

**ILLINOIS HEALTH FACILITIES AND SERVICES REVIEW BOARD
APPLICATION FOR PERMIT**

SECTION I. IDENTIFICATION, GENERAL INFORMATION, AND CERTIFICATION

This Section must be completed for all projects.

Facility/Project Identification

Facility Name: UroPartners Prostate Center at the Glenn		
Street Address: 2634 Patriot Blvd. Unit J		
City and Zip Code: Glenview 60026		
County: Cook	Health Service Area: VII	Health Planning Area: 031

Applicant(s) [Provide for each applicant (refer to Part 1130.220)]

Exact Legal Name: UroPartners, LLC
Street Address: 2245 Enterprise Dr. Suite 4506
City and Zip Code: Westchester, Illinois 60154
Name of Registered Agent: Neal T. Goldstein
Registered Agent Street Address: 200 S. Wacker Dr. Suite 2700
Registered Agent City and Zip Code: Chicago, Illinois 60606
Name of Chief Executive Officer: Richard G. Harris, M.D.
CEO Street Address: 2245 Enterprise Dr. Suite 4506
CEO City and Zip Code: Westchester, Illinois 60154
CEO Telephone Number: (708) 492-0502

Type of Ownership of Applicants

☐ Non-profit Corporation	☐ Partnership
☐ For-profit Corporation	☐ Governmental
☒ Limited Liability Company	☐ Sole Proprietorship ☐ Other
- Corporations and limited liability companies must provide an Illinois certificate of good standing. - Partnerships must provide the name of the state in which they are organized and the name and address of each partner specifying whether each is a general or limited partner.	
APPEND DOCUMENTATION AS ATTACHMENT 1 IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.	

Primary Contact [Person to receive ALL correspondence or inquiries]

Name: Nick Radonjic
Title: General Counsel/Chief Operating Officer
Company Name: UroPartners, LLC
Address: 2245 Enterprise Dr. Suite 4506, Westchester, Illinois 60154
Telephone Number: (708) 273-3031
E-mail Address: NRadonjic@UroPartners.com
Fax Number: (708) 492-0565

Additional Contact [Person who is also authorized to discuss the application for permit]

Name: Mark J. Silberman and Juan Morado Jr.
Title: Partner
Company Name: Benesch Friedlander Coplan & Aronoff
Address: 71 S. Wacker Dr. Suite 1600 Chicago IL 60606
Telephone Number: (312) 212-4952 and (312) 212-4967
E-mail Address: MSilberman@beneschlaw.com and JMorado@beneschlaw.com
Fax Number: (877) 357-4913

Post Permit Contact

[Person to receive all correspondence subsequent to permit issuance-**THIS PERSON MUST BE EMPLOYED BY THE LICENSED HEALTH CARE FACILITY AS DEFINED AT 20 ILCS 3960**]

Name: Nick Radonjic
Title: General Counsel/Chief Operating Officer
Company Name: UroPartners, LLC
Address: 2245 Enterprise Dr. Suite 4506, Westchester, Illinois 60154
Telephone Number: (708) 273-3031
E-mail Address: NRadonjic@UroPartners.com
Fax Number: (708) 492-0565

Site Ownership

[Provide this information for each applicable site]

Exact Legal Name of Site Owner: UroPartners Investments, LLC
Address of Site Owner: 2245 Enterprise Dr. Suite 4506, Westchester, Illinois 60154
Street Address or Legal Description of the Site: 2600 Patriot Blvd. Suite J, Glenview, Illinois 60026 Proof of ownership or control of the site is to be provided as Attachment 2. Examples of proof of ownership are property tax statements, tax assessor's documentation, deed, notarized statement of the corporation attesting to ownership, an option to lease, a letter of intent to lease, or a lease.
APPEND DOCUMENTATION AS ATTACHMENT 2 , IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Operating Identity/Licensee

[Provide this information for each applicable facility and insert after this page.]

Exact Legal Name: UroPartners, LLC	
Address: 2245 Enterprise Dr. Suite 4506, Westchester, Illinois 60154	
☐ Non-profit Corporation ☐ For-profit Corporation ☒ Limited Liability Company ☐ Other	☐ Partnership ☐ Governmental ☐ Sole Proprietorship
- Corporations and limited liability companies must provide an Illinois Certificate of Good Standing. - Partnerships must provide the name of the state in which organized and the name and address of each partner specifying whether each is a general or limited partner. Persons with 5 percent or greater interest in the licensee must be identified with the % of ownership.	
APPEND DOCUMENTATION AS ATTACHMENT 3 , IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.	

Organizational Relationships

Provide (for each applicant) an organizational chart containing the name and relationship of any person or entity who is related (as defined in Part 1130.140). If the related person or entity is participating in the development or funding of the project, describe the interest and the amount and type of any financial contribution.

APPEND DOCUMENTATION AS ATTACHMENT 4 , IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.
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Flood Plain Requirements

[Refer to application instructions.]

Provide documentation that the project complies with the requirements of Illinois Executive Order #2006-5 pertaining to construction activities in special flood hazard areas. As part of the flood plain requirements, please provide a map of the proposed project location showing any identified floodplain areas. Floodplain maps can be printed at www.FEMA.gov or www.illinoisfloodmaps.org. **This map must be in a readable format.** In addition, please provide a statement attesting that the project complies with the requirements of Illinois Executive Order #2006-5 (<http://www.hfsrb.illinois.gov>).

APPEND DOCUMENTATION AS ATTACHMENT 5, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

Historic Resources Preservation Act Requirements

[Refer to application instructions.]

Provide documentation regarding compliance with the requirements of the Historic Resources Preservation Act.

APPEND DOCUMENTATION AS ATTACHMENT 6, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

DESCRIPTION OF PROJECT**1. Project Classification**

[Check those applicable - refer to Part 1110.20 and Part 1120.20(b)]

Part 1110 Classification:

- ☐ Substantive
- ☒ Non-substantive

2. Narrative Description

In the space below, provide a brief narrative description of the project. Explain **WHAT** is to be done in **State Board defined terms, NOT WHY** it is being done. If the project site does NOT have a street address, include a legal description of the site. Include the rationale regarding the project's classification as substantive or non-substantive.

The applicant is proposing to acquire a new linear accelerator, that will be housed in a vault to be constructed at 2634 Patriot Boulevard, Unit J, in Glenview, Illinois. This location is the site of an existing physician office of UroPartners where patients are able to receive treatments for various urological conditions, but the primary focus is the treatment of conditions related to Prostate Cancer. The cost associated with the acquisition of this medical equipment and buildout of the vault are in excess of the capital expenditure threshold for projects by physician group applicants. The acquisition of major medical equipment is classified as a non-substantive project.

Project Costs and Sources of Funds

Complete the following table listing all costs (refer to Part 1120.110) associated with the project. When a project or any component of a project is to be accomplished by lease, donation, gift, or other means, the fair market or dollar value (refer to Part 1130.140) of the component must be included in the estimated project cost. If the project contains non-reviewable components that are not related to the provision of health care, complete the second column of the table below. Note, the use and sources of funds must be equal.

Project Costs and Sources of Funds			
USE OF FUNDS	CLINICAL	NONCLINICAL	TOTAL
Preplanning Costs	0	0	0
Site Survey and Soil Investigation	0	0	0
Site Preparation	0	0	0
Off Site Work	0	0	0
New Construction Contracts	0	0	0
Modernization Contracts	\$2,215,149	0	\$2,215,149
Contingencies	\$220,000	0	\$220,000
Architectural/Engineering Fees	\$200,000	0	\$200,000
Consulting and Other Fees	\$200,000	0	\$200,000
Movable or Other Equipment (not in construction contracts)	\$1,700,000	0	\$1,700,000
Bond Issuance Expense (project related)			
Net Interest Expense During Construction (project related)	\$75,000	0	\$75,000
Fair Market Value of Leased Space or Equipment	\$370,000	0	\$370,000
Other Costs To Be Capitalized	0	0	0
Acquisition of Building or Other Property (excluding land)	0	0	0
TOTAL USES OF FUNDS	\$4,980,149	\$0	\$4,980,149
SOURCE OF FUNDS	CLINICAL	NONCLINICAL	TOTAL
Cash and Securities	\$510,149	0	\$510,149
Pledges	0	0	0
Gifts and Bequests	0	0	0
Bond Issues (project related)	0	0	0
Mortgages	\$4,100,000	0	\$4,100,000
Leases (fair market value)	\$370,000	0	\$370,000
Governmental Appropriations	0	0	0
Grants	0	0	0
Other Funds and Sources	0	0	0
TOTAL SOURCES OF FUNDS	\$4,980,149	0	\$4,980,149
NOTE: ITEMIZATION OF EACH LINE ITEM MUST BE PROVIDED AT ATTACHMENT 7, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.			

Related Project Costs

Provide the following information, as applicable, with respect to any land related to the project that will be or has been acquired during the last two calendar years:

Land acquisition is related to project ☐ Yes ☒ No Purchase Price: Not Applicable Fair Market Value: <u>FMV evidenced per existing lease</u>
The project involves the establishment of a new facility or a new category of service ☐ Yes ☒ No If yes, provide the dollar amount of all non-capitalized operating start-up costs (including operating deficits) through the first full fiscal year when the project achieves or exceeds the target utilization specified in Part 1100. Estimated start-up costs and operating deficit cost is \$ <u>100,000</u> .

Project Status and Completion Schedules

For facilities in which prior permits have been issued please provide the permit numbers.
Indicate the stage of the project's architectural drawings: ☐ None or not applicable ☐ Preliminary ☒ Schematics ☐ Final Working
Anticipated project completion date (refer to Part 1130.140): July 2, 2021
Indicate the following with respect to project expenditures or to financial commitments (refer to Part 1130.140): ☐ Purchase orders, leases or contracts pertaining to the project have been executed. ☐ Financial commitment is contingent upon permit issuance. Provide a copy of the contingent "certification of financial commitment" document, highlighting any language related to CON Contingencies ☒ Financial Commitment will occur after permit issuance.
APPEND DOCUMENTATION AS <u>ATTACHMENT 8</u> , IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

State Agency Submittals [Section 1130.620(c)]

Are the following submittals up to date as applicable: ☒ Cancer Registry APPLICABLE ONLY TO ASC OWNED BY PHYSICIAN GROUP- UROPARTNERS SURGERY CENTER ☐ APORS NOT APPLICABLE ☒ All formal document requests such as IDPH Questionnaires and Annual Bed Reports been submitted APPLICABLE ONLY TO ASC OWNED BY PHYSICIAN GROUP- UROPARTNERS SURGERY CENTER ☐ All reports regarding outstanding permits NOT APPLICABLE Failure to be up to date with these requirements will result in the application for permit being deemed incomplete.

Cost Space Requirements

Provide in the following format, the **Departmental Gross Square Feet (DGSF)** or the **Building Gross Square Feet (BGSF)** and cost. The type of gross square footage either **DGSF** or **BGSF** must be identified. The sum of the department costs **MUST** equal the total estimated project costs. Indicate if any space is being reallocated for a different purpose. Include outside wall measurements plus the department's or area's portion of the surrounding circulation space. **Explain the use of any vacated space.**

Dept. / Area	Cost	Gross Square Feet		Amount of Proposed Total Gross Square Feet That Is:			
		Existing	Proposed	New Const.	Modernized	As Is	Vacated Space
REVIEWABLE							
Diagnostic Radiology-Linear Accelerator	\$4,980,149	1350	0	0	1350	0	0
Total Clinical	\$4,980,149	1350	0	0	1350	0	0
NON REVIEWABLE							
Total Non-clinical	0						
TOTAL	\$4,980,149	1350	0	0	1350	0	0
APPEND DOCUMENTATION AS <u>ATTACHMENT 9</u> , IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.							

ILLINOIS HEALTH FACILITIES AND SERVICES REVIEW BOARD

APPLICATION FOR PERMIT- 10/2019 Edition

CERTIFICATION

The Application must be signed by the authorized representatives of the applicant entity. Authorized representatives are:

- o in the case of a corporation, any two of its officers or members of its Board of Directors;
- o in the case of a limited liability company, any two of its managers or members (or the sole manager or member when two or more managers or members do not exist);
- o in the case of a partnership, two of its general partners (or the sole general partner, when two or more general partners do not exist);
- o in the case of estates and trusts, two of its beneficiaries (or the sole beneficiary when two or more beneficiaries do not exist); and
- o in the case of a sole proprietor, the individual that is the proprietor.

This Application is filed on the behalf of UROPARTNERS, LLC in accordance with the requirements and procedures of the Illinois Health Facilities Planning Act. The undersigned certifies that he or she has the authority to execute and file this Application on behalf of the applicant entity. The undersigned further certifies that the data and information provided herein, and appended hereto, are complete and correct to the best of his or her knowledge and belief. The undersigned also certifies that the fee required for this application is sent herewith or will be paid upon request.

SIGNATURE

Richard G. Harris, M.D.
PRINTED NAME

CEO/ Member
PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 8 day of July

Signature of Notary

Seal

OFFICIAL SEAL
AMANDA TRIBUZIO
NOTARY PUBLIC - STATE OF ILLINOIS
MY COMMISSION EXPIRES: 07/16/23

*Insert the EXACT legal name of the applicant

SIGNATURE

John J. Cudecki, M.D.
PRINTED NAME

Member
PRINTED TITLE

Notarization:
Subscribed and sworn to before me
this 7 day of July

Signature of Notary

Seal

OFFICIAL SEAL
AMANDA TRIBUZIO
NOTARY PUBLIC - STATE OF ILLINOIS
MY COMMISSION EXPIRES: 07/16/23

SECTION III. BACKGROUND, PURPOSE OF THE PROJECT, AND ALTERNATIVES - INFORMATION REQUIREMENTS

This Section is applicable to all projects except those that are solely for discontinuation with no project costs.

