A RAndomizeD Intervention for CArdiovascular and Lifestyle Risk Factors in Prostate Cancer Patients

RADICAL PC2

Darryl P. Leong, MBBS, MPH, M.Biostat, PhD
Population Health Research Institute
McMaster University and Hamilton Health Sciences
On behalf of the RADICAL PC2 Investigators

30 August 2026

Background

- In US patients with non-metastatic prostate cancer, cardiovascular disease accounts 23% of deaths (prostate cancer accounted for 17% of deaths)
- Cardiovascular risk factor control suboptimal in majority of patients with prostate cancer
- Diagnosis & treatment of prostate cancer may represent a “teachable moment”

Weiner *et al. Cancer* 2021; 127(16): 2895
Sun, *et al. JAMA Netw Open* 2021; 4(2):e210070
Klimis, *et al. JACC CardioOncol* 2023; 5(1): 70

Objectives

1. To determine whether routine referral of patients with prostate cancer to a cardiologist/internist - to implement a systematic cardiovascular risk factor strategy - would improve risk factor control and reduce adverse CV outcomes compared with usual care
2. To identify easily recognizable clinical subgroups that might benefit most from this intervention

Methods

Pragmatic randomized, controlled clinical trial

Inclusion Criteria

At least one of:

- Prostate cancer diagnosed within 12 months
- First treated with androgen deprivation therapy within 6 months
- Plan to receive androgen deprivation therapy for the first time within next 1 month

Exclusion Criteria

Any of:

- Age <45 years
- Consulting cardiologist annually
- On statin with systolic blood pressure ≤130mmHg

Intervention

Control group

- Could be referred to cardiologist or internist by usual physicians if clinically indicated
- Otherwise managed according to usual standard-of-care

Intervention group

- Referred to cardiologist or internist
- Statin irrespective of cholesterol levels & guideline recommendations
- Target systolic blood pressure ≤130mmHg with blood pressure-lowering medications as needed
- Diet and exercise guidance including printed materials
- Support to quit smoking using locally available resources

