Diet and Physical Activity in Men with Prostate Cancer: From Observational to Intervention Research

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On behalf of the BRU Prostate Cancer Group

Bristol Nutrition BRU
PCa incidence per 100,000: UK, 1975-2010

- 40,975 new cases in 2010
- 1 in 8 lifetime prevalence
- 1 in 30 lifetime risk of PCa death
Surgery little better than watchful waiting in low-risk PCa

- Prostate Cancer Intervention vs Observation (PIVOT) Trial
- 731 men assigned radical prostatectomy v observation
- T1a disease: 50%
- Median 10 yrs follow-up

Wilt et al. NEJM 2012;367:203
Localised prostate cancer

- Medium-term outlook favourable but aggressive disease develops long-term
- Limited number of deaths potentially avoidable by radical treatment
- An aggressive approach to all men entails substantial overtreatment
- Challenge is to maximise survival without extensive overtreatment & related side effects
> 50% of men with PCa take non-prescription supplements

Meta-analysis of 9 studies, n=69,000: no effect of vitamin supplements on cancer death

HR 0.96 (0.88-1.04)

Lifestyle guidelines for people with cancer

American Cancer Society

• Achieve and maintain a healthy weight
• 30 mins mod-vigorous ‘intentional’ physical activity 5+ d/week; avoid sedentary
• Eat plant-based foods (veg, fruit, whole grain); limit red/processed meat
Lifestyle guidelines for people with cancer

WCRF/AICR

- Regular physical activity / weight control may prevent breast cancer recurrence
- Cancer survivors should follow recommendations for cancer prevention
Modest vigorous activity (bike, tennis, jog, swim) ≥ 3h vs 1h/wk: 49% reduction in all-cause & 61% reduction in PCa deaths

Brisk walking for 3+h/wk halved progression rates vs easy-paced walking <3h/wk

- Richman et al. Cancer Res; 71; 3889–95
Aims of BRU prostate cancer theme

• Evaluate feasibility & impact of diet / activity interventions
• Delineate mechanisms by which cancer progression is modified
• Provide information to design definitive trials with ca endpoints (prognosis / survival)
Strategy

- Systematic reviews
- Mendelian randomization - causal effects
- Current patterns of diet and exercise
- Qualitative interviews – attitudes, barriers, facilitators
- Feasibility RCTs:
  - recruitment, randomisation, retention, acceptability
  - Proof of efficacy (surrogates of proliferation)
  - Impact on nutrient levels & biomarkers (mechanisms)
- Underpinned by PPI
Clinical cohort of 194 men with advanced disease: associations of IGF-I with progression to mortality

<table>
<thead>
<tr>
<th>Model</th>
<th>Prostate cancer specific mortality (n=60)</th>
<th>All cause mortality (n=104)</th>
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<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-value</td>
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<tr>
<td>Model 1</td>
<td>1.22 (0.93, 1.59)</td>
<td>0.1</td>
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<tr>
<td>Model 2</td>
<td>1.23 (0.94, 1.62)</td>
<td>0.1</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.59 (1.11, 2.28)</td>
<td>0.01</td>
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</tbody>
</table>

Odds ratio (OR) per 1 standard deviation (SD) increase in IGF-I

**Adjustments:**
Model 1: Adjusted for age
Model 2: Adjusted for age, stage, Gleason, smoking, treatment & PSA
Model 3: Adjusted for age, stage, Gleason, smoking, treatment, PSA & IGFBP-3

*Rowlands M-A et al. Cancer Causes & Control 2011*
mild exercise no longer cuts it—
to live longer you must jog or
take up vigorous sports!

Marge! do I have a will?
Men with prostate cancer make positive dietary changes following
diagnosis and treatment

Kerry N. L. Avery · Jenny L. Donovan · Rebecca Gilbert · Michael Davis ·
Pauline Emmett · Liz Down · Steven Oliver · David E. Neal · Freddie C. Hamdy ·
J. Athene Lane

Is a cancer diagnosis a trigger for health
behaviour change? Findings from a
prospective, population-based study

K Williams¹, A Steptoe² and J Wardle*¹
PrEvENT framework for a nested feasibility trial

Clinical cohort of men listed for RP – consent for baseline bloods, questionnaire, measures, follow-up for mechanistic studies & re-contact (n ≈ 150)

RP – FFPE tissue for observational mechanistic studies

Randomise post RP (2nd consent, bloods, questionnaire)

Test feasibility of dietary / PA intervention
- factorial design
- follow-up 3 & 6 mo; bloods at 6 mo

Research objectives:
- Feasibility: recruitment, randomisation, retention, delivery, acceptability, adherence, tolerability, quality of life
- Impact on nutrient levels & biomarkers (mechanisms)
- Proof of efficacy on surrogates of cancer proliferation
Current BRU & related projects

**Intervention(s)**
- Systematic reviews (Hackshaw, Perry)
- Molecular & nutrition epi (Holly, Jeffrey, Lane, Penfold)
- Mendelian randomization (Lewis: WCRF funded)

**Delivery & feasibility**
- Qualitative (Persad: UHBristol, Hackshaw, Er, Sutton)
- PrEvENT – recruitment/ acceptability/ retention (Hackshaw, Lane, Martin, PCa Group)

**Mechanistic targets**
- Systematic reviews (Lewis, Gardner, Gaunt: WCRF)
- Molecular responses (Holly, Perks, Biernacka)
- Methylation & ‘omics (Relton, Davey Smith: IEU)

**Surrogate outcomes**
- Serial PSA (Tilling, Simpkin: NIHR SDO&HSR)
- IGF (Holly, Perks, Biernacka)

**Definitive trial**
- BRU Prostate Cancer Group
Summary

• Diet & PA are potential new therapies in PCa
• The BRU will:
  – Identify the most promising interventions
  – Investigate molecular effects
  – Assess feasibility of delivering long-term diet / PA therapies
• Establish the basis for later definitive RCTs assessing impact on progression
• Collaborations very welcome
Acknowledgements

• **BRU staff/affiliates:** Amit Bahl, Kalina Biernacka, Ashley Cooper, George Davey Smith, Jenny Donovan, Vanessa Er, Ola Frankow, Dave Gillatt, Richard Hocking, Lucy Hackshaw, Jeff Holly, Mona Jeffreys, Shirley Jenkins, Melissa Ke, Athene Lane, Andy Ness, Jon Oxley, Chris Penfold, Claire Perks, Rachel Perry, Raj Persad, Tony Rhodes, Eileen Sutton, Steve Thomas, Pat Turton

• **Related projects:** Rob Andrews, Verity Andrews, Kerry Avery, Carolina Bonilla, Neil Davies, Freddie Hamdy, Mike Gardner, Tom Gaunt, Sarah Lewis, David Neal, Mari-Anne Rowlands

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