1110.110(a) – Background of the Applicant

READ THE REVIEW CRITERION and provide the following required information:

BACKGROUND OF APPLICANT

1. A listing of all health care facilities owned or operated by the applicant, including licensing, and certification if applicable.
2. A listing of all health care facilities currently owned and/or operated in Illinois, by any corporate officers or directors, LLC members, partners, or owners of at least 5% of the proposed health care facility.
3. For the following questions, please provide information for each applicant, including corporate officers or directors, LLC members, partners and owners of at least 5% of the proposed facility. A health care facility is considered owned or operated by every person or entity that owns, directly or indirectly, an ownership interest.
 - a. A certified listing of any adverse action taken against any facility owned and/or operated by the applicant, directly or indirectly, during the three years prior to the filing of the application.
 - b. A certified listing of each applicant, identifying those individuals that have been cited, arrested, taken into custody, charged with, indicted, convicted or tried for, or pled guilty to the commission of any felony or misdemeanor or violation of the law, except for minor parking violations; or the subject of any juvenile delinquency or youthful offender proceeding. Unless expunged, provide details about the conviction and submit any police or court records regarding any matters disclosed.
 - c. A certified and detailed listing of each applicant or person charged with fraudulent conduct or any act involving moral turpitude.
 - d. A certified listing of each applicant with one or more unsatisfied judgements against him or her.
 - e. A certified and detailed listing of each applicant who is in default in the performance or discharge of any duty or obligation imposed by a judgment, decree, order or directive of any court or governmental agency.
4. Authorization permitting HFSRB and DPH access to any documents necessary to verify the information submitted, including, but not limited to official records of DPH or other State agencies; the licensing or certification records of other states, when applicable; and the records of nationally recognized accreditation organizations. **Failure to provide such authorization shall constitute an abandonment or withdrawal of the application without any further action by HFSRB.**
5. If, during a given calendar year, an applicant submits more than one application for permit, the documentation provided with the prior applications may be utilized to fulfill the information requirements of this criterion. In such instances, the applicant shall attest that the information was previously provided, cite the project number of the prior application, and certify that no changes have occurred regarding the information that has been previously provided. The applicant is able to submit amendments to previously submitted information, as needed, to update and/or clarify data.

APPEND DOCUMENTATION AS ATTACHMENT 11, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM. EACH ITEM (1-4) MUST BE IDENTIFIED IN ATTACHMENT 11.

Criterion 1110.110(b) & (d)**PURPOSE OF PROJECT**

1. Document that the project will provide health services that improve the health care or well-being of the market area population to be served.
2. Define the planning area or market area, or other relevant area, per the applicant's definition.
3. Identify the existing problems or issues that need to be addressed as applicable and appropriate for the project.
4. Cite the sources of the documentation.
5. Detail how the project will address or improve the previously referenced issues, as well as the population's health status and well-being.
6. Provide goals with quantified and measurable objectives, with specific timeframes that relate to achieving the stated goals **as appropriate**.

For projects involving modernization, describe the conditions being upgraded, if any. For facility projects, include statements of the age and condition of the project site, as well as regulatory citations, if any. For equipment being replaced, include repair and maintenance records.

NOTE: Information regarding the "Purpose of the Project" will be included in the State Board Staff Report.

APPEND DOCUMENTATION AS ATTACHMENT 12, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM. EACH ITEM (1-6) MUST BE IDENTIFIED IN ATTACHMENT 12.

ALTERNATIVES

- 1) Identify **ALL** of the alternatives to the proposed project:
 Alternative options **must** include:
 - A) Proposing a project of greater or lesser scope and cost;
 - B) Pursuing a joint venture or similar arrangement with one or more providers or entities to meet all or a portion of the project's intended purposes; developing alternative settings to meet all or a portion of the project's intended purposes;
 - C) Utilizing other health care resources that are available to serve all or a portion of the population proposed to be served by the project; and
 - D) Provide the reasons why the chosen alternative was selected.
- 2) Documentation shall consist of a comparison of the project to alternative options. The comparison shall address issues of total costs, patient access, quality and financial benefits in both the short-term (within one to three years after project completion) and long-term. This may vary by project or situation. **FOR EVERY ALTERNATIVE IDENTIFIED, THE TOTAL PROJECT COST AND THE REASONS WHY THE ALTERNATIVE WAS REJECTED MUST BE PROVIDED.**
- 3) The applicant shall provide empirical evidence, including quantified outcome data that verifies improved quality of care, as available.

APPEND DOCUMENTATION AS ATTACHMENT 13, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION IV. PROJECT SCOPE, UTILIZATION, AND UNFINISHED/SHELL SPACE**Criterion 1110.120 - Project Scope, Utilization, and Unfinished/Shell Space**

READ THE REVIEW CRITERION and provide the following information:

SIZE OF PROJECT:

1. Document that the amount of physical space proposed for the proposed project is necessary and not excessive. **This must be a narrative and it shall include the basis used for determining the space and the methodology applied.**
2. If the gross square footage exceeds the BGSF/DGSF standards in Appendix B, justify the discrepancy by documenting one of the following:
 - a. Additional space is needed due to the scope of services provided, justified by clinical or operational needs, as supported by published data or studies and certified by the facility's Medical Director.
 - b. The existing facility's physical configuration has constraints or impediments and requires an architectural design that delineates the constraints or impediments.
 - c. The project involves the conversion of existing space that results in excess square footage.
 - d. Additional space is mandated by governmental or certification agency requirements that were not in existence when Appendix B standards were adopted.

Provide a narrative for any discrepancies from the State Standard. A table must be provided in the following format with Attachment 14.

SIZE OF PROJECT				
DEPARTMENT/SERVICE	PROPOSED BGSF/DGSF	STATE STANDARD	DIFFERENCE	MET STANDARD?
Radiation Therapy (Linear Accelerator)	1350 GSF	2400 GSF maximum	-1050	YES

APPEND DOCUMENTATION AS ATTACHMENT 14. IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

PROJECT SERVICES UTILIZATION:

This criterion is applicable only to projects or portions of projects that involve services, functions or equipment for which HFSRB has established utilization standards or occupancy targets in 77 Ill. Adm. Code 1100.

Document that in the second year of operation, the annual utilization of the service or equipment shall meet or exceed the utilization standards specified in 1110.Appendix B. **A narrative of the rationale that supports the projections must be provided.**

A table must be provided in the following format with Attachment 15.

UTILIZATION					
	DEPT./ SERVICE	HISTORICAL UTILIZATION (PATIENT DAYS) (TREATMENTS) ETC.	PROJECTED UTILIZATION	STATE STANDARD	MEET STANDARD?
YEAR 1	Linear Accelerator	12,180 Treatments	6,500	7,500 Treatments	YES
YEAR 2	Linear Accelerator	12,180 Treatments	7,280	7,500 Treatments	YES

APPEND DOCUMENTATION AS ATTACHMENT 15. IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

UNFINISHED OR SHELL SPACE: NOT APPLICABLE

Provide the following information:

1. Total gross square footage (GSF) of the proposed shell space.
2. The anticipated use of the shell space, specifying the proposed GSF to be allocated to each department, area or function.
3. Evidence that the shell space is being constructed due to:
 - a. Requirements of governmental or certification agencies; or
 - b. Experienced increases in the historical occupancy or utilization of those areas proposed to occupy the shell space.
4. Provide:
 - a. Historical utilization for the area for the latest five-year period for which data is available; and
 - b. Based upon the average annual percentage increase for that period, projections of future utilization of the area through the anticipated date when the shell space will be placed into operation.

APPEND DOCUMENTATION AS ATTACHMENT 16, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

ASSURANCES: NOT APPLICABLE

Submit the following:

1. Verification that the applicant will submit to HFSRB a CON application to develop and utilize the shell space, regardless of the capital thresholds in effect at the time or the categories of service involved.
2. The estimated date by which the subsequent CON application (to develop and utilize the subject shell space) will be submitted; and
3. The anticipated date when the shell space will be completed and placed into operation.

APPEND DOCUMENTATION AS ATTACHMENT 17, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

M. Criterion 1110.270 - Clinical Service Areas Other than Categories of Service

1. Applicants proposing to establish, expand and/or modernize Clinical Service Areas Other than categories of service must submit the following information:
2. Indicate changes by Service: Indicate # of key room changes by action(s):

Service	# Existing Key Rooms	# Proposed Key Rooms
☒ Radiation Therapy (Linear Accelerator)	1	1
☐		
☐		

3. READ the applicable review criteria outlined below and submit the required documentation for the criteria:

Project Type	Required Review Criteria
New Services or Facility or Equipment	(b) – Need Determination – Establishment
Service Modernization	(c)(1) – Deteriorated Facilities
	AND/OR
	(c)(2) – Necessary Expansion
	PLUS
	(c)(3)(A) – Utilization – Major Medical Equipment
	OR
	(c)(3)(B) – Utilization – Service or Facility
APPEND DOCUMENTATION AS <u>ATTACHMENT 30</u> , IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.	

The following Sections **DO NOT** need to be addressed by the applicants or co-applicants responsible for funding or guaranteeing the funding of the project if the applicant has a bond rating of A- or better from Fitch's or Standard and Poor's rating agencies, or A3 or better from Moody's (the rating shall be affirmed within the latest 18-month period prior to the submittal of the application):

- Section 1120.120 Availability of Funds – Review Criteria
- Section 1120.130 Financial Viability – Review Criteria
- Section 1120.140 Economic Feasibility – Review Criteria, subsection (a)

VI. 1120.120 - AVAILABILITY OF FUNDS

The applicant shall document that financial resources shall be available and be equal to or exceed the estimated total project cost plus any related project costs by providing evidence of sufficient financial resources from the following sources, as applicable [Indicate the dollar amount to be provided from the following sources]:

<u>\$510,149</u>	a) Cash and Securities – statements (e.g., audited financial statements, letters from financial institutions, board resolutions) as to: 1) the amount of cash and securities available for the project, including the identification of any security, its value and availability of such funds; and 2) interest to be earned on depreciation account funds or to be earned on any asset from the date of applicant's submission through project completion;
_____	b) Pledges – for anticipated pledges, a summary of the anticipated pledges showing anticipated receipts and discounted value, estimated time table of gross receipts and related fundraising expenses, and a discussion of past fundraising experience.
_____	c) Gifts and Bequests – verification of the dollar amount, identification of any conditions of use, and the estimated time table of receipts;
<u>\$4,470,000</u>	d) Debt – a statement of the estimated terms and conditions (including the debt time period, variable or permanent interest rates over the debt time period, and the anticipated repayment schedule) for any interim and for the permanent financing proposed to fund the project, including: 1) For general obligation bonds, proof of passage of the required referendum or evidence that the governmental unit has the authority to issue the bonds and evidence of the dollar amount of the issue, including any discounting anticipated; 2) For revenue bonds, proof of the feasibility of securing the specified amount and interest rate; 3) For mortgages, a letter from the prospective lender attesting to the expectation of making the loan in the amount and time indicated, including the anticipated interest rate and any conditions associated with the mortgage, such as, but not limited to, adjustable interest rates, balloon payments, etc.; 4) For any lease, a copy of the lease, including all the terms and conditions, including any purchase options, any capital improvements to the property and provision of capital equipment;

[illegible]

SECTION VII. 1120.130 - FINANCIAL VIABILITY

All the applicants and co-applicants shall be identified, specifying their roles in the project funding or guaranteeing the funding (sole responsibility or shared) and percentage of participation in that funding.

Financial Viability Waiver

The applicant is not required to submit financial viability ratios if:

1. "A" Bond rating or better
2. All of the projects capital expenditures are completely funded through internal sources
3. The applicant's current debt financing or projected debt financing is insured or anticipated to be insured by MBIA (Municipal Bond Insurance Association Inc.) or equivalent
4. The applicant provides a third party surety bond or performance bond letter of credit from an A rated guarantor.

See Section 1120.130 Financial Waiver for information to be provided

APPEND DOCUMENTATION AS ATTACHMENT 34, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

The applicant or co-applicant that is responsible for funding or guaranteeing funding of the project shall provide viability ratios for the latest three years for which **audited financial statements are available and for the first full fiscal year at target utilization, but no more than two years following project completion.** When the applicant's facility does not have facility specific financial statements and the facility is a member of a health care system that has combined or consolidated financial statements, the system's viability ratios shall be provided. If the health care system includes one or more hospitals, the system's viability ratios shall be evaluated for conformance with the applicable hospital standards.

	Historical 3 Years			Projected
Enter Historical and/or Projected Years:	2017	2018	2019	Year 1
Current Ratio	1.62	1.80	1.48	1.63
Net Margin Percentage	29.1	25.8	23.2	22.7
Percent Debt to Total Capitalization	2.1	.60	.60	37.1
Projected Debt Service Coverage	26.95	25.74	726.15	30.17
Days Cash on Hand	34	34	31	47
Cushion Ratio	5.93	6.79	188.40	12.23

Provide the methodology and worksheets utilized in determining the ratios detailing the calculation and applicable line item amounts from the financial statements. Complete a separate table for each co-applicant and provide worksheets for each.

Variance

Applicants not in compliance with any of the viability ratios shall document that another organization, public or private, shall assume the legal responsibility to meet the debt obligations should the applicant default.

APPEND DOCUMENTATION AS ATTACHMENT 35, IN NUMERICAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION VIII.1120.140 - ECONOMIC FEASIBILITY

This section is applicable to all projects subject to Part 1120.

A. Reasonableness of Financing Arrangements

The applicant shall document the reasonableness of financing arrangements by submitting a notarized statement signed by an authorized representative that attests to one of the following:

- 1) That the total estimated project costs and related costs will be funded in total with cash and equivalents, including investment securities, unrestricted funds, received pledge receipts and funded depreciation; or
- 2) That the total estimated project costs and related costs will be funded in total or in part by borrowing because:
 - A) A portion or all of the cash and equivalents must be retained in the balance sheet asset accounts in order to maintain a current ratio of at least 2.0 times for hospitals and 1.5 times for all other facilities; or
 - B) Borrowing is less costly than the liquidation of existing investments, and the existing investments being retained may be converted to cash or used to retire debt within a 60-day period.

B. Conditions of Debt Financing

This criterion is applicable only to projects that involve debt financing. The applicant shall document that the conditions of debt financing are reasonable by submitting a notarized statement signed by an authorized representative that attests to the following, as applicable:

- 1) That the selected form of debt financing for the project will be at the lowest net cost available;
- 2) That the selected form of debt financing will not be at the lowest net cost available, but is more advantageous due to such terms as prepayment privileges, no required mortgage, access to additional indebtedness, term (years), financing costs and other factors;
- 3) That the project involves (in total or in part) the leasing of equipment or facilities and that the expenses incurred with leasing a facility or equipment are less costly than constructing a new facility or purchasing new equipment.

C. Reasonableness of Project and Related Costs

Read the criterion and provide the following:

1. Identify each department or area impacted by the proposed project and provide a cost and square footage allocation for new construction and/or modernization using the following format (insert after this page).

COST AND GROSS SQUARE FEET BY DEPARTMENT OR SERVICE									
Department (list below)	A	B	C	D	E	F	G	H	Total Cost (G + H)
	Cost/Square Foot New	Mod.	Gross Sq. Ft. New Circ.*		Gross Sq. Ft. Mod. Circ.*		Const. \$ (A x C)	Mod. \$ (B x E)	
Linear Accelerator		\$1,640.85			1350			\$2,215,149	\$2,215,149
Contingency		\$162.96			0			\$220,000	\$220,000
TOTALS		\$1,803.81			1350			\$2,435,149	\$2,435,149

* Include the percentage (%) of space for circulation

D. Projected Operating Costs

The applicant shall provide the projected direct annual operating costs (in current dollars per equivalent patient day or unit of service) for the first full fiscal year at target utilization but no more than two years following project completion. Direct cost means the fully allocated costs of salaries, benefits and supplies for the service.

