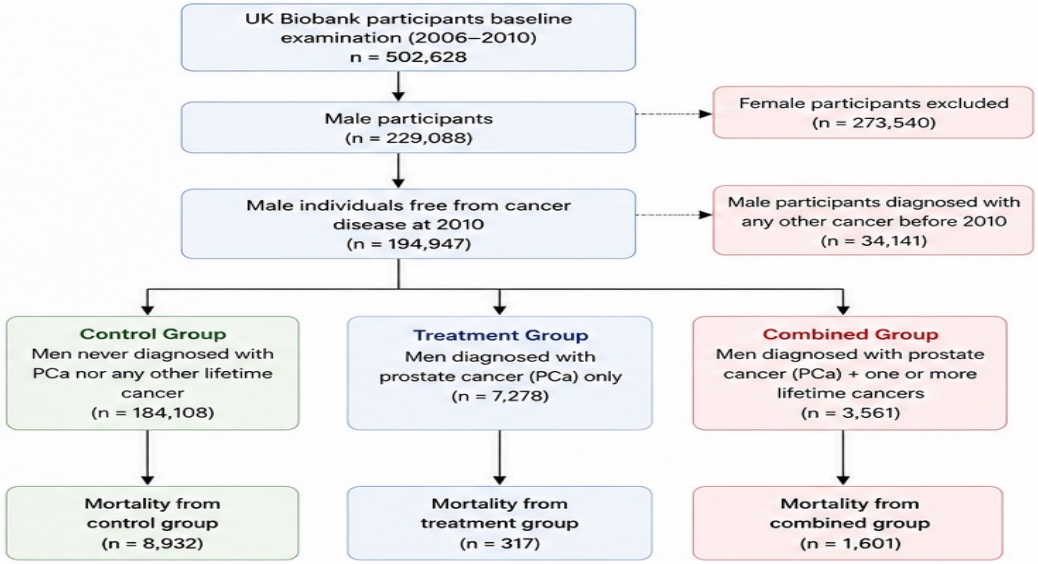
Combined Group — n = 3,561
Prostate cancer + one or more other cancers

Median Follow-up
11.9 years

Study Period
Baseline: 2007–2010
Follow-up: to 2020

Data Sources
Self-report &
National Registries

COHORT SELECTION FLOWCHART



KEY DATA COLLECTED

- **Physical Activity:** International Physical Activity Questionnaire (IPAQ)
- **Muscle Strength:** Handgrip strength measured by dynamometer
- **Outcome:** All-cause mortality from national death registries

PCa = Prostate cancer

Source: Figure adapted from study flow diagram (Figure 4.1).

Physical Activity and Handgrip Strength Assessment

PHYSICAL ACTIVITY ASSESSMENT

Physical activity was assessed using the **International Physical Activity Questionnaire (IPAQ) – short form.**

MET-minutes/day were calculated from **walking, moderate, and vigorous activity.**

Participants with implausible total physical activity values were **excluded** from analysis.

IPAQ SHORT FORM – SAMPLE ITEMS

1. During the last 7 days, on how many days did you walk for at least 10 minutes at a time?	☐ days
2. During the last 7 days, on how many days did you do moderate intensity activities for at least 10 minutes at a time? (e.g., cycling at a regular pace, swimming, doubles tennis)	☐ days
3. During the last 7 days, on how many days did you do vigorous intensity activities for at least 10 minutes at a time? (e.g., running, aerobics, fast cycling, heavy lifting)	☐ days

MET **Total Physical Activity (MET-min/day)** = Walking (METs) + Moderate (METs) + Vigorous (METs)

HANDGRIP STRENGTH ASSESSMENT

Handgrip strength was measured **bilaterally** using a **calibrated hydraulic** dynamometer.

Two trials were taken for each hand with standardized instructions and seated position.

The **highest value** from either hand was used in analysis.

Handgrip strength was analyzed as a continuous variable.

Both physical activity and handgrip strength were treated as continuous variables in all analyses.

