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# Optimizing outcomes in men with prostate cancer: the cardiovascular event lowering (CaELO) pathways

E. David Crawford, MD,<sup>1</sup> David Albala, MD,<sup>2</sup> Marc B. Garnick, MD,<sup>3</sup> Andrew W. Hahn, MD,<sup>4</sup> Paul Maroni, MD,<sup>5</sup> Rana R. McKay, MD,<sup>6</sup> Martin Miner, MD,<sup>7</sup> Peter Orio III, MD,<sup>8</sup> Kshitij Pandit, MD,<sup>1</sup> Scott Sellinger, MD,<sup>9</sup> Evan Y. Yu, MD,<sup>10</sup> Robert H. Eckel, MD<sup>11</sup>

<sup>1</sup>Department of Urology, University of California San Diego, La Jolla, California, USA; <sup>2</sup>Department of Urology, Downstate Health Sciences Center, Brooklyn, New York, USA; <sup>3</sup>Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA; <sup>4</sup>Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; <sup>5</sup>Department of Surgery, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA; <sup>6</sup>Department of Urology, Department of Medicine, University of California San Diego, La Jolla, California, USA; <sup>7</sup>Warren Alpert School of Medicine, Brown University, Providence, Rhode Island, USA; <sup>8</sup>Dana-Farber Brigham Cancer Center, Harvard Medical School, Boston, Massachusetts, USA; <sup>9</sup>Advanced Urology Institute, Tallahassee, Florida, USA; <sup>10</sup>University of Washington, Fred Hutchinson Cancer Center, Seattle, Washington, USA; <sup>11</sup>Division of Endocrinology, Metabolism, and Diabetes, Anschutz Medical Center, University of Colorado, Denver, Colorado, USA

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**Introduction:** Risk of cardiovascular disease is higher among men with prostate cancer than men without, and prostate cancer treatments (especially those that are hormonally based) are associated with increased cardiovascular risk.

**Materials and methods:** An 11-member panel of urologic, medical, and radiation oncologists (along with a men's health specialist and an endocrinologist/preventive cardiologist) met to discuss current practices and challenges in the management of cardiovascular risk in prostate cancer patients who are taking androgen deprivation therapies (ADT) including LHRH analogues, alone and in combination with androgen-targeted therapies (ATTs).

**Results:** The panel developed an assessment algorithm to categorize patients by risk and deploy a risk-adapted management strategy, in collaboration with other healthcare providers (the patient's healthcare "village"), with the goal of preventing as well as reducing cardiovascular events. The panel also developed a patient questionnaire for cardiovascular risk as well as a checklist to ensure that all aspects of cardiovascular disease risk reduction are completed and monitored.

**Conclusions:** Prostate cancer patients receiving ADT with or without ATT need to be more zealously assessed for prevention and aggressively managed to reduce cardiovascular events. This can and should include participation from the entire multidisciplinary healthcare team.

**Key Words:** prostate cancer, cardiovascular disease, risk assessment, hormonal therapy, lifestyle risk reduction

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Address correspondence to Dr. E. David Crawford, Dept. of Urology, University of California San Diego, Koman Family Outpatient Pavilion, La Jolla, CA 92037 USA

## Introduction

Cardiovascular (CVD) and prostate cancer are inextricably linked, on several levels. Firstly, the most common non-prostate cancer cause of death in men with prostate cancer is CVD.<sup>1,2</sup> Simply because of their age, men with prostate cancer are at higher risk of CVD. However, androgen deprivation therapy (ADT), a mainstay of prostate cancer treatment throughout the disease process, is associated with adverse metabolic and CV effects such as increased fat mass, insulin resistance, as well as increased CVD including coronary heart disease (CHD),<sup>3</sup> stroke,<sup>4</sup> and heart failure,<sup>5</sup> especially in men with pre-existing heart disease and weight gain.<sup>6</sup> Beyond clinically localized disease, ADT can be combined with androgen-targeted therapies (ATT), as well as chemotherapy and immunotherapy, each of which are associated with increased CV risk.<sup>7</sup> Several clinical trials are evaluating novel hormone monotherapy in men with localized prostate cancer. Doublet therapy is also now approved for use earlier in the disease course for curative intent, in nonmetastatic hormone-sensitive prostate cancer with biochemical recurrence at high risk for metastasis, which will prolong duration of exposure to potential CV risk-increasing agents.