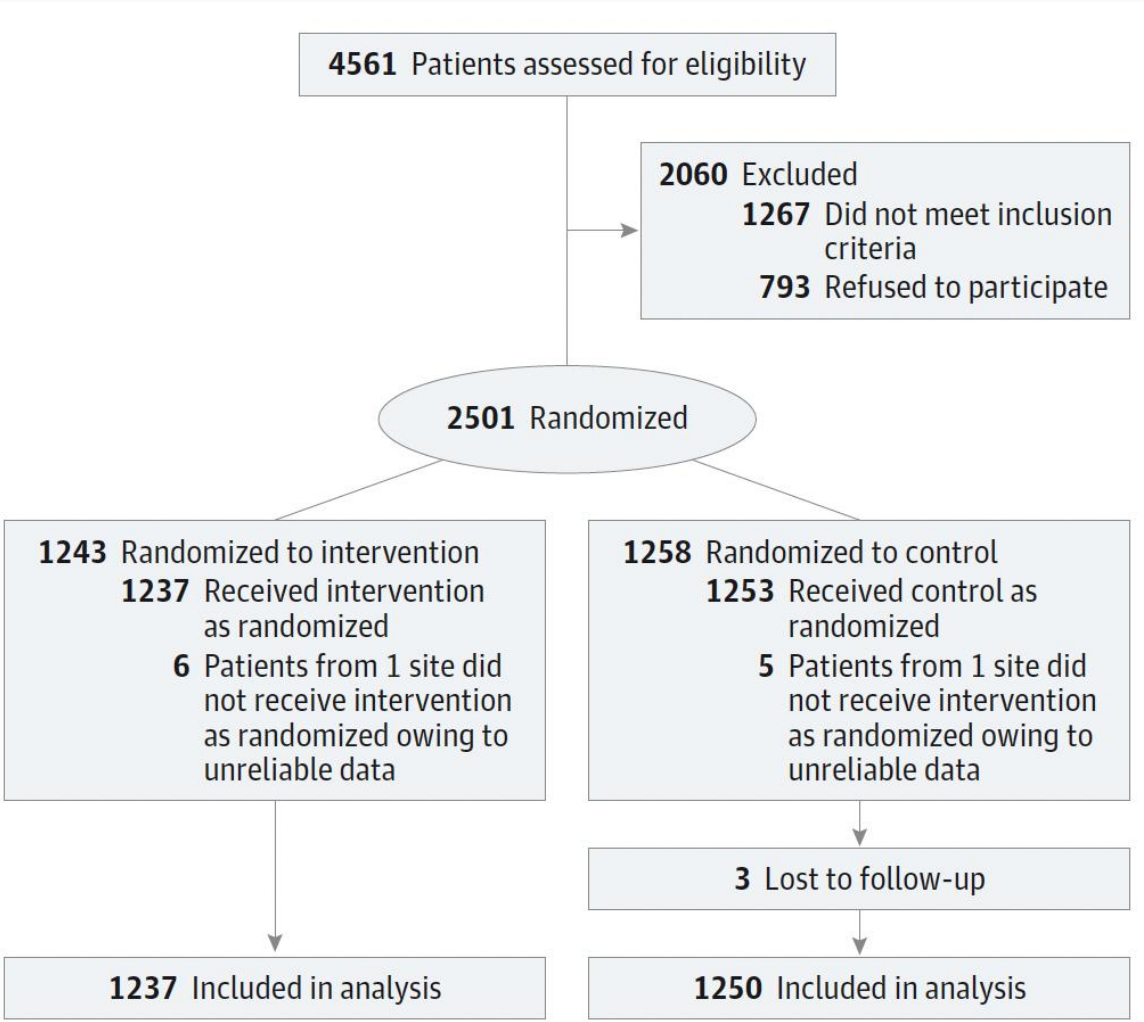
Outcomes

1. First primary: hierarchical composite of cardiovascular death, MI, stroke, heart failure, suboptimal cholesterol (>4mmol/L) and suboptimal blood pressure (SBP >130mmHg) by win ratio
2. Second primary: time-to-cardiovascular death, MI, stroke and heart failure by competing risks analysis
3. Exploratory: each component of the first primary outcome

Results

55 sites

8 countries



Baseline Characteristics

Characteristic	Control Group N=1250	Intervention Group N=1237
Mean±SD age, years	68±8	68±8
Race/Ethnicity		
Black	79 (6%)	97 (8%)
Latino	79 (6%)	64 (5%)
White	1034 (83%)	1028 (83%)
Other	53 (4%)	45 (4%)
Employed	456 (36%)	480 (39%)

Baseline Characteristics

Characteristic	Control Group N=1250	Intervention Group N=1237
Prostate cancer characteristics		
NCCN low risk	104 (8%)	82 (7%)
NCCN intermediate risk	455 (37%)	500 (41%)
NCCN high risk	504 (40%)	499 (40%)
Metastases	184 (15%)	153 (12%)
Prostate cancer treatment		
Prostatectomy	326 (26%)	343 (28%)
Prostate radiotherapy	338 (27%)	349 (29%)
Observation	138 (11%)	111 (9%)
ADT		
GnRH agonist	345 (28%)	332 (27%)
GnRH antagonist	54 (4%)	49 (4%)

Baseline Cardiovascular Risk Factors

Characteristic	Control Group N=1250	Intervention Group N=1237
Tobacco		
Never	571 (46%)	549 (44%)
Former	530 (42%)	565 (46%)
Current	146 (12%)	119 (10%)
Medical history		
Coronary artery disease	56 (4%)	57 (5%)
Stroke	33 (3%)	25 (2%)
Peripheral arterial disease	17 (1%)	15 (1%)
Heart failure	16 (1%)	15 (1%)
Diabetes	172 (14%)	187 (15%)
Hypertension	501 (40%)	536 (43%)

Adoption of Interventions – median f/u 5.8 years

Component	Overall Baseline	Control Group Closeout	Intervention Group Closeout
Consulted cardiologist/ internist	-	21%	90%
Median (IQR) number of cardiologist/internist visits	-	3 (1-6)	4 (3-6)
Statin	30%	40%	63%
BP-lowering medication	45%	49%	56%
Antiplatelet medication	16%	14%	19%
Anticoagulant	3%	7%	7%