E. Total Effect of the Project on Capital Costs

The applicant shall provide the total projected annual capital costs (in current dollars per equivalent patient day) for the first full fiscal year at target utilization but no more than two years following project completion.

APPEND DOCUMENTATION AS ATTACHMENT 36, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION IX. SAFETY NET IMPACT STATEMENT- NOT APPLICABLE FOR NON-SUBSTANTIVE PROJECT

SAFETY NET IMPACT STATEMENT that describes all the following must be submitted for **ALL SUBSTANTIVE PROJECTS AND PROJECTS TO DISCONTINUE HEALTH CARE FACILITIES [20 ILCS 3960/5.4]:**

1. The project's material impact, if any, on essential safety net services in the community, to the extent that it is feasible for an applicant to have such knowledge.
2. The project's impact on the ability of another provider or health care system to cross-subsidize safety net services, if reasonably known to the applicant.
3. How the discontinuation of a facility or service might impact the remaining safety net providers in a given community, if reasonably known by the applicant.

Safety Net Impact Statements shall also include all of the following:

1. For the 3 fiscal years prior to the application, a certification describing the amount of charity care provided by the applicant. The amount calculated by hospital applicants shall be in accordance with the reporting requirements for charity care reporting in the Illinois Community Benefits Act. Non-hospital applicants shall report charity care, at cost, in accordance with an appropriate methodology specified by the Board.
2. For the 3 fiscal years prior to the application, a certification of the amount of care provided to Medicaid patients. Hospital and non-hospital applicants shall provide Medicaid information in a manner consistent with the information reported each year to the Illinois Department of Public Health regarding "Inpatients and Outpatients Served by Payor Source" and "Inpatient and Outpatient Net Revenue by Payor Source" as required by the Board under Section 13 of this Act and published in the Annual Hospital Profile.
3. Any information the applicant believes is directly relevant to safety net services, including information regarding teaching, research, and any other service.

A table in the following format must be provided as part of Attachment 37.

Safety Net Information per PA 96-0031			
CHARITY CARE			
Charity (# of patients)	Year	Year	Year
Inpatient			
Outpatient			
Total			
Charity (cost in dollars)			
Inpatient			
Outpatient			
Total			
MEDICAID			
Medicaid (# of patients)	Year	Year	Year
Inpatient			
Outpatient			
Total			

	Medicaid (revenue)				
	Inpatient				
	Outpatient				
	Total				

APPEND DOCUMENTATION AS ATTACHMENT 37, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

SECTION X. CHARITY CARE INFORMATION

Charity Care information **MUST** be furnished for **ALL** projects [1120.20(c)].

1. All applicants and co-applicants shall indicate the amount of charity care for the latest three **audited** fiscal years, the cost of charity care and the ratio of that charity care cost to net patient revenue.
2. If the applicant owns or operates one or more facilities, the reporting shall be for each individual facility located in Illinois. If charity care costs are reported on a consolidated basis, the applicant shall provide documentation as to the cost of charity care; the ratio of that charity care to the net patient revenue for the consolidated financial statement; the allocation of charity care costs; and the ratio of charity care cost to net patient revenue for the facility under review.
3. If the applicant is not an existing facility, it shall submit the facility's projected patient mix by payer source, anticipated charity care expense and projected ratio of charity care to net patient revenue by the end of its second year of operation.

Charity care" means care provided by a health care facility for which the provider does not expect to receive payment from the patient or a third-party payer (20 ILCS 3960/3). Charity Care **must** be provided at cost.

A table in the following format must be provided for all facilities as part of Attachment 39.

The applicant, UroPartners, LLC is a physician practice group. The applicant is providing charity care data for UroPartners Surgery Center, LLC (a wholly owned subsidiary) of UroPartners Investments, LLC which operates the ASC UroPartners Surgery Center and has identical ownership as the applicant.

CHARITY CARE			
	2016	2017	2018
Net Patient Revenue	N/A	0	0
Amount of Charity Care (charges)	N/A	0	0
Cost of Charity Care	N/A	0	0

APPEND DOCUMENTATION AS **ATTACHMENT 38**, IN NUMERIC SEQUENTIAL ORDER AFTER THE LAST PAGE OF THE APPLICATION FORM.

After paginating the entire completed application indicate, in the chart below, the page numbers for the included attachments:

INDEX OF ATTACHMENTS			
ATTACHMENT NO.			PAGES
1	Applicant Identification including Certificate of Good Standing		23
2	Site Ownership		24-27
3	Persons with 5 percent or greater interest in the licensee must be identified with the % of ownership.		28
4	Organizational Relationships (Organizational Chart) Certificate of Good Standing Etc.		29
5	Flood Plain Requirements		30
6	Historic Preservation Act Requirements		31-35
7	Project and Sources of Funds Itemization		36-37
8	Financial Commitment Document if required		
9	Cost Space Requirements		38
10	Discontinuation		
11	Background of the Applicant		39-42
12	Purpose of the Project		43-151
13	Alternatives to the Project		152
14	Size of the Project		153
15	Project Service Utilization		154-156
16	Unfinished or Shell Space		
17	Assurances for Unfinished/Shell Space		
	Service Specific:		
18	Medical Surgical Pediatrics, Obstetrics, ICU		
19	Comprehensive Physical Rehabilitation		
20	Acute Mental Illness		
21	Open Heart Surgery		
22	Cardiac Catheterization		
23	In-Center Hemodialysis		
24	Non-Hospital Based Ambulatory Surgery		
25	Selected Organ Transplantation		
26	Kidney Transplantation		
27	Subacute Care Hospital Model		
28	Community-Based Residential Rehabilitation Center		
29	Long Term Acute Care Hospital		
30	Clinical Service Areas Other than Categories of Service		157-159
31	Freestanding Emergency Center Medical Services		
32	Birth Center		
	Financial and Economic Feasibility:		
33	Availability of Funds		160-161
34	Financial Waiver		
35	Financial Viability		162
36	Economic Feasibility		163-165
37	Safety Net Impact Statement		166
38	Charity Care Information		167

**ATTACHMENT 1 - UROPARTNERS, LLC
CERTIFICATE OF GOOD STANDING**

File Number 0142447-5



To all to whom these Presents Shall Come, Greeting:

***I, Jesse White, Secretary of State of the State of Illinois, do hereby
certify that I am the keeper of the records of the Department of
Business Services. I certify that***

UROPARTNERS, LLC, HAVING ORGANIZED IN THE STATE OF ILLINOIS ON FEBRUARY
10, 2005, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED
LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD
STANDING AS A DOMESTIC LIMITED LIABILITY COMPANY IN THE STATE OF ILLINOIS.



Authentication #: 2017502212 verifiable until 06/23/2021
Authenticate at: <http://www.cyberdriveillinois.com>

***In Testimony Whereof, I hereto set
my hand and cause to be affixed the Great Seal of
the State of Illinois, this 23RD
day of JUNE A.D. 2020 .***

Jesse White

SECRETARY OF STATE

ATTACHMENT 2 - SITE OWNERSHIP

The land in which the linear accelerator will be located is owned by UroPartners Investments, LLC, an Illinois Limited Liability Company that has identical ownership (both owners and percentage of ownership) as the applicant UroPartners, LLC, an Illinois Limited Liability Company. Attached as evidence of control is a copy of the Warranty Deed.

#20-034

② 28040309/STSI00706

ILLINOIS STATUTORY
WARRANTY DEED

=====

This instrument was prepared by:
Stewart F. Schechter, Esq.
Schechter & Associates
555 Skokie Boulevard, Suite 260
Northbrook, Illinois 60062

After recording, return to:
Glenn T. Garfinkel, Esq.
Levick, Timm & Garfinkel, LLC
770 Lake Cook Road, Suite 150
Deerfield, Illinois 60015

Tax statements should be sent to:
UroPartners, LLC
2634 Patriot Blvd.
Glenview, Illinois 60026



Doc#: 0822740073 Fee: \$52.00
Eugene "Gene" Moore RHSP Fee: \$10.00
Cook County Recorder of Deeds
Date: 08/14/2008 11:25 AM Pg: 1 of 9

RECORDER'S STAMP

SPECIAL WARRANTY DEED

THIS INDENTURE WITNESSETH THAT THE GRANTOR, PATRIOT COURTYARDS INVESTORS, LLC, a limited liability company created and existing under and by virtue of the laws of the State of Arizona ("Grantor"), and duly authorized to transact business in the State of Illinois, whose address is 20 Great Oaks Boulevard, Suite 230, San Jose, California 95119, for and in consideration of Ten Dollars and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, does hereby **GRANT, BARGAIN, SELL, CONVEY and WARRANT** unto: UROPARTNERS INVESTMENTS, LLC, an Illinois Limited Liability Company ("Grantee"), whose address is 675 W. North Avenue, Suite 605, Melrose Park, Illinois 60160, the following described Real Estate, situated in the County of Cook and State of Illinois, which is legally described on Exhibit A, attached hereto and thereby made a part hereof (the "Real Estate"), to have and to hold the Real Estate aforesaid, with all and singular the hereditaments, rights, privileges, appurtenances and immunities thereto belonging or in anywise appertaining unto said Grantee, and unto its successors and assigns forever; said Grantee hereby covenanting that the said Real Estate is free and clear from any encumbrances done or suffered by Grantor, and that Grantor will warrant and defend the title to the said Real Estate unto said Grantee and unto its successors and assigns forever, against the lawful claims and demands of all persons claiming by, through or under Grantor but none other, except for the encumbrances set forth in Exhibit B attached hereto and thereby made a part hereof.

1

8/14

BOX 333-CT

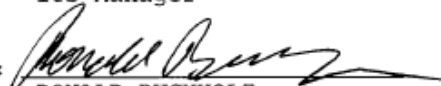
0822740073D Page: 2 of 9

Permanent Real Estate Index: 04-22-101-047-1021

Address of Premises: 2634 Patriot Blvd., Glenview, Illinois 60026

In witness whereof, Grantor has caused its name to be signed
to these presents this 8 day of July, 2008

PATRIOT COURTYARDS INVESTORS, LLC
an Arizona Limited Liability Company
By: EQUITY ENTERPRISES - NEVADA, INC.
a Nevada Corporation
its Manager

By: 
RONALD BUCHHOLZ
President

STATE OF CALIFORNIA)
) SS
COUNTY OF SANTA CLARA)

I, the undersigned, a Notary Public in and for said County and State aforesaid, DO HEREBY CERTIFY that RONALD BUCHHOLZ, as President of EQUITY ENTERPRISES - NEVADA, INC., a Nevada Corporation, as Manager of PATRIOT COURTYARDS INVESTORS, LLC, an Arizona Limited Liability Company, personally known to me to be the same person whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledged that he signed, sealed and delivered the said instrument as his free and voluntary act for the uses and purposes therein set forth.



Given under my hand and seal this 8th day
of July, 2008

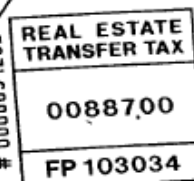
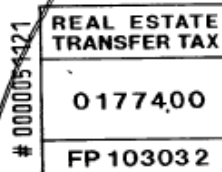

Notary Public

My commission expires: July 28, 2011

STATE OF ILLINOIS



AUG. 12. 08

REAL ESTATE TRANSFER TAX
DEPARTMENT OF REVENUE

0822740073D Page: 3 of 9

EXHIBIT A TO WARRANTY DEED
FROM PATRIOT COURTYARDS INVESTORS, LLC ("GRANTOR")
TO UROPARTNERS, LLC ("GRANTEE")

Legal Description

UNIT J IN THE PATRIOT COURTYARDS CONDOMINIUMS, AS
DELINEATED ON A PLAT OF SURVEY OF THE FOLLOWING DESCRIBED
REAL TRACT OF LAND: LOT 2 OF PRAIRIE GLEN CORPORATE
CAMPUS, PHASE 1, UNIT 1, A RESUBDIVISION OF A PORTION OF
LOT 4 IN GLENVIEW NAVAL AIR STATION SUBDIVISION NO. 2,
BEING A SUBDIVISION OF PART OF SECTIONS 15, 21, 22, 23,
26, 27, 28, AND 34, TOWNSHIP 42 NORTH, RANGE 12 EAST OF
THE THIRD PRINCIPAL MERIDIAN, IN COOK COUNTY, ILLINOIS,
WHICH PLAT OF SURVEY IS ATTACHED AS EXHIBIT "D" TO THE
DECLARATION OF CONDOMINIUM OF PATRIOT COURTYARDS OFFICE
CONDOMINIUM ASSOCIATION RECORDED JANUARY 6, 2006, AS
DOCUMENT NO. 0600627031, AS AMENDED FROM TIME TO TIME,
TOGETHER WITH ITS UNDIVIDED PERCENTAGE INTEREST IN THE
COMMON ELEMENTS

Permanent Real Estate Index: 04-22-101-047-1021

Address of Premises: 2634 Patriot Blvd., Glenview, Illinois 60026

**ATTACHMENT 3 - UROPARTNERS, LLC
CERTIFICATE OF GOOD STANDING**

File Number 0142447-5



To all to whom these Presents Shall Come, Greeting:

***I, Jesse White, Secretary of State of the State of Illinois, do hereby
certify that I am the keeper of the records of the Department of
Business Services. I certify that***

UROPARTNERS, LLC, HAVING ORGANIZED IN THE STATE OF ILLINOIS ON FEBRUARY
10, 2005, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED
LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD
STANDING AS A DOMESTIC LIMITED LIABILITY COMPANY IN THE STATE OF ILLINOIS.



Authentication #: 2017502212 verifiable until 06/23/2021
Authenticate at: <http://www.cyberdriveillinois.com>

***In Testimony Whereof, I hereto set
my hand and cause to be affixed the Great Seal of
the State of Illinois, this 23RD
day of JUNE A.D. 2020 .***

Jesse White

SECRETARY OF STATE

ATTACHMENT 4 - ORGANIZATIONAL CHART

UroPartners, LLC is an Illinois Limited Liability Company that is wholly owned in equal shares by physicians who are active members of the practice. A list of those physicians their percentage of ownership is list below. The individual physician owners maintain identical ownership (both owners and percentage of ownership) in UroPartners Investments, LLC as indicated in Attachment 2. UroPartners Investments, LLC in turn is the sole owner of an ASC, UroPartners Surgery Center, LLC.