IPAQ = International Physical Activity Questionnaire
MET = Metabolic Equivalent of Task

Source: IPAQ Research Committee. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) – Short and Long Forms. 2005. www.ipaq.ki.se

Statistical Analysis

Survival modelling and prognostic interaction analysis in UK Biobank cohort

SURVIVAL MODELLING

- **Cox proportional hazards** regression models
- **Time-to-event** mortality analysis
- **Age-adjusted** hazard ratios (HRs)

EFFECT MODIFICATION

- Interaction terms:
  - Physical activity × cancer group
  - Handgrip strength × cancer group

OUTCOMES REPORTED

- HRs with **95% confidence intervals**
- **Kaplan–Meier** survival estimates
- Statistical significance threshold: **P < 0.05**

VARIABLES INCLUDED

- Mortality
- Age
- Physical activity (MET.min.day^{-1})
- Peak handgrip strength (kg)

KEY STATISTICAL FINDING

Men with prostate cancer **plus additional cancers** demonstrated substantially reduced survival probability over time compared with **controls** and **prostate-cancer-only groups**.

MODEL
Cox proportional hazards model

OUTCOME
Incident mortality

POPULATION
UK Biobank (n = 7,153 men)

SIGNIFICANCE LEVEL
P < 0.05

IPAQ = International Physical Activity Questionnaire
MET = Metabolic Equivalent of Task

Source: Cox DR. Regression models and life-tables. J R Stat Soc Series B. 1972;34(2):187–220.
Kleinbaum DG, Klein M. Survival Analysis: A Self-Learning Text. 3rd ed. Springer; 2012.

Participant Characteristics

Summary of baseline characteristics by study group

Baseline characteristics of participants across treatment, control, and combined groups.
Values are presented as **mean ± standard deviation (SD)** unless otherwise specified.

Group	N	Age (mean ± SD)	MET.min/day (mean ± SD)	Grip Strength (kg) (mean ± SD)	Mortality %
Treatment	7,278	60.7 ± 5.9	334 ± 408	40.8 ± 8.6	4.3%
Control	184,108	55.7 ± 8.2	336 ± 414	41.9 ± 9.1	4.9%
Combined	3,561	62.9 ± 5.1	339 ± 339	40.1 ± 8.5	37.1%

- The combined group (prostate cancer + additional cancers) had the **highest mortality rate (37.1%)**.
- The treatment group (prostate cancer only) showed the **lowest mortality rate (4.3%)**.
- Average physical activity (MET.min/day) and grip strength were comparable across groups.

MET = Metabolic Equivalent of Task
SD = Standard Deviation

Source: Adapted from Table 3.1
Data presented as mean ± SD unless otherwise specified.

Survival Outcomes – Kaplan–Meier Curves

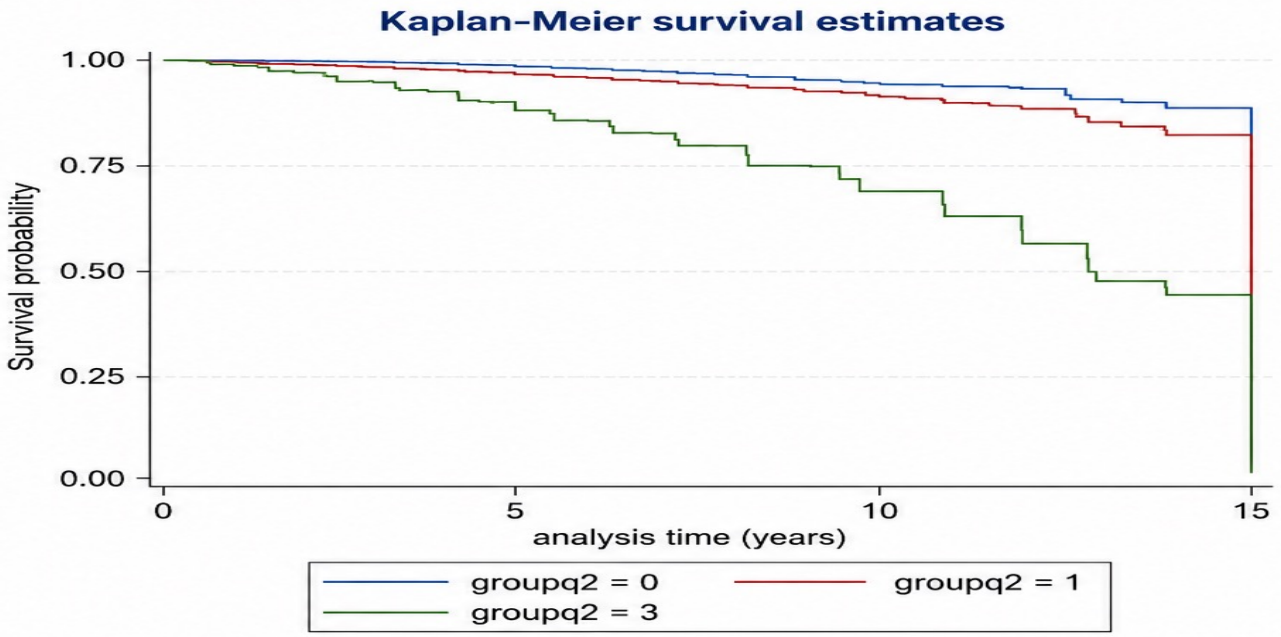
Survival probability over 12 years by group