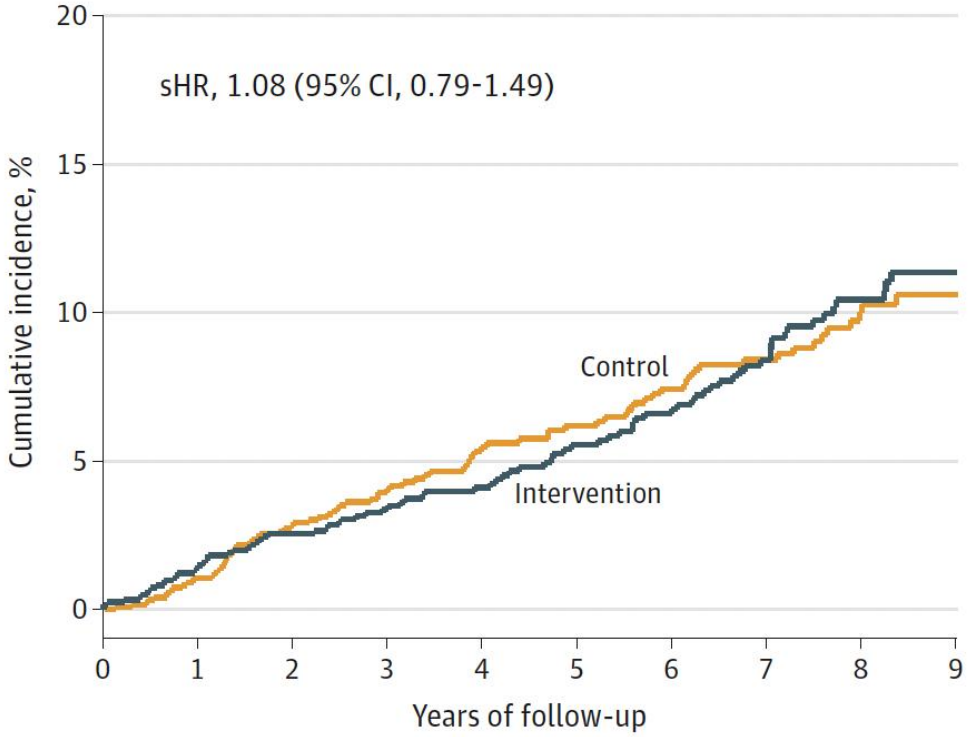
Win ratio at median 5.8 years

Among control-intervention pairs that are not tied at the end of follow-up:

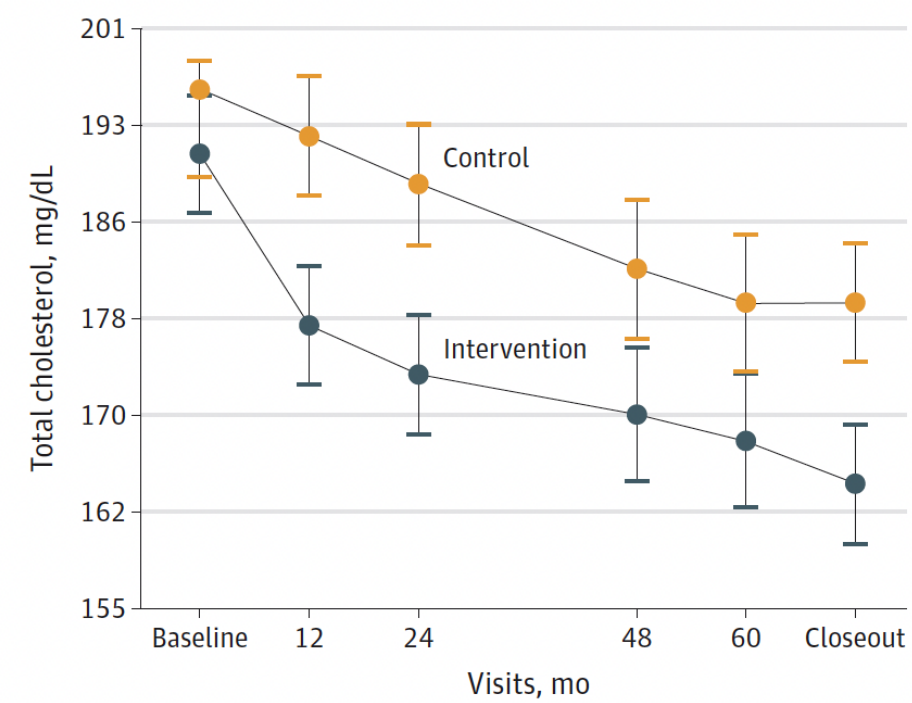
$$\textbf{Win ratio} = \frac{\textit{Wins in intervention group}}{\textit{Wins in control group}}$$