For many, CV risk begins with the increasingly prevalent metabolic syndrome, a cluster of conditions that occur together and may be associated with increased risk of heart disease, stroke, and type 2 diabetes. These conditions include abdominal adiposity/large waist, high triglyceride levels, low high-density lipoprotein cholesterol levels, hypertension, and elevated fasting blood sugar.<sup>5,8,9,10</sup> Metabolic syndrome is associated with a pro-inflammatory state as measured by several pro-inflammatory biomarkers, leading to increased vascular endothelial dysfunction, increased vascular inflammation, oxidative stress and decreased coronary flow reserve. The end result is atherosclerosis and CVD.<sup>6</sup> Patients with cancer also have a hypercoagulable/prothrombotic state, which can increase risk independently.<sup>6</sup>

CV risk is an important issue in men both being considered for ADT and those who are established ADT patients. Anecdotally, the panel noted that CV risk assessment and management in current clinical practice is not standardized and often performed ad hoc. While there exist guidelines and risk calculating tools in the US for CV risk reduction in prostate cancer patients taking ADT, they offer no formalized approach for identification or stratification of CV risk or tools to reduce risk, and are either too vague to be useful for cancer patients or are not easily implemented in busy clinic settings. There is a need for a practical and easily

implemented CV risk assessment tool that is specific to prostate cancer patients.