Treatment (prostate cancer only) had slowest decline in survival.

Combined group had steepest decline, reflecting higher mortality risk.

Control group intermediate survival.

Kaplan–Meier curves compare survival probability over 12 years of follow-up.



The combined group (prostate cancer + additional cancers) demonstrated substantially lower survival probability over time compared with treatment and control groups.

Cox Proportional Hazards Results

Associations of physical activity and handgrip strength with mortality

Cox proportional hazards models were used to estimate hazard ratios (HRs) for mortality. Models were adjusted for age. Results are presented with **95% confidence intervals (CI)**.

Comparison	Physical Activity		Handgrip Strength	
	HR	95% CI	HR	95% CI
Treatment vs Control	1.65	1.48 – 1.85	1.61	1.44 – 1.81
Treatment vs Combined	2.06	1.98 – 2.15	2.06	1.98 – 2.15
Control vs Combined	2.25	2.19 – 2.32	2.27	2.21 – 2.34

- Higher physical activity and greater handgrip strength were associated with **lower mortality risk**.
- The combined group (prostate cancer + additional cancers) had significantly **higher hazard ratios** compared with both **treatment and control groups**.
- Results remained consistent across both exposures.

Men in the combined group had more than double the risk of mortality compared with controls, independent of physical activity and handgrip strength.

HR = Hazard Ratio
CI = Confidence Interval

Models adjusted for age.
Outcome: All-cause mortality

Key Quantitative Findings

Summary of effect sizes and variance explained for mortality outcomes

Physical activity associated with **<1% reduction** in mortality risk

HR ~0.99 per MET.min/day

Handgrip strength accounted for **~4.3% variance** in mortality risk

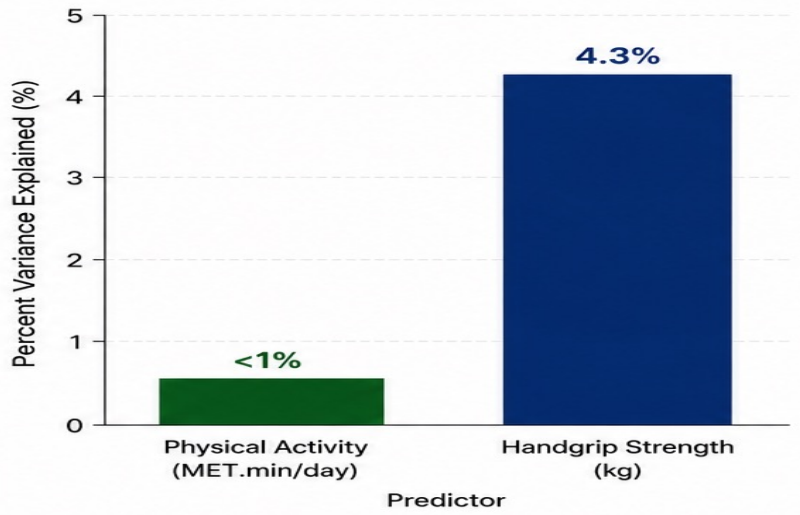
HR ~0.96 per kg increase

Age-adjusted mortality risk significantly higher in **combined cancer group**

HR 8.36 (95% CI: 8.06 – 8.65)

Prostate cancer alone modestly impacts mortality compared to controls

HR 1.65 (95% CI: 1.48 – 1.85)



Mortality Hazard Ratios (Age-Adjusted)

- **Physical Activity** HR ~0.99 per MET.min/day
- **Handgrip Strength** HR ~0.96 per kg increase
- **Combined Cancers** HR 8.36 (95% CI: 8.06 – 8.65)
- **Prostate Cancer Only** HR 1.65 (95% CI: 1.48 – 1.85)

Greater handgrip strength explains substantially more variance in mortality risk (~4.3%) compared to physical activity (<1%). The combined cancer group has the highest mortality risk (HR 8.36), while prostate cancer alone shows a modest increase.