Hierarchical component	Number of events	Component-specific win ratio	Favours
Overall		***1.60 (1.42-1.81)***	***Intervention***
Cardiovascular death	73 (2.9%)	0.75	Control
Myocardial infarction	55 (2.2%)	1.80	Intervention
Stroke	47 (1.9%)	1.07	Neutral
Heart failure	30 (1.2%)	0.57	Control
Cholesterol >4mmol/L		2.24	Intervention
SBP >130mmHg		0.99	Neutral

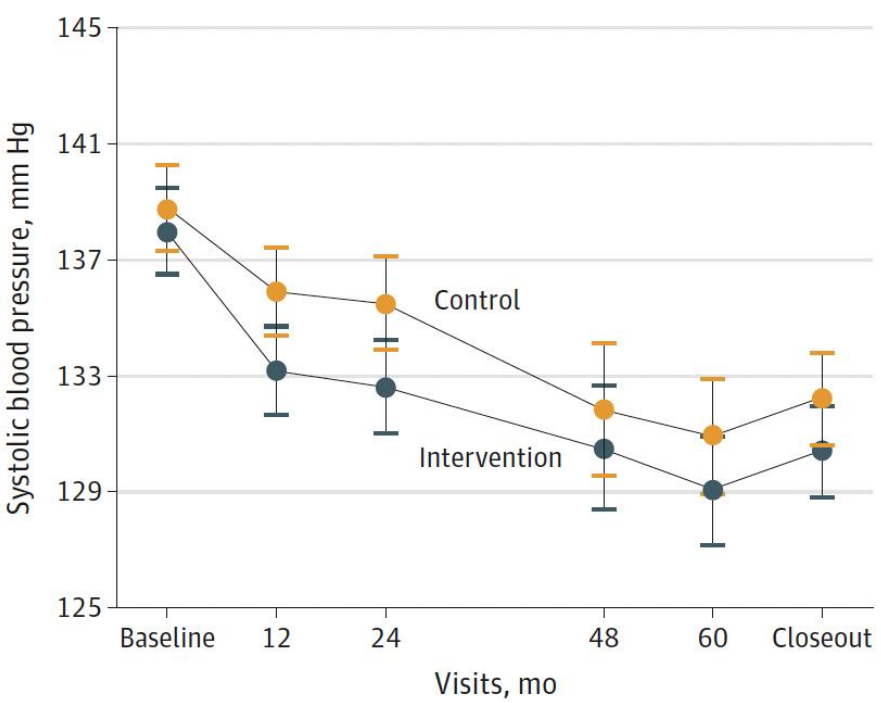
CV Death, MI, Stroke and Heart Failure



Cholesterol



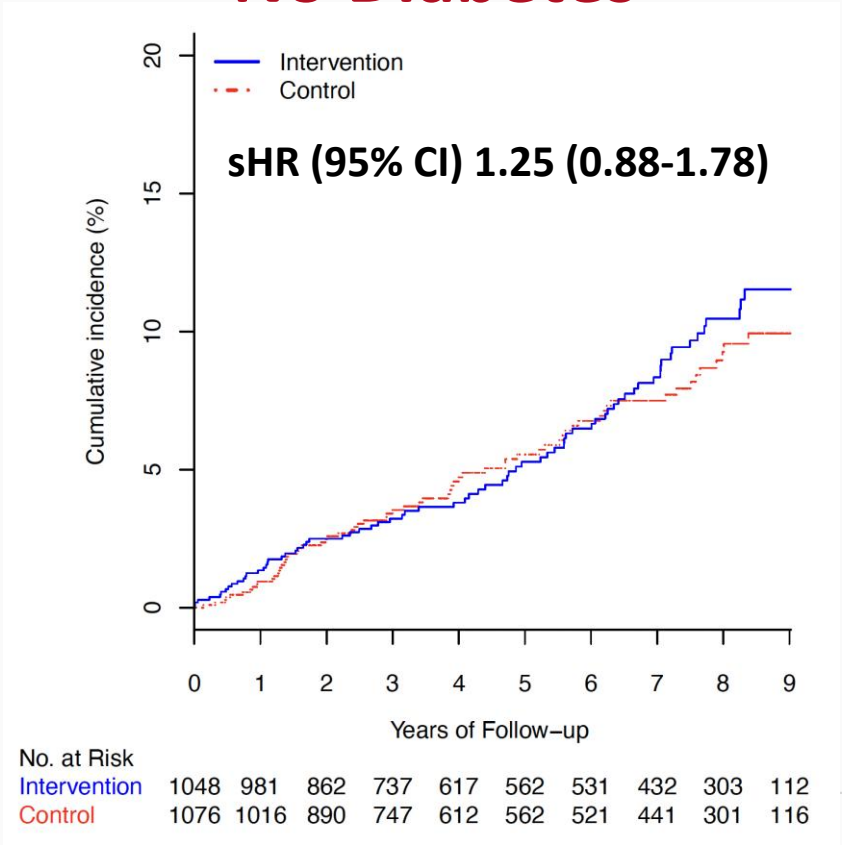
Systolic BP



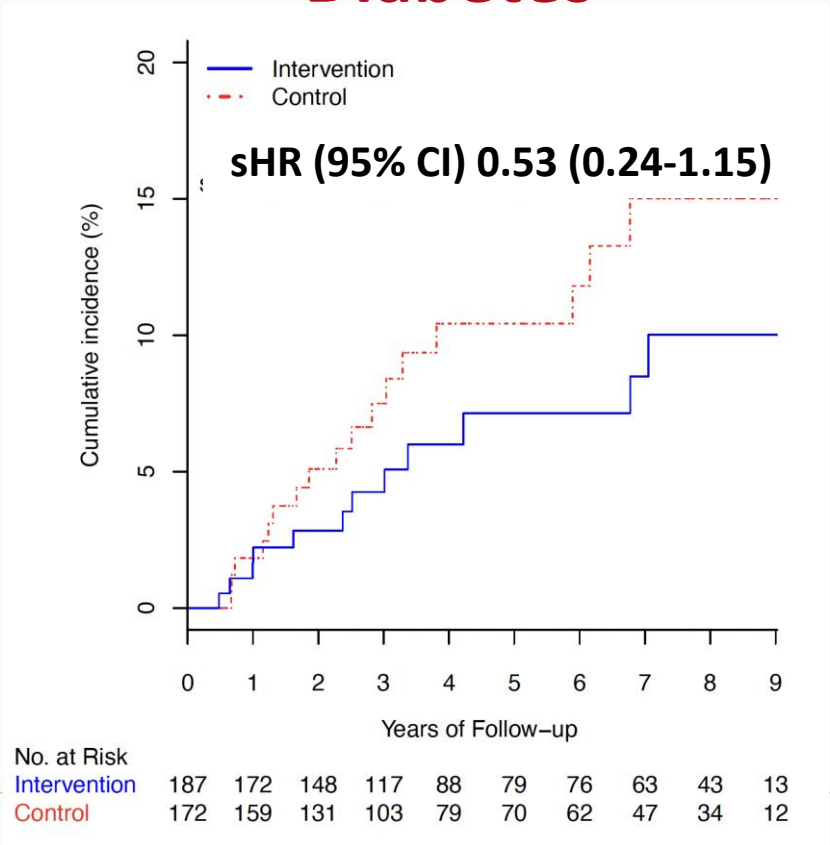
Multiply cholesterol in mg/dL by 0.0259 to convert to mmol/L