Member	Percent of Ownership Interest
Nejd F. Alsikafi, M.D.	2.174%
Kristopher N. Atzeff, M.D.	2.174%
Laurie Bachrach, M.D.	2.174%
Jonas Benson, M.D.	2.174%
Ronald J. Bonaguro, M.D.	2.174%
Mark T. Brandt, M.D.	2.174%
Robert J. Challenger, M.D.	2.174%
Justin J. Cohen, M.D.	2.174%
Christopher L. Coogan, M.D.	2.174%
Joel Z. Cornfield, M.D.	2.174%
John J. Cudecki, M.D.	2.174%
Daniel P. Dalton, M.D.	2.174%
Risha M. Foster, M.D.	2.174%
Gordon R. Gluckman, M.D.	2.174%
Michael S. Gomez, M.D.	2.174%
Richard Harris, M.D.	2.174%
Stephen Hurley, D.O.	2.174%
Robert S. Kaplinsky, M.D.	2.174%
Raza M. Khan, M.D.	2.174%
Ronald J. Kim, M.D.	2.174%
Kyle J. Kiriluk, M.D.	2.174%
Steven Koopman, M.D.	2.174%
Samuel S. Krengel, M.D.	2.174%
John Kritsas, M.D.	2.174%
Ronald D. Lee, M.D.	2.174%
Laurence A. Levine, M.D.	2.174%
William W. Lin, M.D.	2.174%
Kelly M. Maxwell, M.D.	2.174%
Matthew Meadows, M.D.	2.174%
Daniel S. Merrick, M.D.	2.174%
Michael H. Milani, D.O.	2.174%
John Milner, M.D.	2.174%
Steven E. Mutchnik, M.D.	2.174%
Narendra Narepalem, M.D.	2.174%
Jeffrey P. Norris, M.D.	2.174%
Dimitri Papagiannopoulos M.D.	2.174%
Sutchin R. Patel, M.D.	2.174%
Jeffrey A. Pearl, M.D.	2.174%
David A. Rebuck, M.D.	2.174%
Robert S. Saffrin, M.D.	2.174%
David M. Shore, M.D.	2.174%
Scott Tiplitsky, M.D.	2.174%
Brett A. Trockman, M.D.	2.174%
Thomas A. Will, M.D.	2.174%
Paul M. Yonover, M.D.	2.174%
David L. Zumerchik, M.D.	2.174%
	100.000%

ATTACHMENT 6 - HISTORICAL PRESERVATION LETTER

The applicant submitted a request for determination to the Illinois Department of Natural Resources-Preservation Services Division on June 23, 2020. A final determination has not yet been received, however, with the certification made with this application, the applicant certifies that either a determination from the Department will be provided to the HFSRB staff prior to Board review of this CON application or if the HFSRB approves this application, the project will not be obligated until the determination is made by DNR.



Juan Morado, Jr.
71 South Wacker Drive, Suite 1600
Chicago, IL 60606
Direct Dial: 312.212.4967
Fax: 312.757.9192
jmorado@beneschlaw.com

June 23, 2020

VIA EMAIL

Jeffrey Kruchten
Chief Archaeologist
Preservation Services Division
Illinois Historic Preservation Office
Illinois Department of Natural Resources
1 Natural Resources Way
Springfield, IL 62702
Jeffrey.kruchten@illinois.gov

Re: Certificate of Need Application for the Purchase of Major Medical Equipment

Dear Jeffrey:

I am writing on behalf of my client, Uropartners, LLC ("Uropartners") to request a review of the project area under Section 4 of the Illinois State Agency Historic Resources Preservation Act (20 ILCS 3420/1 et. seq.). Uropartners is submitting an application for a Certificate of Need from the Illinois Health Facilities and Services Review Board. Uropartners is proposing to purchase a linear accelerator to allow for treatment of patients for their urology physician group. The equipment will be installed in an existing office building located at 2634 Patriot Boulevard, Unit J, Glenview, Illinois 60026

The proposed equipment will be housed in the existing office building and will involve additional construction on site to ensure that the equipment is properly housed. This will not require the removal of any existing structures. For your reference, we have included pictures of the existing building and a topographic map showing the general location of the project.

www.beneschlaw.com

13561889 v2

June 23, 2020
Page 2

We respectfully request review of the project area and a determination letter at your earliest convenience. Thank you in advance for all of the time and effort that will be going into this review.

Very truly yours,

BENESCH, FRIEDLANDER,
COPLAN & ARONOFF LLP

A handwritten signature in blue ink, appearing to read "Juan Morado, Jr.", is written over a light blue rectangular background.

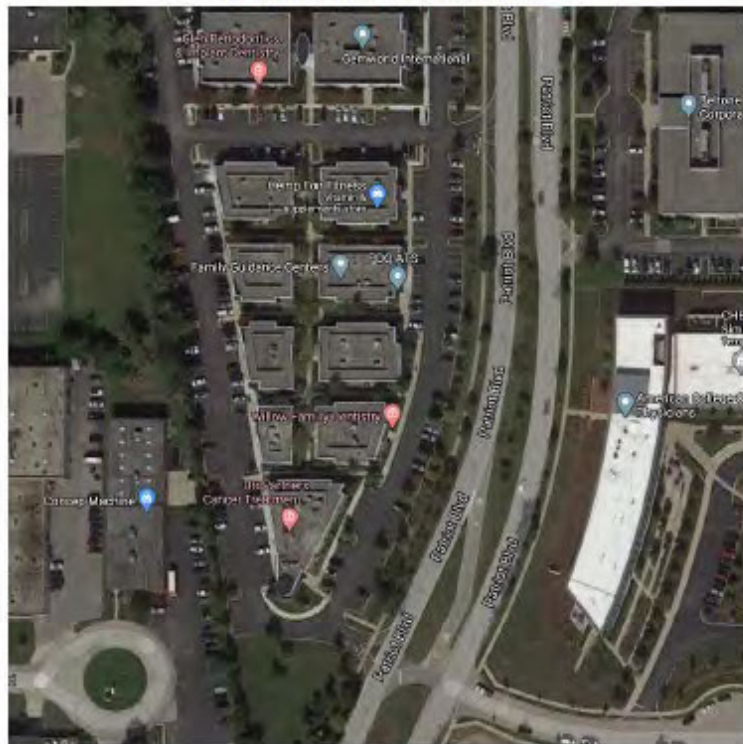
Juan Morado, Jr.

JM:
Enclosures

Side view of Office Building



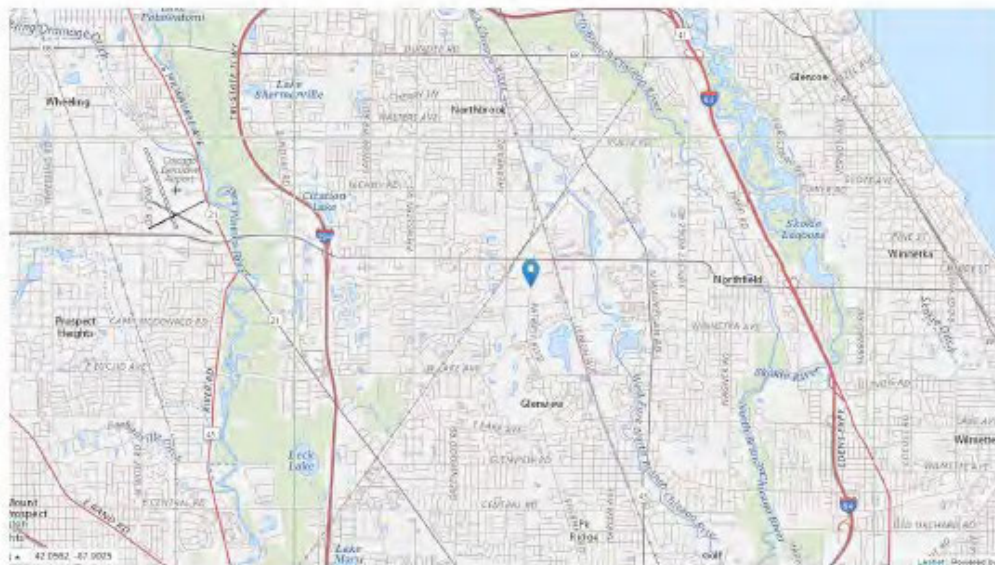
Overhead view of Office Park



Page 34

June 23, 2020
Page 4

Topographic Map



ATTACHMENT 7 - PROJECT COSTS AND SOURCES OF FUNDS

Project Costs and Sources of Funds			
USE OF FUNDS	CLINICAL	NONCLINICAL	TOTAL
Preplanning Costs	0	0	0
Site Survey and Soil Investigation	0	0	0
Site Preparation	0	0	0
Off Site Work	0	0	0
New Construction Contracts	0	0	0
Modernization Contracts	\$2,215,149	0	\$2,215,149
Contingencies	\$220,000	0	\$220,000
Architectural/Engineering Fees	\$200,000	0	\$200,000
Consulting and Other Fees	\$200,000	0	\$200,000
Movable or Other Equipment (not in construction contracts)	\$1,700,000	0	\$1,700,000
Bond Issuance Expense (project related)			
Net Interest Expense During Construction (project related)	\$75,000	0	\$75,000
Fair Market Value of Leased Space or Equipment	\$370,000	0	\$370,000
Other Costs To Be Capitalized	0	0	0
Acquisition of Building or Other Property (excluding land)	0	0	0
TOTAL USES OF FUNDS	\$4,980,149	\$0	\$4,980,149
SOURCE OF FUNDS	CLINICAL	NONCLINICAL	TOTAL
Cash and Securities	\$510,149	0	\$510,149
Pledges	0	0	0
Gifts and Bequests	0	0	0
Bond Issues (project related)	0	0	0
Mortgages	\$4,100,00	0	\$4,100,000
Leases (fair market value)	\$370,000	0	\$370,000
Governmental Appropriations	0	0	0
Grants	0	0	0
Other Funds and Sources	0	0	0
TOTAL SOURCES OF FUNDS	\$4,980,149	0	\$4,980,149

Modernization Contracts	Cost
General Conditions	\$355,000.00
Demolition	\$15,000.00
Carpentry 6100	\$5,500.00
Carpentry 6400	\$5,500.00
Door Installation	\$10,000.00
Drywall	\$48,000.00
Roof Framing & Sheeting	\$30,000.00
Acoustical	\$14,000.00
Temporary Fencing	\$3,500.00
Demolition	\$25,000.00
Concrete & Excavation	\$435,000.00
Masonry	\$16,000.00
Metal	\$42,000.00
Millwork & Installation	\$10,000.00
Roofing	\$102,000.00
Door/Frame/Hardware	\$18,000.00
Painting	\$21,000.00
Flooring	\$35,000.00
Moisture Mitigation	\$5,649.00
Specialty Items	\$10,000.00
Radiation Protection/Shielding	\$132,000.00
Radiation Protection/Sliding Door System	\$175,000.00
Fire Suppression	\$74,000.00
HVAC/Mech/Plumbing	\$300,000.00
Electrical	\$223,000.00
Landscaping Repairs	\$15,000.00
Paving Repairs	\$30,000.00
Misc. Work	\$60,000.00
Subtotal	\$2,215,149.00
Total	\$2,215,149.00
Consulting	\$200,000.00
Net Interest	\$75,000.00
Linear Accelerator	\$1,700,000.00
Contingency	\$220,000.00
FMV of Leased Space	\$370,000.00
A&E Fees	\$200,000.00
Grand Total	<u><u>\$4,980,149.00</u></u>

ATTACHMENT 9 - COST SPACE REQUIREMENTS

The equipment will be installed in existing space that measures at 1350 GSF. The equipment will be installed in physician office space, not a licensed health care facility. As this project only involves major medical equipment there is no non-clinical space involved in this project.

Dept. / Area	Cost	Gross Square Feet		Amount of Proposed Total Gross Square Feet That Is:			
		Existing	Proposed	New Const.	Modernized	As Is	Vacated Space
REVIEWABLE							
Diagnostic Radiology-Linear Accelerator	\$4,980,149	1350	0	0	1350	0	0
Total Clinical	\$4,980,149	1350	0	0	1350	0	0
NON REVIEWABLE							
Total Non-clinical	0						
TOTAL	\$4,980,149	1350	0	0	1350	0	0

ATTACHMENT 11 - BACKGROUND OF THE APPLICANT

The following information is provided to illustrate the qualifications, background and character of the Applicant and to assure the Review Board that the proposed acquisition of major medical equipment will be utilized to provide a proper standard of health care services for the community.

UroPartners, LLC

The proposed project is brought by UroPartners, LLC, an entity owned by physicians who practice through the UroPartners physician group. UroPartners, LLC is owned by in equal shares by the physicians as reflected in Attachment 4.

The individual physician owners of UroPartners, LLC maintain identical ownership (both owners and percentage of ownership) in UroPartners Investments, LLC as indicated in Attachment 4. UroPartners Investments, LLC in turn is the sole owner of an ASC, UroPartners Surgery Center, LLC, which operates the UroPartners Surgery Center located at 2750 South River Road in Des Plaines, Illinois 60018. The applicant certifies that there have been no adverse actions during the three (3) years prior to the filing of this Application. A letter certifying to the above information is attached at Attachment 11.

We have included a letter authorizing access to the HFSRB and IDPH to verify information about UroPartners, LLC at Attachment 11.

Background of UroPartners

UroPartners is the largest urology group in the Midwest, and is made up of over 54 experienced urological specialists. The doctors provides advanced care in urological conditions by some of the most renowned physicians in Chicago. The applicants operate an ambulatory surgery center, three Prostate Centers and dozens of physician offices throughout the Chicagoland locations. UroPartners has experts in urology, pathology, and radiation oncology, and they utilize state of the art techniques to care for patients.

UroPartners has access to its own laboratory and pathologists who provide rapid and reliable test results, which is incredibly important to their patients undergoing treatment and evaluation for cancer and other urological issues. The laboratory is accredited by the College of American Pathologists and staff by full time pathologists and expert technologists in the field of anatomic pathology, cytology/FISH, blood studies, and microbiology. Access to these types of tests combined with other equipment utilized by UroPartners allows them to provide a high level of care to their patient base.

The linear accelerator that is the subject of this application will be installed at the UroPartners Prostate Center in Glenview, Illinois. At the Prostate Center in Glenview, Dr. Parthiv Mehta, a Radiation Oncologist leads the facility specializing in the treatment of prostate cancer. Dr. Mehta is a Board Certified Radiation Oncologist and he has expertise and advanced training in intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), and prostate brachytherapy. After earning his bachelor's degree in engineering from the University of Michigan. Dr. Mehta entered the Medical Scholars Program at the University of Illinois where he completed an M.D. as well as an M.B.A. degree. He completed his residency in radiation oncology at Rush University Medical Center and entered into a brachytherapy fellowship program at Beth Israel Medical Center in New York City. Dr. Mehta is a member of the American Society for Therapeutic Radiology and Oncology, the American Society of Clinical Oncology, the American Medical Association, the Radiological Society of North America, the American College of Radiation Oncology, and the American Brachytherapy Society.