HR = Hazard Ratio
CI = Confidence Interval

Models adjusted for age.
Outcome: All-cause mortality

Interpretation and Context

Integrating findings to understand the relationships between fitness, cancer, and mortality

Prostate cancer alone
has limited impact on mortality in this cohort.

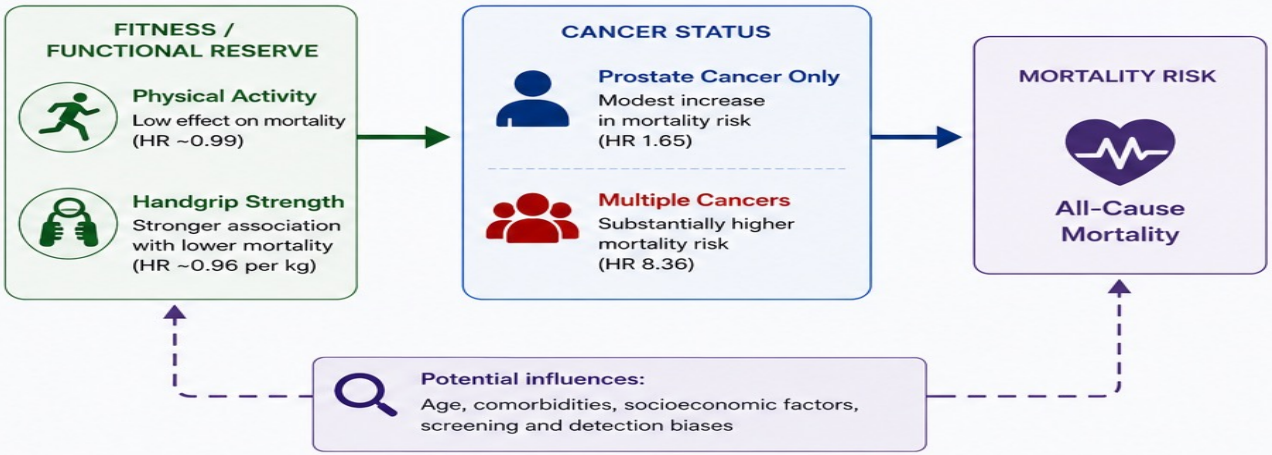
Multiple cancers
greatly increase mortality risk.

Physical activity's
minimal effect may reflect measurement limitations or confounding.

Handgrip strength
likely reflects underlying health and functional reserve.

Screening and detection biases
may influence observed associations with fitness.

Conceptual Pathways Linking Fitness, Cancer, and Mortality



Maintaining functional reserve, reflected by greater handgrip strength, is more strongly associated with lower mortality, while physical activity alone shows minimal impact. The presence of multiple cancers is the strongest driver of increased mortality risk.

HR = Hazard Ratio
CI = Confidence Interval

Models adjusted for age.
Outcome: All-cause mortality

Interpretation considers potential confounding, measurement limitations, and detection biases.

Clinical and Research Implications

Translating findings into patient care and future research

Muscle strength assessment may aid risk stratification in prostate cancer patients.

Physical activity remains important for overall health, but may not strongly alter prostate cancer mortality.

Need for interventions targeting muscle strength and functional status.

Further research on biological mechanisms and role of fitness in cancer progression warranted.

Clinical Pathway: Integrating Fitness Assessment in Prostate Cancer Care

1. Assessment

- Patient evaluation at diagnosis
- Measure handgrip strength
- Assess physical activity level

2. Risk Stratification

- Combine clinical factors with muscle strength
- Identify patients at higher mortality risk
- Inform prognosis and counseling

3. Intervention

- Prescribe resistance training to improve muscle strength
- Encourage regular physical activity
- Address nutrition and other modifiable factors

4. Follow-up

- Reassess muscle strength and function
- Monitor progress and adjust interventions
- Support long-term healthy behaviors

5. Outcomes

- Improved functional status
- Potential reduction in mortality risk
- Better quality of life

Key Takeaway

Incorporating muscle strength assessment into routine prostate cancer care may enhance risk stratification and guide targeted interventions to improve survival and quality of life.