CV Death, MI, Stroke and Heart Failure

No Diabetes

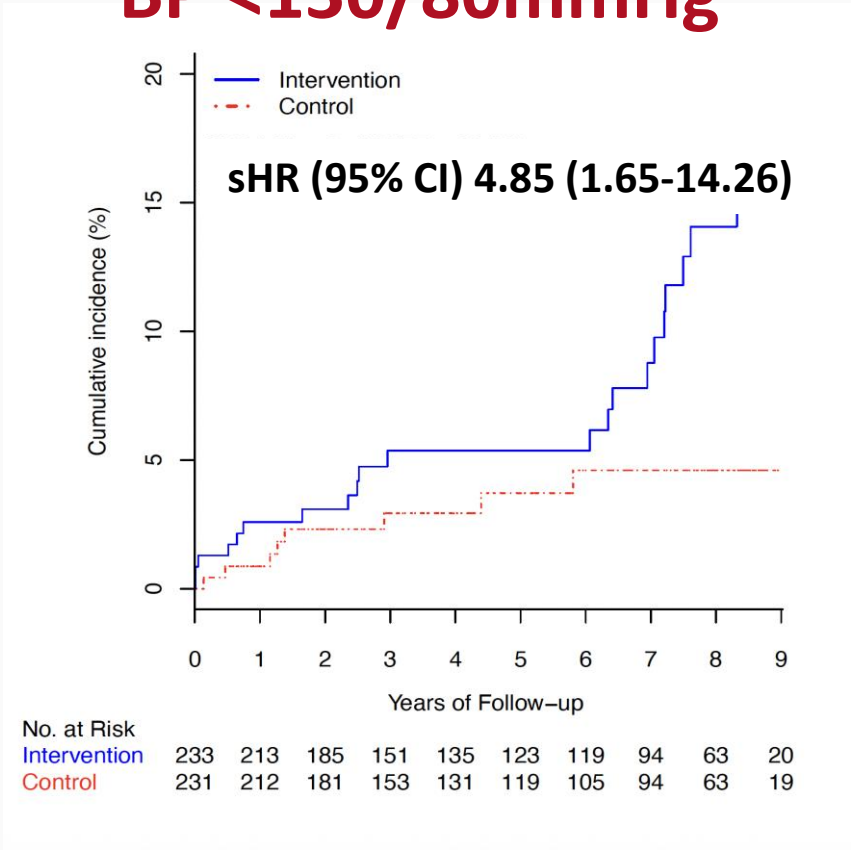


Diabetes

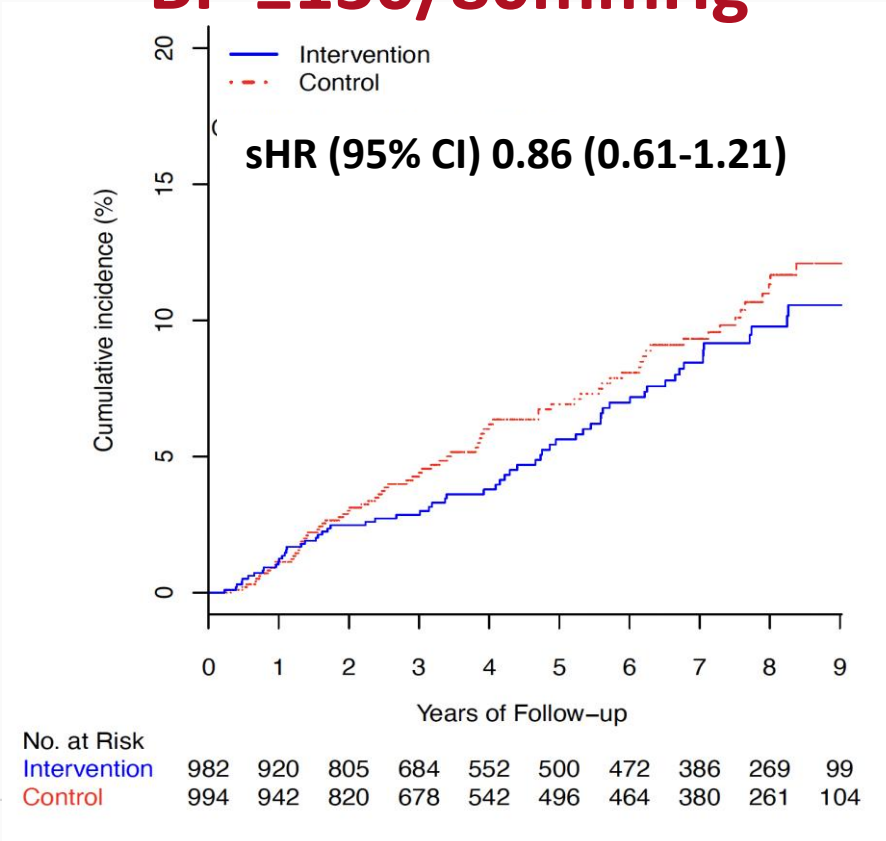


CV Death, MI, Stroke and Heart Failure

BP <130/80mmHg



BP ≥130/80mmHg



Conclusions

Routine referral of patients with prostate cancer to a cardiovascular specialist:

1. Improves outcomes primarily through achieving better cholesterol control
2. Has not been shown to decrease CV death, MI, stroke and heart failure
3. May be of greater benefit in those with
   - Hypertension, SBP ≥130mmHg or DBP ≥80mmHg
   - Diabetes
   - Total cholesterol >4mmol/L

Acknowledgements

- All trial participants

- Canadian Cancer Society and funded by the Movember Foundation (grant #400326)
- Hamilton Health Sciences Strategic Initiative Program
- Canadian Cancer Society (grant #706677)
- Tolmar Pharmaceutiques Canada Inc.
- Population Health Research Institute, Hamilton Health Sciences Research Institute (HHSRI)