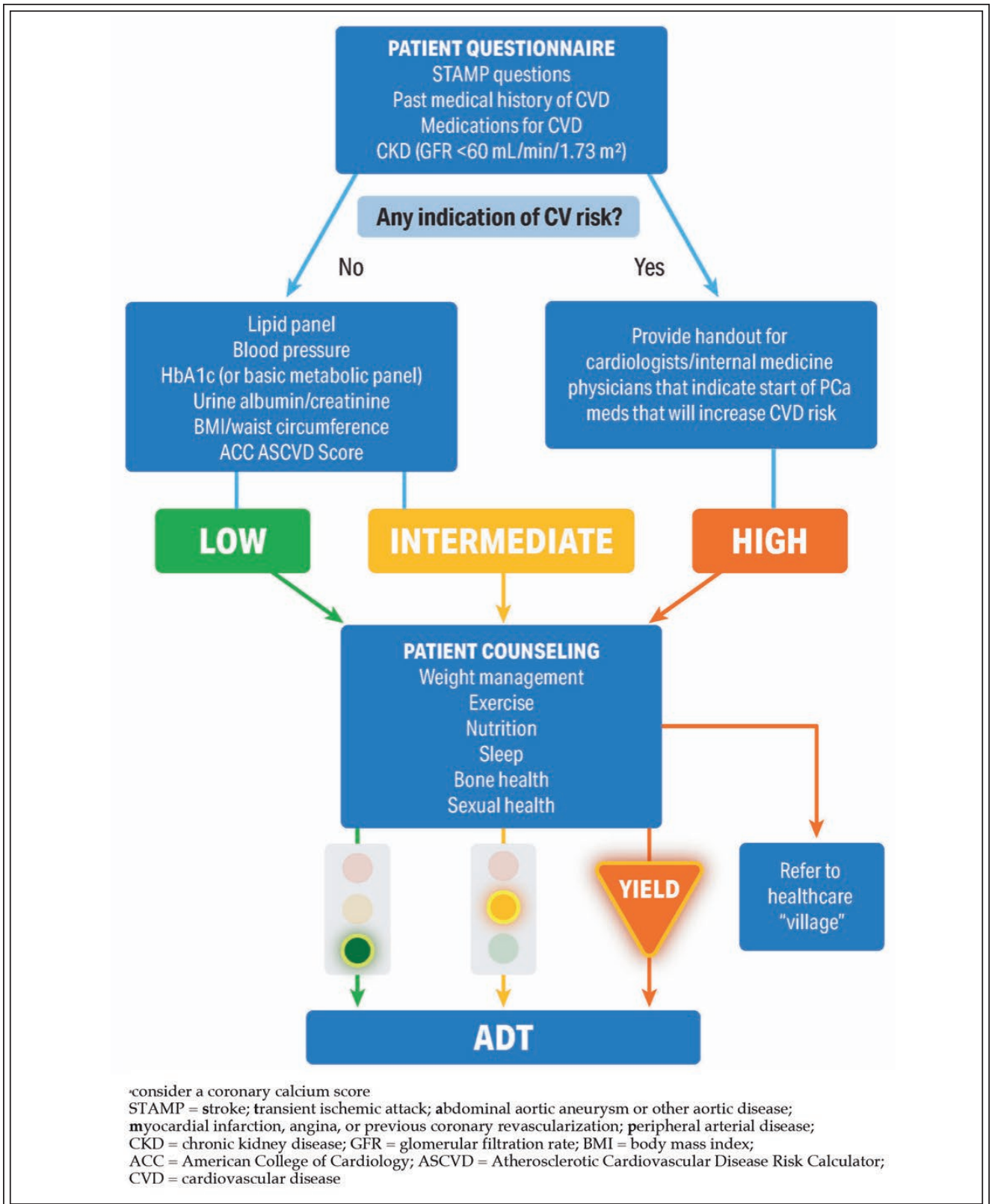
Several of the authors have recently published a proposal for the comprehensive care of men on ADT from the Prostate Cancer 360 Working Group, of which cardiometabolic care is part of the five identified domains for recommended monitoring and assessment.<sup>11</sup> They describe the cardiometabolic changes associated with ADT, noting that ADT use imposes the greatest cardiovascular risk in patients who have pre-existing cardiometabolic comorbidities, of which the vast majority of patients starting ADT have.<sup>11</sup> This article provides practical and easy-to-use strategies to implementing the CV risk tools into clinical practice.

## Materials and methods

A multidisciplinary group of urologic, medical, and radiation oncologists, a men's health specialist, and an endocrinologist/preventive cardiologist, was recruited based on their experience and expertise in the management of prostate cancer to consider the current challenges in managing CV risk in men with prostate cancer being considered for or currently receiving ADT. During the meeting (August 2023), after a brief review of the background/rationale including existing guidelines and materials, panel members were asked a series of questions about their current practices with prostate cancer patients regarding identifying CV risk, stratifying patients based on CV risk, management of CV risk, and the role of other healthcare providers in addressing CV risk in prostate cancer patients. The panel was then divided into three working groups to discuss the following questions: 1) How should prostate cancer patients be stratified based on CV risk?; 2) What operations need to be in place to make this risk assessment more standard practice?; 3) What are the management recommendations for each level of CV risk?

## Results

The panel members developed the following assessment tool to stratify risk in prostate cancer patients in a urology or oncology clinic, for whom hormonally-based treatments (ie, ADT +/- ATT) is being considered, Figure 1. Patients would be given a questionnaire to be completed prior to the visit - The STAMP questions (ie, history of stroke; transient ischemic attack; abdominal aortic aneurysm or other aortic disease; myocardial infarction, angina, or previous coronary revascularization; peripheral



**Figure 1.** CV Event Lowering (CaELO) risk assessment tool for patients with prostate cancer being considered for ADT with or without ATT.

arterial disease); any other past medical history of CVD; any current medications for CVD; and any history of chronic kidney disease.<sup>12</sup> A sample questionnaire can be found in Figure 2. This questionnaire could be integrated into any electronic medical records system.