**ATTACHMENT 11 - CERTIFICATE OF GOOD STANDING
UROPARTNERS SURGERY CENTER, LLC**

File Number 0591690-9



To all to whom these Presents Shall Come, Greeting:

I, Jesse White, Secretary of State of the State of Illinois, do hereby certify that I am the keeper of the records of the Department of Business Services. I certify that

UROPARTNERS SURGERY CENTER, LLC, HAVING ORGANIZED IN THE STATE OF ILLINOIS ON AUGUST 04, 2016, APPEARS TO HAVE COMPLIED WITH ALL PROVISIONS OF THE LIMITED LIABILITY COMPANY ACT OF THIS STATE, AND AS OF THIS DATE IS IN GOOD STANDING AS A DOMESTIC LIMITED LIABILITY COMPANY IN THE STATE OF ILLINOIS.



Authentication #: 2019003338 verifiable until 07/08/2021
Authenticate at: <http://www.cyberdriveillinois.com>

***In Testimony Whereof, I hereto set
my hand and cause to be affixed the Great Seal of
the State of Illinois, this 8TH
day of JULY A.D. 2020 .***

Jesse White

SECRETARY OF STATE

ATTACHMENT 11 - IDPH ASTC LICENSE OF UROPARTNERS SURGERY CENTER



**Illinois Department of
PUBLIC HEALTH** HF 118968

LICENSE, PERMIT, CERTIFICATION, REGISTRATION

The person, firm or corporation whose name appears on this certificate has complied with the provisions of the Illinois statutes, and/or rules and regulations and is hereby authorized to engage in the activity as indicated below.

Ngozi O. Ezike, M.D.
Director

Issued under the authority of
the Illinois Department of
Public Health

EXPIRATION DATE	CATEGORY	LIC. NUMBER
10/30/2020		7003212

Ambulatory Surgery Treatment Center

Effective: 10/31/2019

Uropartners Surgery Center, LLC
2750 S River Rd
Des Plaines, IL 60018

The face of this license has a colored background. Printed by Authority of the State of Illinois • P.O. #19-493-001 10M 9/18

← **DISPLAY THIS PART IN A
CONSPICUOUS PLACE**

Exp. Date 10/30/2020

Lic Number 7003212

Date Printed 10/1/2019

Uropartners Surgery Center, LLC

2750 S River Rd
Des Plaines, IL 60018-4103

FEE RECEIPT NO.

ATTACHMENT 11 - CERTIFICATION AND AUTHORIZATION LETTER

UroPartners, LLC Suite #502 1/1/2020 IL 6018-1 Private TM 4/1/2020 1/1/2020 1/1/2020

July 2, 2020

Courtney Avery
Board Administrator
Illinois Health Facilities and Service Review Board
525 West Jefferson Street, 2nd Floor
Springfield, Illinois 62761

Re: Certification and Authorization

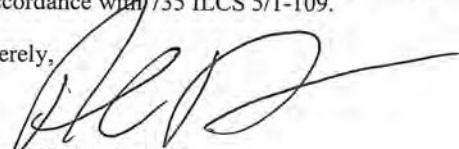
Dear Ms. Avery,

As representative of UroPartners, LLC, I, Richard G. Harris, M.D., give authorization to the Health Facilities and Services Review Board and the Illinois Department of Public Health (IDPH) to access documents necessary to verify the information submitted including, but not limited to: official records of IDPH or other state agencies, the licensing or certification records of other states, and the records of nationally recognized accreditation organizations.

I further verify that, UroPartners, LLC has no ownership interest in a health care facility, and thus has had no adverse action in the past three (3) years.

I hereby certify this is true and based upon my personal knowledge under penalty of perjury and in accordance with 735 ILCS 5/1-109.

Sincerely,


Richard G. Harris, M.D.
CEO
UroPartners, LLC

13562236 v1

ATTACHMENT 12 - PURPOSE OF THE PROJECT

This project involves the acquisition of major medical equipment, a linear accelerator, to be installed in an existing physician office. The physician office where the equipment will be installed operates as one of the UroPartners' practice group Prostate Centers. This office is located in Glenview, Illinois. The physician office is located in Health Service Area 7, and in Planning Service Area 031. The facility serves patients throughout northern Cook County, DuPage County, and southern Lake County.

The applicants currently own and operate a linear accelerator. Combined with Phillips and GE CT scanners, they are able to counsel patients to determine the most appropriate treatment and method for delivering that treatment. Linear accelerators are the most commonly used device for external beam radiation treatments. UroPartners estimates that nearly 95% of all radiation therapy done in the United States utilizes a linear accelerator. The principal reason for this is that these machines have proven effective at shrinking tumors in myriad forms of cancer.

All linear accelerators have a limited life cycle (commonly 10-12 years) and the equipment currently in use at the Prostate Center-Glenview is nearing the end of its life cycle. The existing linear accelerator was acquired on December 1, 2008, it is manufacturer Varian, model number 21iX, and its serial number is 4194. Pursuant to 32 Illinois Admin. Code Section 320 the equipment maintains a registration with Illinois Emergency Management Agency.

The Varian Linear Accelerator utilized by UroPartners is an advanced radiation therapy device that delivers Intensity Modulated Radiation Therapy (IMRT) and Image Guided Radiation Therapy (IGRT) radiation. Utilizing IMRT, UroPartners is able to precisely target cancer cells while sparing healthy tissue nearby. The use of IMRT allows for customization wherein the radiation dose is designed to conform to the 3-dimensional shape of the target volume by modulating or controlling the intensity of the radiation beam. At the Prostate Center-Glenview, led by Dr. Parthiv Mehta, patients are typically receiving treatment for prostate cancer. The location of the prostate between the bladder and rectum means that the prostate may not be in the same position daily. IGRT allows the radiation therapists to visualize the treatment area and ensure that the radiation is accurately delivered.

Newer models of linear accelerators are able to generate more radiation per unit compared to earlier models. New machines also allow for greater focus of radiation on the tumor itself, thereby minimizing as much as possible radiation to healthy cells nearby. UroPartners estimates that at least two thirds of all cancer patients require radiation therapy. The linear accelerator uses microwave technology to accelerate electrons in a part of the accelerator called the "wave guide". The electrons then collide with a heavy metal target to produce high-energy x-rays which can be shaped to attack a patient's tumor. During a procedure a patient lies on a moveable treatment platform and lasers are used to make sure the patient is in the proper position. The beam then comes out of a part of the accelerator called a gantry, and delivers radiation to the tumor from many angles. The fundamental principle is that the high-dose of radiation is restricted to the shape of the target tumor while excluding as much normal tissue from the high-dose radiation as possible. Because these machines have become a regular tool in the delivery of care and have regularly proven to be more precise and less harmful in radiation delivery, it is crucial that patients have access to this type of care.

Consistent with the goals and mission of the Health Facilities and Services Review Board, the applicants have filed this application in advance of their existing machine being rendered unusable. The acquisition of a new linear accelerator will serve the dual purpose of ensuring that the thousands of patients served by UroPartners will continue to have access to life saving treatments offered by the practice. Additionally, the acquisition of a new linear accelerator at this time promotes efficient health planning and allows the UroPartners practice to gradually phase out their existing machine while bringing the new linear accelerator up to full utilization.

This project proposes to address the regular deterioration of existing equipment and allow the patients served by the largest urology practice in the Midwest to continue to benefit from the care available in response to the acquisition of a new state-of-the-art linear accelerator. This will allow the practice to continue performing lifesaving procedures for their patients suffering from prostate cancer and other urological conditions.

Prostate Cancer is the most common non-skin cancer in the United States. The Prostate Cancer Foundation reports that 1 out of every 9 men will be diagnosed with prostate cancer in their lifetime. Typically, men at age 50 begin receive routine screening for prostate cancer. If test results reveal an enlargement or irregularity, physicians perform additional tests to determine if the patient in fact suffers from prostate cancer. According to the Illinois Department of Public Health, African-American and Latinos account for almost 60% of patient deaths due to prostate cancer.

Linear accelerators offer an important balance of safety and quality assurance, each of which are improved with modern equipment. Internal systems are built into each linear accelerator to avoid delivering a higher dose than prescribed by the radiation oncologist. This equipment is maintained and checked by the performance of routine checks, both monthly and daily. Modern linear accelerators have internal checking systems that will not allow the machine to be turned on unless all the prescribed treatment requirements are met.

In addition to safety of the patients, safety of staff and the employees operating a linear accelerator is also important. Linear accelerator are housed in rooms with lead and concrete walls so that the high-energy x-rays are shielded and no one outside of the room will be exposed to the x-rays. Because linear accelerators only emit radiation when being operated, the risk of accidental exposure is extremely low. Nevertheless, radiation therapists operate the machinery from outside the chamber housing the linear accelerator.

Linear accelerators can also be used to treat other cancers with targeted radiation regimens. Nearly 3,000 cases of bladder cancer will be diagnosed in Illinois this year, and radiation therapy will be one of the most common treatments for each person. Over 2,000 Illinois residents are diagnosed with kidney cancer every year, according to IDPH. UroPartners physicians also treat patients suffering from these conditions.

As described in this application, the applicants have an ample patient population that will benefit from this new equipment. The existing equipment is over 11 years old and the typical lifecycle of with regular maintenance of these machine is just over 10-12 years according to the study conducted by the Sarah Cannon Cancer Institute of HCA Healthcare. While the existing machine has received regular maintenance since initial use, over time there have been several developments in linear accelerator technology that would benefit UroPartners patients in the market area.

The applicant proposes to purchase the Varian Truebeam with Calypso. This system is helping providers treat prostate tumors more precisely by providing real-time targeting and motion management as well as accurate and efficient patient setup during radiotherapy. "Smaller than a grain of rice, each Calypso soft tissue beacon transponder continuously transmits location information about the tumor in real-time through a nonionizing signal to the Calypso tracking system. By monitoring a tumor's location—or, in the case of a surface transponder, patient motion that could compromise treatment accuracy—Calypso makes it possible to reduce margins between the clinical target volume (CTV) and the planning target volume (PTV) and provides clinicians with confidence that the prescribed dose is being delivered accurately and precisely."

The Varian Truebeam has multiple built in safety features physical, software, audible, and visual mechanisms specifically designed to help ensure safe operation of the equipment. Those systems as described by the manufacturer include the following:

- The TrueBeam system features collision detectors with touch guard sensors for machine components that may come within close proximity to the patient. These components include the kV imaging panel, kV imaging source, and the MV imaging panel.
- A capacitive collision detection system (CCDS), which is a non-contact layer of safety that stops the motion of the kV imaging source if the active area is encroached upon. The Varian TrueBeam has built-in equipment motion model that provides a 3D representation of the mechanical aspects of the entire system and prevents component-to-component collision.

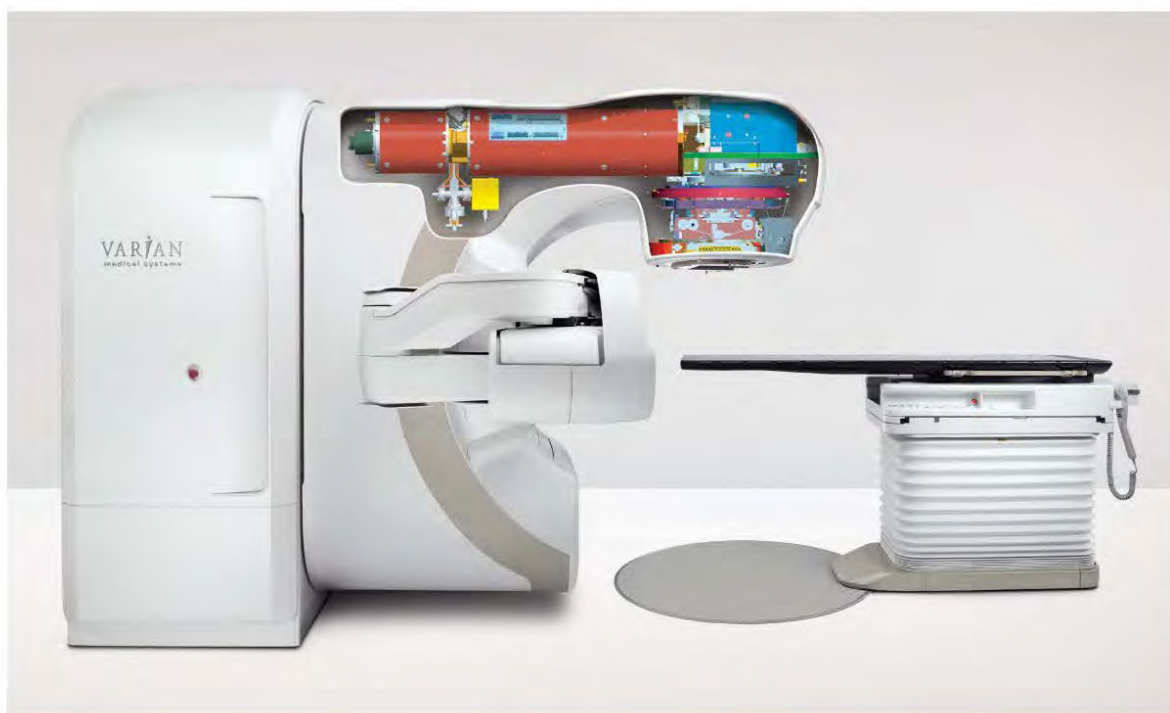
- Another feature of the machine are integrated zone rules that prevent hardware collisions. These built-in rules restrict any remote and some targeted motions from being performed during patient setup and treatment delivery if the system detects that a collision is possible.
- The live view monitoring system includes a radiation hardened camera focused on the patient. Directional arrows are projected onto the real-time image, located in the center of the treatment application monitor, indicating the targeted motions that are about to be executed. The system acts as a virtual presence, allowing therapists to remain focused on the patient. Visual and audio monitoring system Closed-circuit televisions enable the therapist to monitor the patient at all times. This “visual” safety mechanism affords the user ample coverage of the treatment room with pan, tilt, and zoom capabilities for optimal viewing. An integrated audio system built into the treatment control console enables constant interaction between the patient and therapist. Standardized user interfaces. The pendants, couch side panel, and treatment control console are all icon driven and use the same optical indicators for consistency and ease of recognition.
- Pre-treatment dry run functionality moves all TrueBeam external motion axes through their planned movements for the entire treatment, but does not deliver any dose to the patient. Dry run can be implemented as a motion review of the entire plan or a motion review of selected treatment fields and/or treatment field transitions.
- LaserGuard II is an integrated patient and equipment collision detection system. The system uses an infrared laser scanning device that continuously monitors the contoured region between the collimator face and the patient. If an object enters its protection zone, then LaserGuard II stops or inhibits motion prior to a potential collision. This is particularly useful when performing remote gantry rotations, whether from the treatment console or during an automated treatment sequence. LaserGuard II usability features include:
 - Deactivation when treatment door is open for easy patient setup and automated re-activation when door is closed;
 - Automated activation when a patient is loaded into the system and during a dry run (when the dry run mode is selected);
 - Remote clearance override of LaserGuard II, with the appropriate user rights, which allows motion to continue when the system is close to the patient;
 - Patient clearance and system usability are maximized through the design of the protection zone. The three-degree inclined protection zone plane includes a conformal notch contour which allows maximum clearance for patient treatment setup;
 - Works with the machine motion model and touch guards.