Acknowledgements

- **Steering Committee:** Darryl P. Leong, Jehonathan H. Pinthus, P.J. Devereaux, Vincent Fradet, Laurence Klotz, Himu Lukka, Marina Mourtzakis, Joseph Selvanayagam, Avirup Guha, Celestia Higano, Alvaro Avezum, Ludhmila Hajjar
- **Adjudication Committee:** Kelvin K.H. Ng (Chair), Pablo Lamellas, David Margel, Francois Caron, Malik Farooqi, Som Mukherjee, Germano Dallegrave Cavalli, Rocio Consuelo Baro Vila, Cristina Cano Garcia, Alexander Benz, Filipe Cirne, Rachel Richard
- **Data Safety Monitoring Board (DSMB):** George Wells (Chair), Jean Rouleau, Michael L. Cher
- **Statisticians Reporting to DSMB:** Kumar Balasubramanian
- **Study Statisticians & Programmers:** Rajibul Mian, Cissy Tang, Mark Molec, Nishitha Jeyachandradhas
- **ICT:** Matthew Smart, Les Farago, Gianluca Rigitano, Miroslaw Malysz, Shrouk Saed, Nidhi Jethoo
- **Project Office Study Staff:** Sumathy Rangarajan (Program Director), Sarah Karampatos, Steven Agapay, Peter Accardo, Amanda DeJesus, Maxwell Crispo, Rhonda Masney, Sabrina Woolgar, Ruchi Patel, Edith Wagan, Kayla Pohl, Sara Chenier, Steven Chen (Student Volunteer), Riya Srivastava (Student), Shauna Szendrey, Shraddha Sawant, Nadra Yasmin, Aaron Donst
- **Cardio-Oncology Trainees:** Nazanin Aghel, Frances Carandang, Germano Dallegrave Cavalli, Filipe Cirne, Cristina Cano Garcia, Enrique Gonzalez, Harry Klimis, Jose Patricio Lopez-Lopez, Sophia Laird, Rocio Consuelo Baro Vila, Rachel Richard

JAMA Internal Medicine

Leong DP, Higano C, Garcia CC, et al; for the RADICAL PC Investigators

Specialist Referral for Cardiovascular Risk in Patients With Prostate Cancer

A Randomized Clinical Trial

Published online August 30, 2026

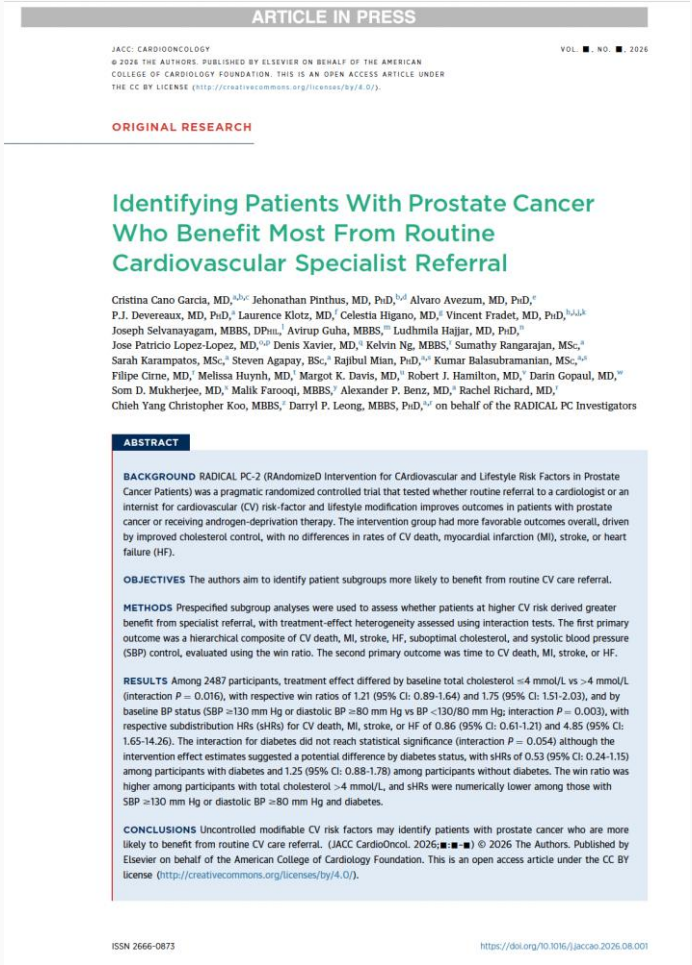
European Society of Cardiology

Available at jamainternalmedicine.com

Scan to read the article

Simultaneously published in JACC: CardioOncology

10.1016/j.jaccao.2026.08.001



ARTICLE IN PRESS

JACC: CARDIOONCOLOGY VOL. ■, NO. ■, 2026

ORIGINAL RESEARCH

Identifying Patients With Prostate Cancer Who Benefit Most From Routine Cardiovascular Specialist Referral