For patients who have no history of CVD, a standard pre-treatment work up should include a lipid panel, measurement of blood pressure, an HbA1c measurement (or basic metabolic panel, depending on patient insurance), urinary albumin/creatinine measurement, determination of body mass index and waist circumference, and use these data for a CVD risk calculator such as the American College

of Cardiology (ACC) Atherosclerotic Cardiovascular Disease Risk Calculator (ASCVD), which determines the 10-year risk for CVD. Based on those results, the patient will be considered either low, intermediate, or high risk for CVD – a stratification that can serve as a guide for further patient management. Those with no indication of CV risk based on the STAMP question responses and normal values in the pre-treatment work up are considered low risk. Those with no STAMP indication of CV risk but some abnormal results the pre-treatment work up are considered intermediate risk. Those whose STAMP profile indicates CV risk are automatically considered high risk.

Today's date:

Patient name:

Patient date of birth:

1. Do you have a history of any of the following types of cardiovascular disease?

	Yes	No
Stroke		
Transient ischemic attack or "mini stroke"		
Abdominal aortic aneurysm		
Myocardial infarction		
Angina		
Previous coronary artery stent or bypass surgery		
Valvular heart disease		
Cardiac arrhythmias and/or prolonged QT interval		
Peripheral arterial disease		

2. Do you have a history of chronic kidney disease?    Yes    No

3. Are you currently taking any of the following medications?

	Yes	No
Cholesterol-lowering therapy (eg, statins)		
Aspirin and/or other medications that affect clotting		
Obesity medications		
Diabetes medications		

*From the Cardiovascular Event Lowering (CaELO) Advisory Panel.*

**Figure 2.** Cardiovascular Risk Evaluation (CARE) questionnaire for men with prostate cancer.

Test	First test	Follow up	Date last performed	By which provider?
Family history of CVD	Baseline	NA		
Lipid panel	Baseline	At least annually		
HbA1c (or basic metabolic panel)	Baseline	At least annually		
eGFR	Baseline	At least annually		
Weight	Baseline	Every visit		
Waist circumference	Baseline	If weight changes		
10-year ASCVD risk	Baseline	Annually		

\*the measurement frequency of tests done at least annually needs to be individually determined.  
*From the Cardiovascular Event Lowering (CaELO) Advisory Panel.*

**Figure 3.** The Cardiovascular Risk Evaluation (CARE) monitoring schedule for patients with prostate cancer\*

For those without known CVD and who are considered intermediate risk, a coronary calcium score can be considered for further clarification of CVD risk; consider also additional testing to determine if a statin is needed. Of note, most prostate cancer patients will be considered intermediate or high risk. A high-risk patient can be given a handout to give to his cardiologist and/or internal medicine/primary care physician (PCP) discussing the type of medications that will be initiated and their associated CVD risks, as provided by Crawford et al.<sup>11</sup> In the panel's view, men at high risk of CVD should have their cardiovascular health managed by a PCP or cardiologist, which is why the handout explaining the new medications should be provided.

All patients being considered for prostate cancer treatment would receive counseling on reducing CVD risk factors through lifestyle modification, such as smoking cessation, improved nutrition, increased physical activity, sleep hygiene, as well as bone and sexual health.

Those deemed low and intermediate risk can proceed to ADT initiation. Those in the high-risk group can still receive ADT, but a "yield" sign indicates that referrals to a "village" of other healthcare providers for further follow up will be required, and possible treatment recommendations to reduce CVD risk. This provider "village" includes any or all of the following practitioners: cardiologist, PCP, cardio-oncologist, endocrinologist, nurse practitioner, physician assistant, pharmacist, nutritionist, physical therapist, fitness trainer, psychologist/psychiatrist, social worker, nurse navigator, dentist, and/or financial planner (for discussion of healthcare costs associated with treatment). This multidisciplinary team is essential

because urologists, radiation oncologists, and medical oncologists are seldom equipped to address all of health risk factors and possible medication side effects with their patients (due to limitations in staffing resources, time, and specialty support) and so must rely on this outside team. Some healthcare providers may wish to treat some of the CV risk factors directly. Importantly, this tool should be used at least annually but can be implemented more frequently (eg, every visit), depending on the preference of the provider. A sample checklist and timeline for assessments can be found in Figure 3; this could also be integrated into an EMR system.