We have included materials from the manufacturer regarding the Varian Truebeam machine with Calypso technology that is currently offered.



A beam generation technology like no other

At the heart of the TrueBeam™ system is a groundbreaking beam generation technology, radically different from any other on the market. Built upon years of experience, it provides superior performance in beam delivery. It's fast. It delivers higher doses. It has more energies. It gives radiation oncologists the tools and flexibility to design new treatment options that can make all the difference.



Customizable for flexible energy selection

The TrueBeam system is fully customizable with four flat-field X-ray energies and two flattening filter free energies (High-Intensity Mode), and gives you the ability to choose the number of electron energies from zero to eight. You can now tailor your radiation treatment program almost without limitation.

This type of flexibility can only be found in the TrueBeam system. Additionally, you can do energy upgrades in the field without a guide change, giving you unmatched versatility. You can buy what you need now and add more later or exchange energies if appropriate.

High-Intensity Mode, the game-changer

The patented High-Intensity Mode is an exciting clinical capability, and it is now available on TrueBeam.

High-Intensity Mode has a peaked beam profile with the maximum intensity at the center of the field and a natural intensity falloff at the edge of the field. This beam profile is ideal for small fields, but also has advantages for larger fields. Small field treatments benefit from a high dose rate at the center of the beam by being able to be treated faster.

High-Intensity Mode can increase the speed of delivery by 40–140% because of a higher dose rate. Small field intensity modulated treatment techniques (IMRT, VMAT, RapidArc® radiotherapy technology) benefit from a high dose rate in the middle of the beam and a steeper intensity drop-off at the edge of treatment/tumor volume, as this can provide better normal tissue and critical structure dose sparing. Finally, treatment delivery with High-Intensity Mode benefits both free-breathing and breath-hold techniques for SBRT and radiotherapy by allowing treatment delivery under respiratory gated conditions without significantly lengthening overall treatment delivery times.

High-Intensity Mode has a maximum field size of 40 x 40 cm² and is not limited to a smaller field size. With dose rates extending from 400 MU/min through the maximum dose rate, these intensity-modulated energy configurations can be used for both radiosurgery and radiotherapy treatments. The highest dose rates achievable at the available energies are 1,400 MU/min for 6x and 2,400 MU/min at 10x.

Exceptional performance and technology without compromise**Important features of the TrueBeam system include:**

- Redesigned accelerator guide. This revolutionary, patented flat-field coupled guide allows tuning to a continuum of energies.
- Variable energy switch. The variable energy switch technology provides the “energy continuum” tuning capability. In other radiotherapy and radiosurgery technologies, tuning is limited to three energies.
- Simplified and integrated bend magnet. This patented technology ensures a narrow energy spectrum for each energy configuration. The narrow energy spectrum ensures stable and consistent beam output.
- Enhanced energy filter/foil carousel and target system. These enable the large selection of traditional energy configurations for both X-rays and electrons, in addition to the new High-Intensity Mode X-ray energy configurations.

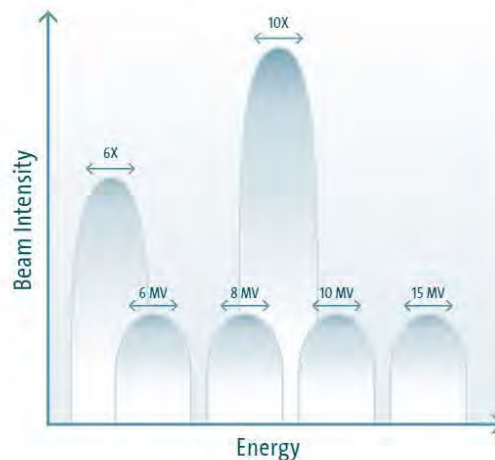
- Real-time electron gun gating. Treatment beam gating is accomplished by gating the electron gun in real time.
- Maximum flexibility in dosimetry. TrueBeam's dosimetry system is designed to support low dose rates (<5 MU/min) all the way up to high dose rates of 2,400 MU/min.

Advances in integrated gating technology

Varian is an industry leader when it comes to high-speed gating of treatment beams, gating the beam within 10 ms and precisely orchestrating system motion with respiratory gating. Respiratory gated treatment delivery is now compatible with all treatment techniques, including arc treatments (arc, dynamic conformal arc, VMAT and RapidArc).

Fully integrated respiratory gating, supported by the Eclipse™ treatment planning system and ARIA® oncology information system, ensures delivery of respiratory gated treatments and acquisition of respiration synchronized images, as defined by the treatment plan. If the treatment plan calls for respiratory gating, TrueBeam requires respiratory gating to be set up and respiration tracking active in order for treatment to be delivered. Images can be acquired, synchronized with respiration or automatically triggered by respiratory gating before, after, and now, during treatment delivery.

Redesigned inside and out, TrueBeam delivers the power and performance you expect from Varian technology while giving you the control and versatility to unlock new treatment options for your patients.



VARIAN
medical systems

A partner for life

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PerfectPitch 6 degrees of freedom couch Advanced robotics for accurate patient setup

Accurate and reproducible patient setups can potentially reduce harm to critical organs during radiation treatment. Patient set-up accuracy is especially critical for high-intensity treatments, such as intensity-modulated radiation therapy (IMRT), stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT)¹⁻³. Increasing clinical evidence suggests that a robotic couch with 6 degrees of freedom used in conjunction with cone-beam computed tomography (CBCT) may reduce patient set-up errors and improve target positioning for high-dose stereotactic treatments and IMRT⁴⁻⁶.

The Varian PerfectPitch™ 6 degrees of freedom (6DoF) couch is designed to deliver advanced radiation therapy techniques with a high level of accuracy and reproducibility. Allowing for two additional axes of rotation, pitch and roll, the 6DoF couch adjusts seamlessly on six axes, facilitating isocenter-focused shifts. With the 6DoF couch, CBCT image-guided target location, isocenter correction, treatment review, treatment delivery, and axes recording can all be accomplished without re-entering the treatment room or changing the control console. As a result, it may be possible to treat more patients with a higher degree of accuracy and reduce treatment margins in selected clinical cases.

Full system integration and easy workflow

When the PerfectPitch 6DoF couch is used with the Varian TrueBeam™ system, the TrueBeam STx™ system, or the Varian Edge™ radiosurgery system, couch operation and verification are fully integrated into the system user interface, enabling a seamless workflow. The patient shift can be calculated based on a CBCT or on two planar radiographs. Remote patient re-positioning can be performed in all six degrees. All shifts are saved and automatically recorded in the ARIA® oncology information system.



For Healthcare Professionals Only



User-friendly design for both clinician and patient

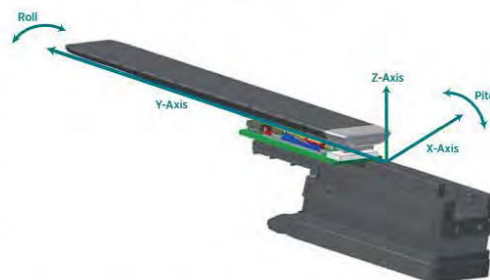
The Varian 6DoF couch is designed with both clinicians and patients in mind. The isocenter-focused couch movement reduces position correction and streamlines setup, which may contribute to increased treatment throughput. More importantly, with fast positioning, patients may spend less time on the treatment couch.

References

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SPECIFICATIONS

- Travel range: pitch and roll ± 3 degrees
- Velocity: up to 1.0 degrees/second
- 6DoF positioning accuracy: ≤ 0.5 mm (within precision load range) and ≤ 0.7 mm (full load range)
- Longitudinal and lateral couch range: same as standard TrueBeam couch
- Safe working load (using the integrated image-guided radiation therapy (IGRT) couchtop): 200 kg/440 lbs.
- Couchtop compatibility: Integrated IGRT, kVue™ IGRT couchtop and kVue™ Calypso® couchtop, including Pivotal™ treatment solution for prone breast care



The 6DoF couch adjusts seamlessly on six axes, facilitating isocenter-focused shifts.

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10/2013

Calypso

Precise localization and tracking for lung, soft tissues, and surface motion helps you optimize treatment delivery.



1 **Highly accurate tracking**

Calypso's GPS for the Body® technology detects the slightest patient movement to help you deliver tighter treatment margins.

2 **Automatic real-time correction**

Radiation delivery pauses when the target moves outside the clinician-defined threshold and resumes when moved back within the threshold.

3 No additional ionizing radiation

Calypso tracks using RF waves, so your patients won't experience unnecessary dose from imaging.

4 SBRT treatments

Accelerate prostate and lung treatments with more concentrated dose, reduced CTV-to-PTV margins, and reduced treatment-related side effects.

5 Multiple transponder options

Track motion for treatment to lung, prostate, and other soft tissue locations using internal or surface transponders.

PROSTATE CANCER IN ILLINOIS

FACTS AND FIGURES

PROSTATE CANCER IS A CANCER THAT AFFECTS
MEN AND STARTS IN THE PROSTATE GLAND.



#1

CAUSE OF CANCER AMONG MEN IN
ILLINOIS

DIAGNOSED IN ABOUT

7,665

MEN EVERY YEAR

97%

OF MEN DIAGNOSED
WITH PROSTATE
CANCER DO NOT DIE OF
IT WITHIN 5 YEARS

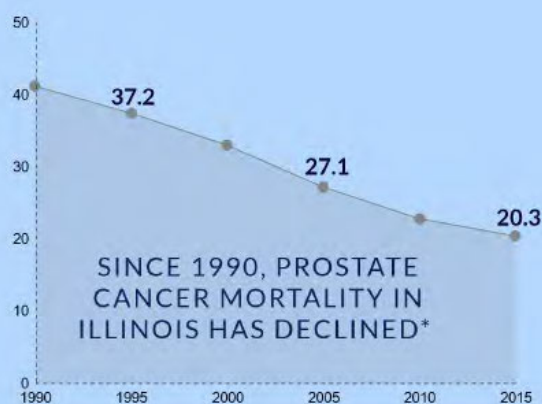
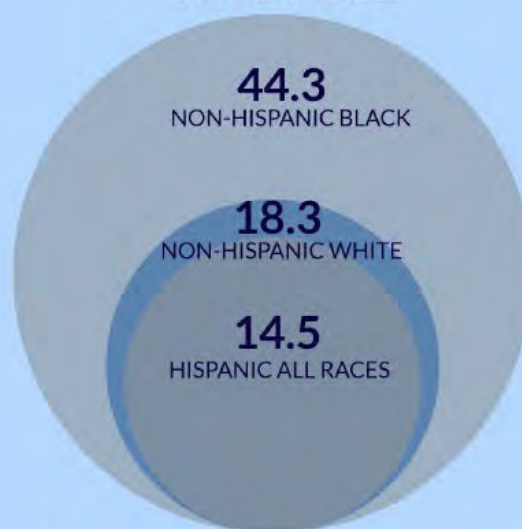


PROSTATE CANCER MORTALITY

PROSTATE CANCER CAN BE FATAL



MORTALITY RATES* VARY BY RACE



MORTALITY RATES ARE OVER **TWICE AS HIGH** IN BLACK MEN THAN IN WHITE MEN

*RATES ARE PER 100,000 PEOPLE IN THE POPULATION

SCREENING & PREVENTION

AVOIDING RISK FACTORS CAN HELP REDUCE THE RISK AND IMPACT OF PROSTATE CANCER



RISK FACTORS



FAMILY OR PERSONAL HISTORY OF CANCER



POOR DIET & OBESITY



NOT GETTING REGULAR EXERCISE



INHERITED GENETIC SYNDROMES (e.g. BRCA GENE MUTATIONS, LYNCH SYNDROME)



SMOKING



CHEMICAL EXPOSURE SUCH AS AGENT ORANGE (VIETNAM WAR)

NOTE: All cancer incidence and mortality data are specific to Illinois residents. Five-year survival estimates reflect age-standardized, relative survival. Methods are described in the 'Cancer in North America: 2011-2015' report, cited below. All presented rates are per 100,000 and are age-adjusted to the 2000 U.S. standard million population. Unless otherwise noted, displayed incidence and mortality rates have been calculated for calendar year 2015.

REFERENCES:

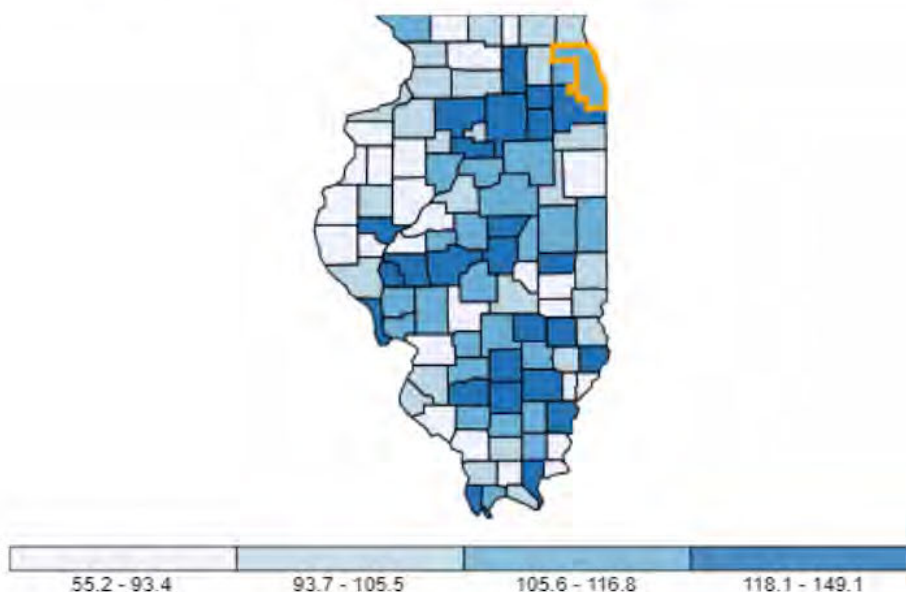
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Rate of New Cancers in Cook County, Illinois

Prostate, All Ages, All Races/Ethnicities, Male, 2013-2017



Rate per 100,000 people

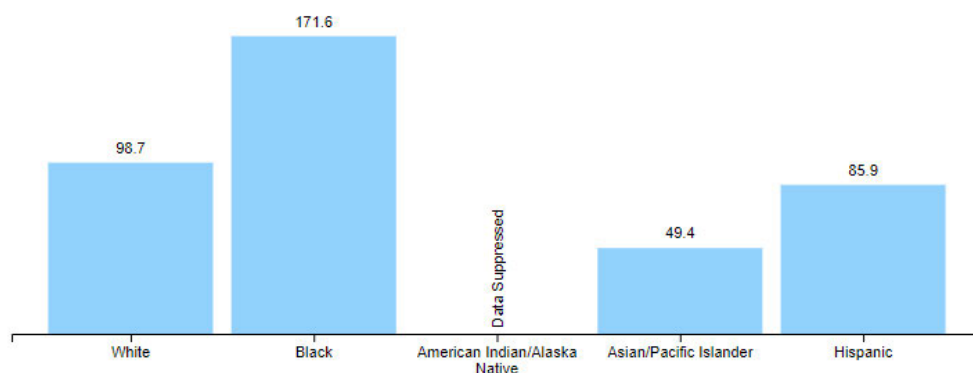
Data source – U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on November 2019 submission data (1999-2017); U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; <https://www.cdc.gov/cancer/dataviz/>, June 2020.