Cristina Cano Garcia, MD,[a,b,y,c] Jehonathan Pinthus, MD, PhD,[b,d] Alvaro Avezum, MD, PhD,[e] P.J. Devereaux, MD, PhD,[a] Laurence Klotz, MD,[f] Celestia Higano, MD,[g] Vincent Fradet, MD, PhD,[h,i,j,k] Joseph Selvanayagam, MBBS, DPhil,[l] Avirup Guha, MBBS,[m] Ludhmila Hajjar, MD, PhD,[n] Jose Patricio Lopez-Lopez, MD,[o,p] Denis Xavier, MD,[q] Kelvin Ng, MBBS,[r] Sumathy Rangarajan, MSc,[a] Sarah Karampatos, MSc,[s] Steven Agapay, BSc,[a] Rajibul Mian, PhD,[a,t] Kumar Balasubramanian, MSc,[a,t] Filipe Cirne, MD,[r] Melissa Huynh, MD,[r] Margot K. Davis, MD,[u] Robert J. Hamilton, MD,[v] Darin Gopaul, MD,[w] Som D. Mukherjee, MD,[s] Malik Farooqi, MBBS,[s] Alexander P. Benz, MD,[a] Rachel Richard, MD,[r] Chieh Yang Christopher Koo, MBBS,[r] Darryl P. Leong, MBBS, PhD,[a,r] on behalf of the RADICAL PC Investigators

ABSTRACT

BACKGROUND RADICAL PC-2 (RAndomizeD Intervention for CArdiovascular and Lifestyle Risk Factors in Prostate Cancer Patients) was a pragmatic randomized controlled trial that tested whether routine referral to a cardiologist or an internist for cardiovascular (CV) risk-factor and lifestyle modification improves outcomes in patients with prostate cancer or receiving androgen-deprivation therapy. The intervention group had more favorable outcomes overall, driven by improved cholesterol control, with no differences in rates of CV death, myocardial infarction (MI), stroke, or heart failure (HF).

OBJECTIVES The authors aim to identify patient subgroups more likely to benefit from routine CV care referral.

METHODS Prespecified subgroup analyses were used to assess whether patients at higher CV risk derived greater benefit from specialist referral, with treatment-effect heterogeneity assessed using interaction tests. The first primary outcome was a hierarchical composite of CV death, MI, stroke, HF, suboptimal cholesterol, and systolic blood pressure (SBP) control, evaluated using the win ratio. The second primary outcome was time to CV death, MI, stroke, or HF.

RESULTS Among 2487 participants, treatment effect differed by baseline total cholesterol ≤4 mmol/L vs >4 mmol/L (interaction $P = 0.016$), with respective win ratios of 1.21 (95% CI: 0.89-1.64) and 1.75 (95% CI: 1.51-2.03), and by baseline BP status (SBP ≥130 mm Hg or diastolic BP ≥80 mm Hg vs BP <130/80 mm Hg; interaction $P = 0.003$), with respective subdistribution HRs (sHRs) for CV death, MI, stroke, or HF of 0.86 (95% CI: 0.61-1.21) and 4.85 (95% CI: 1.65-14.26). The interaction for diabetes did not reach statistical significance (interaction $P = 0.054$) although the intervention effect estimates suggested a potential difference by diabetes status, with sHRs of 0.53 (95% CI: 0.24-1.15) among participants with diabetes and 1.25 (95% CI: 0.88-1.78) among participants without diabetes. The win ratio was higher among participants with total cholesterol >4 mmol/L, and sHRs were numerically lower among those with SBP ≥130 mm Hg or diastolic BP ≥80 mm Hg and diabetes.

CONCLUSIONS Uncontrolled modifiable CV risk factors may identify patients with prostate cancer who are more likely to benefit from routine CV care referral. (JACC CardioOncol. 2026;■:■-■) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

ISSN 2666-0873 https://doi.org/10.1016/j.jaccao.2026.08.001