## Discussion

This assessment tool identifies the CV risks evident in many men with prostate cancer, which can be exacerbated by treatment. It also empowers urologic oncology providers who are comfortable with managing CV risk factors to provide comprehensive care to their prostate cancer patients, and also ensures continuity of care when prostate cancer treatment providers communicate CV risk to other providers. Two processes are essential to the successful implementation of this tool: 1) good communication between the urologist/oncologist and the provider "village" and 2) delegation when possible to medical assistants (MAs) and advanced practice providers (APPs) to complete the assessments, provide education, communicate with other providers, and ensure that patients are going forward with their referrals. Moreover, CV risk in prostate cancer patients is not static; it changes with age, disease progression, and prostate cancer treatments, so CV risk must be continually assessed over the course of the patient's life.

## Conclusion

There is an urgent need for a practical CV risk assessment algorithm based on the increased CVD risk in prostate cancer patients. This increased risk occurs with many prostate cancer treatments, as well as with the possible earlier use of ADT with or without ATT in the disease process and therefore longer exposure to treatment over time. These simple tools can be used and integrated into any practice setting and will remain relevant throughout the disease process for each patient. □

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## References

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1. Leong DP, Fradet V, Shayegan B et al. Cardiovascular risk in men with prostate cancer: Insights from the RADICAL PC Study. *J Urol* 2020;203(6):1-8.
2. Elmehraath AO, Afifi AM, Al-Husseini MJ et al. Causes of death among patients with metastatic prostate cancer in the US from 2000 to 2016. *JAMA Netw Open* 2021;4(8):e2119568.
3. Roge M, Guimas V, Rio E et al. Cardiologist-performed baseline evaluation with an assessment of coronary status for prostate cancer patients undergoing androgen deprivation therapy: impact on newly diagnosed coronary artery disease. *Cancers* 2023;15(16):4157.
4. Meng F, Zhu S, Zhao J et al. Stroke related to androgen deprivation therapy for prostate cancer: a meta-analysis and systematic review. *BMC Cancer* 2016;16:180.
5. Kim J, Freeman K, Ayala A, Mullen M, Sun Z, Rhee JW. Cardiovascular impact of androgen deprivation therapy: from basic biology to clinical practice. *Curr Oncol Rep* 2023;25(9): 965-977.
6. Higano CS. Update on cardiovascular and metabolic risk profiles of hormonal agents used in managing advanced prostate cancer. *Urol Oncol* 2020;38(12):912-917.
7. Wilk M, Wasko-Grabowska A, Szmit S. Cardiovascular complications of prostate cancer treatment. *Front Pharmacol* 2020;11:555475.
8. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365(9468):1415-1428.
9. Albert KGMM, Eckel RH, Grundy SM et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and the International Association for the Study of Obesity. *Circulation* 2009;120(16): 1640-1645.
10. Okwuosa TM, Morgans A, Rhee JW et al. Impact of hormonal therapies for treatment of hormone-dependent cancers (breast and prostate) on the cardiovascular system: effects and modifications. *Circ Genom Precis Med* 2021;14:e000082.
11. Crawford ED, Garnick MB, Eckel RH et al. A proposal for the comprehensive care of men on androgen deprivation therapy: recommendations from the multidisciplinary Prostate Cancer 360 Working Group. *Urol Pract* 2024;11(1):18-29.
12. Kenk M, Gregoire JC, Cote, MA et al. Optimizing screening and management of cardiovascular health in prostate cancer: a review. *Can Urol Assoc J* 2020;14(9):E458-E464.