According to the Centers for Disease Control, in Cook County, the age adjusted rate of new prostate cancer cases was 114.6 per 100,000 men. Between 2013-2017 there were 15,341 new cases of prostate cancer. During this same period of time 2,561 men died of prostate cancer. For every 100,00 men in Cook County, 23 men died of prostate cancer.

Rate of New Cancers by Race/Ethnicity, Both Sexes

Prostate
Rate per 100,000 men

Chart Table Export



Using Data to Create a Focused Radiation Oncology Service Line Across 46 Facilities: The HCA Sarah Cannon Story

Centerline

November 22, 2017

In 2015, Sarah Cannon, the Cancer Institute of HCA Healthcare, announced a new initiative to create an infrastructure and tools to assess and improve the quality, safety and outcomes across HCA Healthcare's network of 46 radiation oncology centers.

"The long-term goal was to accomplish a full programmatic build, bringing health systems into a collaborative service line to share best practices and to reduce variation across the 46 facilities," said Andrew Kennedy, MD, FACRO, Physician-in-Chief, Radiation Oncology, Sarah Cannon and Director, Radiation Oncology Research, Sarah Cannon Research Institute.

ARIA Consolidation and Utilization

An important strategy to accomplish this goal was to use data analytics to drive quality and operational enhancements as well as greater utilization of advanced technologies and best practices across all sites. That meant first consolidating and standardizing the ARIA® oncology information system (OIS) across the network and deploying InSightive™ software for mining the ARIA database to generate actionable insights.

"Current data are invaluable for informing how we can improve treatments for future patients," said Jason Pawlowski, MS, PhD, DABR, Senior Director, Radiation Oncology Services at Sarah Cannon. "We are committed to using analytics to improve outcomes and to identify best practices for the greatest clinical impact."

"We are working to establish a data-centric culture within our radiation oncology program," Dr. Kennedy elaborated. "We wanted to make sure that clinical staff viewed the routine capture of clinical information as an essential task that would impact our ability not only to complete treatments, but also to improve the treatment of future patients."

Prior to the OIS consolidation, there was no standardization or interconnectivity between sites, and the oncology information systems were managed by the local site physics teams with the support of IT departments. Consequently, there were limitations in areas like economies of scale, data sharing, and disaster recovery planning.

According to Dr. Kennedy, when disparate sites were consolidated on the ARIA OIS, a standard configuration could be adopted for the network and rates of compliance began to be measured to ensure that all sites were using ARIA tools like "Encounters," "Activities" and "Care Paths" in the same way. In addition, new software deployments, upgrades and disaster recovery are now managed by Varian within the data centers, freeing up IT resources and allowing the medical physics staff to focus on clinical issues.

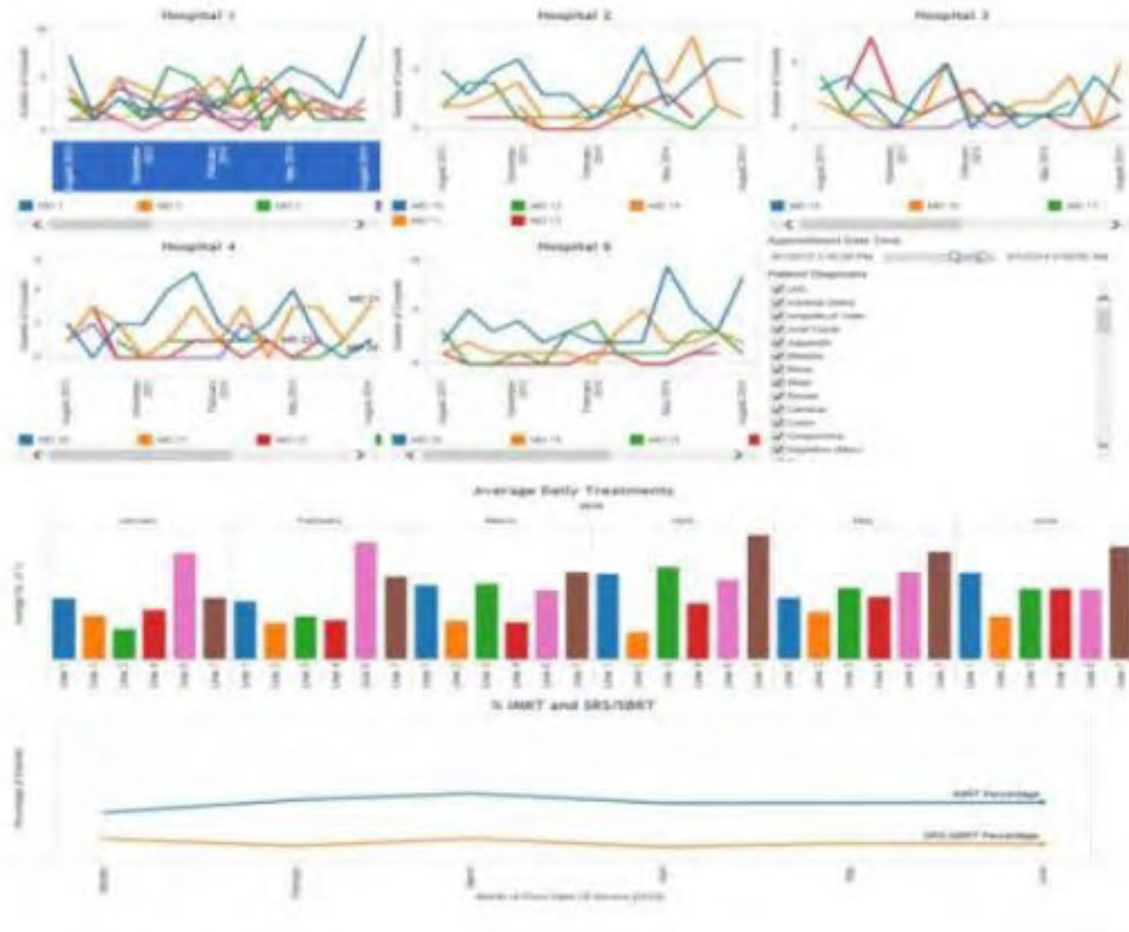
Using InSightive analytics, the Sarah Cannon team created dashboards that enable them to identify trends and assess how sites are performing relative to benchmarks. This makes it possible to discover operational inefficiencies and to identify best practices that can help improve performance across the network.

Clinician-Led Governance

Sarah Cannon adopted a clinician-led governance model to oversee the project. "Clinician-led governance has been the foundation of our build," said Dr. Kennedy. "Our clinicians lead decision making through expert consensus focused on improving quality, safety and outcomes. Capitalizing on the expertise of our

clinicians, we are giving our facilities the tools to meet benchmarks by measuring themselves against their peers and learning best practices from each other.”

The governance team worked together to determine what would be measured to assess and improve clinical quality, operational efficiency and business performance. Additionally, they determined that the project should include deployment of RapidPlan™ knowledge-based treatment planning to reduce variability in plan quality, and enable rapid adoption of new treatment modalities.



During a pilot project conducted in advance of the systemwide rollout, Sarah Cannon measured 15 benchmarks in three areas: operational analysis, business performance and clinical quality. That meant looking at, among other metrics, asset utilization, modality mix, patient satisfaction and retention, radiation toxicities, accreditation status, adherence to agreed-upon data entry requirements, RapidPlan adoption for approved disease site models, financial performance, and linac replacement performance, which examined utilization of new linear accelerators for a 12-month period post-installation. As facilities adopted modern technologies and best practices, InSightive enabled them to measure how they were performing in the 15 benchmarks compared to their peers.

RapidPlan™ Knowledge-Based Treatment Planning

Nine facilities deployed RapidPlan during the pilot program. More than 350 clinically-used patient plans were optimized during the pilot project using RapidPlan. By the end of the pilot, the RapidPlan adoption rate amongst the pilot sites ranged from 45% to 85%.

“The performance of RapidPlan in our pilot testing, in terms of efficiency and dosimetric superiority compared with manual planning, gave us the data needed to increase the adoption of RapidPlan in our clinics. We now couple a license for RapidPlan with every linear accelerator replacement across our

network. By the end of 2017, 40% of facilities across our system will be utilizing this technology,” said Dr. Pawlowski.

Asset Replenishment and Utilization

At the start of this project, the average linear accelerator (linac) age across Sarah Cannon’s network exceeded 9 years, and 15% of the conventional linacs were equipped to offer stereotactic radiosurgery (SRS) or stereotactic body radiotherapy (SBRT). A systematic asset replenishment strategy was implemented in 2015 and by the end of 2017, 62% of linacs, and 83% of radiation oncology departments will be equipped to perform these procedures.

“Seventy-five percent of our 46 radiation oncology facilities are single-vault departments. By focusing on multi-functional linear accelerators that enable a full range of treatment options spanning conventional radiotherapy to SRS and SBRT, we have significantly improved access to essential treatments for our patients and physicians,” said Dr. Pawlowski.

According to analytics monitoring, the Sarah Cannon team reports that asset utilization across the system (based on the average number of patients treated per day or the number of patients receiving a given treatment) has been steadily improving due to the initiative.

Summary

“Initial results show us that the infrastructure we are putting in place across the network allows us to use important data for continuous enhancements,” said Dr. Kennedy. “By analyzing operational and quality clinical metrics in real-time, we can provide timely feedback to our facilities, enhancing the ability to make adjustments and changes.”

“By implementing systems for quality and operational measurement, establishing a governance to identify best practices, and providing tools to our clinicians and leadership teams across the network, we have seen significant improvements in our programs across the U.S. and look forward to continuously measuring the impact for our patients,” added Dr. Pawlowski.

Source: <https://www.varian.com/resources-support/blogs/clinical-oncology-news/using-data-create-focused-radiation-oncology-service>

PROSTATE CANCER

PATIENT GUIDE

A comprehensive resource on diagnosis, treatment, side effects, and risk factors for patients and families with a history of prostate cancer.



**“Be vigilant, live healthy,
and don’t give up. This disease
can be conquered.”**

— FORMER COMBAT MARINE, KOREAN WAR

About this guide

There are no two ways about it: being diagnosed with cancer is hard and it is life-changing. Despite increasing optimism about treatment, today's cancer landscape can be challenging, as patients have access to an unprecedented amount of information. There are literally millions of cancer-related webpages, blogs, and videos available at your fingertips. But it's important to acknowledge that this isn't always a helpful thing. A cancer diagnosis can be disorienting, and for many, the overwhelming volume of information available can be more of a burden than an aid.

This guide focuses all of the information available about contemporary prostate cancer research, treatment, and lifestyle factors into one consolidated resource. It is for any man who has been newly diagnosed, who is in treatment, or is concerned about a rising PSA. Beyond that, it's for any loved one or caregiver who wants to cut through the information noise and get directly to need-to-know information for prostate cancer patient navigation. Lastly, as we are beginning to recognize the genetic underpinnings of cancer, this guide is for any family member who might want to understand how their shared genes affect their own short- and long-term risk factors — and whether they should be screened as well.

We gratefully acknowledge the scholarly expertise and contributions of our Editors, who are world leaders in prostate cancer research: Daniel Spratt, MD (University of Michigan); Andrea Miyahira, PhD (Prostate Cancer Foundation); Heather Cheng, MD, PhD (University of Washington, Fred Hutchinson Cancer Research Center); Stacy Loeb, MD, MSc (New York University); Matthew Cooperberg, MD, MPH, (University of San Francisco); Alicia Morgans, MD (Northwestern University); Arthur Burnett, MD, MBA (Johns Hopkins University); Nima Sharifi, MD (Cleveland Clinic); William Aronson, MD (UCLA); Angelo Baccala Jr., MD, FACS, MBA (Lehigh Valley Health Network); Neal Shore, MD, FACS (Carolina Urologic Research Center); James Schraidt & Chuck Strand (UsTOO); Andrew Armstrong, MD (Duke University); Bill Curry; Izak Faiena, MD (University of California, Los Angeles); Christopher Sweeney, MBBS (Dana-Farber Cancer Institute, Harvard Medical School); Howard Soule, PhD (Prostate Cancer Foundation); Stuart Holden, MD (Prostate Cancer Foundation); Jonathan Simons, MD (Editor-in-Chief, Prostate Cancer Foundation); Rebecca Campbell, MD, MPH (Co-Editor, Prostate Cancer Foundation) and Julie DiBiase, PhD (Co-Editor, Prostate Cancer Foundation).

This guide was originally released in 2017, updated for print in January 2019, and most recently updated in pdf in May 2020 by the Prostate Cancer Foundation (PCF). The Prostate Cancer Foundation is the world's leading philanthropic organization funding and accelerating prostate cancer research. Since its beginning in 1993, the Prostate Cancer Foundation has funded key research leading to many of the treatments used by doctors today to improve the lives of patients, with the mission that someday, soon, no man will die of this disease.

Subjects depicted are models and are used for illustrative purposes only. Prostate cancer standards of practice change regularly. For the most up-to-date information, please register for updates at pcf.org.