Research Priorities

- Elucidate biological mechanisms linking muscle strength to cancer outcomes
- Evaluate effectiveness of strength training interventions on survival
- Explore interactions between fitness, treatment, and cancer progression
- Address measurement limitations and reduce residual confounding in future studies

These findings highlight the importance of **muscle health** in prostate cancer prognosis and support a broader focus on **fitness** as a key component of comprehensive cancer care.

Strengths and Limitations

Balanced appraisal of study design and data considerations

STRENGTHS

Large, well-characterized cohort
Included >190,000 men with up to 15 years of follow-up.

Objective handgrip strength measurement
Assessed using a calibrated hydraulic dynamometer.

Comprehensive mortality data linkage
Linked to national death registry ensuring high completeness and accuracy.

Long follow-up duration
Extended follow-up allowed for robust assessment of long-term outcomes.

LIMITATIONS

Self-reported physical activity prone to bias
Subject to recall bias and misclassification, potentially attenuating associations.

Observational design limits causal inference
Associations cannot be interpreted as causal relationships.

Potential residual confounding
Unmeasured factors (e.g., diet, comorbidities, screening behavior) may influence results.

Limited data on cancer treatment and severity
Lack of detailed clinical information may affect risk estimates.

This study leverages a large cohort and objective fitness measures but is limited by self-reported activity and observational design. Findings should be interpreted with consideration of potential biases.

Strengths enhance the reliability and generalizability of results.

Limitations highlight areas for future research and data improvement.

Balanced interpretation is essential for informed conclusions.

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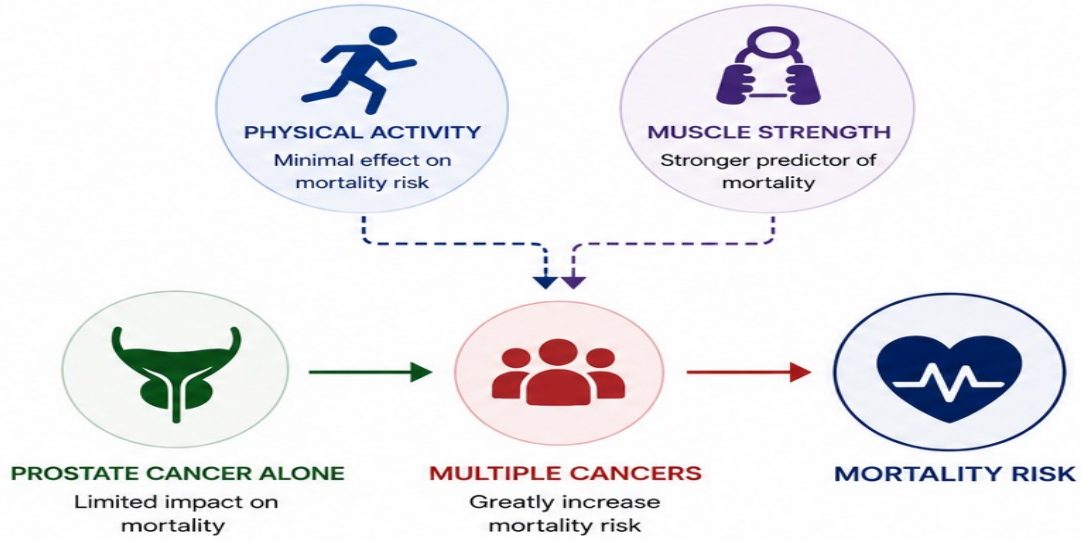
Summary and Conclusions

Key takeaways from the study

1. Prostate cancer alone has limited mortality impact.
2. Multiple cancers greatly increase mortality risk.
3. Physical activity shows minimal effect on mortality.
4. Handgrip strength is a stronger, independent predictor of mortality.
5. Findings highlight the complexity of fitness–cancer interactions; further research is needed.



Muscle strength is a **key marker of survival**, beyond traditional cancer characteristics.
Integrating strength assessment into care may improve risk prediction and personalized management.

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Questions

Disclaimers