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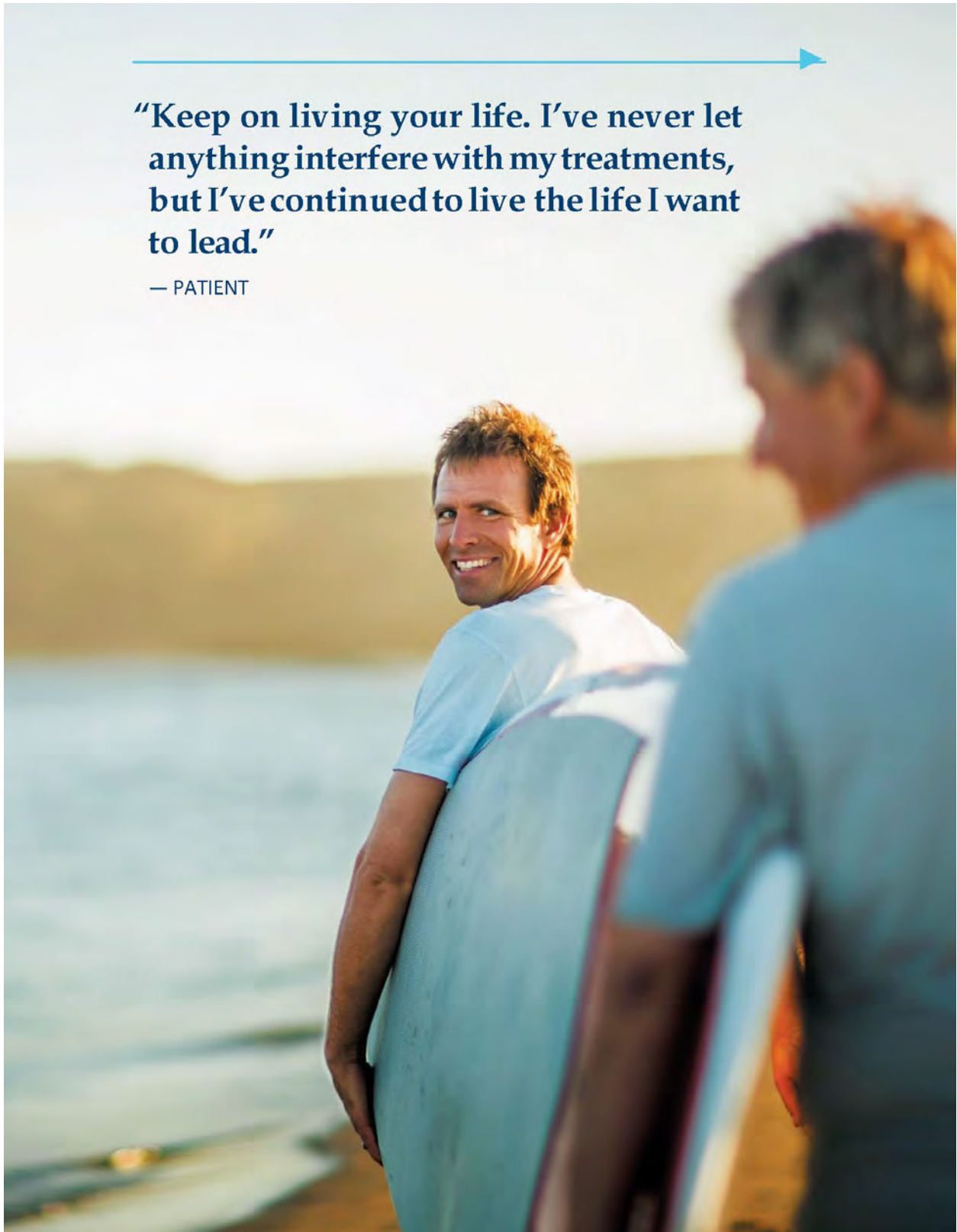
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“Keep on living your life. I’ve never let anything interfere with my treatments, but I’ve continued to live the life I want to lead.”

— PATIENT



1 ► ABOUT YOU AND PROSTATE CANCER

See Appendix for 2020 COVID-19 Updates.

GENERAL INFORMATION

What is Prostate Cancer?

In general, **cancer** is a condition in which a normal cell becomes abnormal and starts to grow uncontrollably without having the signals or “brakes” that stop typical cell growth. Prostate cancer starts in the **prostate**, a small gland located below the bladder that is responsible for secreting one of the components of semen. Prostate cancer cells form masses of abnormal cells known as **tumors**.

Prostate cancer, therefore, is when a normal prostate cell becomes altered and starts growing in an uncontrolled way.

In many cases, prostate cancer is relatively slow-growing, which means that it takes a number of years to become large enough to be detectable, and even longer to spread outside the prostate, or **metastasize**. However, some cases are more aggressive and need more urgent treatment.

Surviving Prostate Cancer

More than 90% of all prostate cancers are detected when the cancer is in the prostate or the region around it, so treatment success rates are high compared to most other types of cancer in the body. **The 5-year relative survival rate in the United States for men diagnosed with prostate cancer is 99%.** In other words, the chances of the cancer spreading or men dying from their prostate cancer is generally low. However, prostate cancer comes in many forms and some men can have aggressive prostate cancer even when it appears to be confined to the prostate.

Amidst much optimism and progress in the last 10 years, it's important to keep in mind that prostate cancer is still a deadly disease for some men, and it is the second leading cause of cancer death among men in the U.S., with nearly 87 men dying from it every day.

In general, the earlier the cancer is caught and treated, the more likely the patient will remain disease-free. In fact, many men with “low-risk” tumors, which are the most common type of prostate cancer, can safely undergo active surveillance, in which they are monitored without immediate treatment (and treatment-related side effects) while still preserving their chance of long-term survival if the cancer becomes aggressive enough to require treatment.

Rates of Diagnosis

Prostate cancer is the third most prevalent type of cancer in the U.S. and the fourth most common worldwide. Nearly 175,000 new cases are estimated in the U.S. for 2019, and about 1.27 million men were diagnosed globally in 2018. Approximately one in nine men in the U.S. will be diagnosed with prostate cancer at some point in their lives. The older you are, the more likely you are to be diagnosed with prostate cancer.

Although only about 1 in 437 men under age 50 will be diagnosed, the rate shoots up to 1 in 59 for ages 50 to 59, 1 in 22 for ages 60 to 69, and 1 in 13 for men 70 and older. Nearly 60% of all prostate cancers are diagnosed in men over the age of 65.

IS THERE A CURE FOR PROSTATE CANCER?

When people think about cancer treatment success, they often think of the word “cure.” Thanks to advances in treatment in the last 15 years, it is often possible to say that a man has been “cured” of prostate cancer. However, more often statisticians think of “cure” as a function of time: is 5 years without a cancer recurrence equal to a cure? Or is it 10 years? Unfortunately, in some men, prostate cancers can recur even 10 years after treatment. So instead of using the term “cure,” doctors commonly use terms such as *biochemical control* (PSA levels kept at bay) or *freedom from developing metastatic disease* (the cancer has not spread to distant organs) to help quantify the success of prostate cancer treatment.

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20 genes

that run in families have been discovered that have overlap from prostate cancer to other cancers.



Prostate cancer can be silent — it's important to get checked, even if you have no symptoms.

Prostate cancer has one of the highest survival rates of any cancer.

Since 1993, deaths from prostate cancer have been cut in half.



99%

Prostate cancer is 99% treatable if detected early.

10 THINGS TO KNOW

A man of African descent is 76% more likely to develop prostate cancer.

76%

As men age, their risk of developing prostate cancer increases exponentially.

Thanks to emerging science, in the next 5 years, we may see an end to all incurable prostate cancer.



In the U.S., prostate cancer is the **most common** non-skin cancer in men.

2x

Men with relatives with a history of prostate cancer may be twice as likely to develop the disease.

Prostate cancer is almost always diagnosed with a biopsy. The most common reason for a man to undergo a prostate biopsy is due to an elevated prostate-specific antigen level, or PSA, determined by a blood test. Recent changes in PSA screening recommendations have impacted the rates of prostate cancer diagnosis (see [Screening for Prostate Cancer](#), page 75).

Risk Factors

As indicated by the rates of diagnosis, **age** is the biggest—but not the only—risk factor for prostate cancer. Other important factors include family history, genetic factors, race, and lifestyle and dietary habits.

Genes that increase risk for disease can run in families. Genetic factors contribute to about 40% of all prostate cancers, which makes prostate cancer the most “inheritable” of all cancers. Men who have a close relative with prostate cancer may be twice as likely to develop the disease, while those with 2 or more relatives are nearly 4 times as likely to be diagnosed. The risk is even higher if the affected family members were diagnosed before age 65. Men may also be at increased risk of prostate cancer if they have a strong family history of other cancers, such as breast cancer, ovarian cancer, colon cancer, or pancreatic cancer. Because family members share many genes, there may be multiple genetic factors that contribute to the overall risk of prostate cancer in a family. However, there are also some individual genes that we now know increase the risk of prostate cancer, and men with these genes may need to undergo genetic counseling, be screened differently, or consider changes in treatment. For more on family risk, see [The Genetics of Risk](#), page 75.

It is still a scientific mystery, but African American men are 76% more likely to develop prostate cancer compared with white men, and 2.2 times more likely to die from the disease.

Prostate cancer appears to develop about 3 years earlier among African American men, on average, than among white men. Whether this phenomenon is due to environmental factors—such as diet, stress, and exercise; socioeconomic factors—such as those related to access to healthcare; or genetic factors—such as genes that run

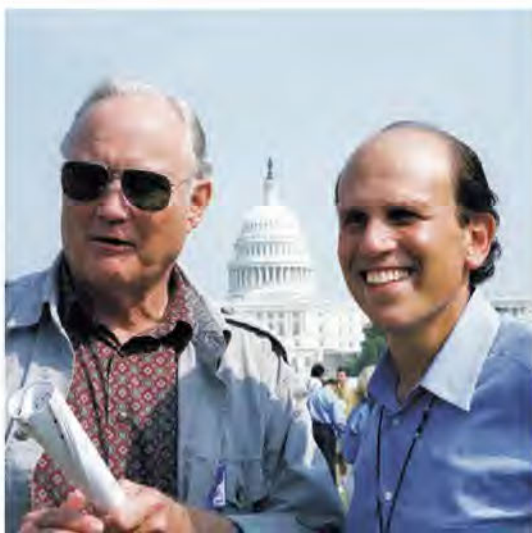
in families, remains unclear. Improving understanding about the origins of risk will help inform better treatments and is an active area of research for the Prostate Cancer Foundation. In the meantime, it is important to keep in mind that not every African American man will get prostate cancer, and that all prostate cancer has a better chance of being managed effectively and cured if it is detected early.

Other risk factors for prostate cancer are [social and environmental factors](#)—particularly a high-fat, high-processed-carbohydrate diet—and lifestyle. Men who are overweight or obese are at greater risk of ultimately developing an aggressive form of prostate cancer. Research has shown that in obese men, recovery from surgery tends to be longer and more difficult, and the risk of dying from prostate cancer can be higher.

Symptoms

If you’ve recently been diagnosed with prostate cancer, you may be asking yourself if there were warning signs or symptoms you should have noticed earlier. Unfortunately, there usually aren’t any early warning signs for prostate cancer. The growing tumor usually does not push against anything to cause pain, so for many years the disease may be silent. That’s why [screening](#) for prostate cancer is such an important topic for all men and their families. In rare cases, typically when the disease has advanced, prostate cancer can cause symptoms that include:

- ▶ A need to urinate frequently, especially at night, sometimes urgently
- ▶ Difficulty starting or holding back urination
- ▶ Weak, dribbling, or interrupted flow of urine
- ▶ Painful or burning urination
- ▶ Difficulty in having an erection
- ▶ A decrease in the amount of fluid ejaculated
- ▶ Painful ejaculation
- ▶ Blood in the urine or semen
- ▶ Pressure or pain in the rectum
- ▶ Pain or stiffness in the lower back, hips, pelvis, or thighs



PCF founder and chairman Michael Milken is joined by General Norman Schwarzkopf in 1998 on the Mall in Washington for "THE MARCH: Coming Together To Conquer Cancer."

Keep in mind that urinary symptoms don't necessarily mean you have cancer. Prostatitis and BPH (**Benign Prostatic Hypertrophy**, also known as enlargement of the prostate) are common and benign diseases that can cause similar symptoms.

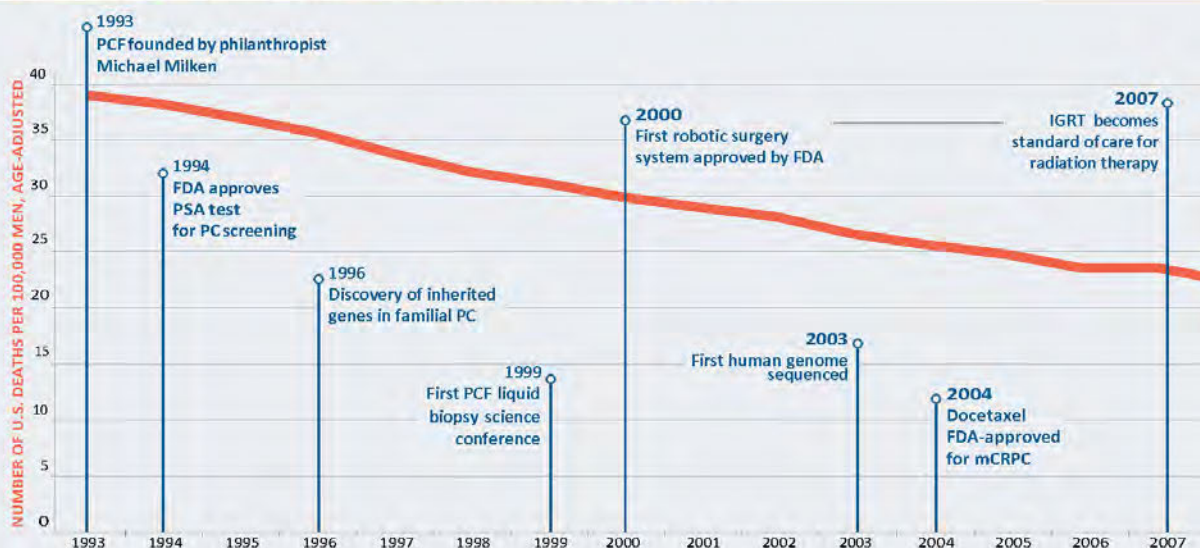
What about difficulty in having an erection? Again, this is most likely not caused by prostate cancer but by other factors such as diabetes, smoking, high blood pressure, cardiovascular disease, medications, or aging.

Remember: Symptoms are symptoms, and no matter what's most likely to be causing them, you should get them checked out by a doctor.

History & Progress

Modern prostate cancer research was framed in the 1940s by the discovery that hormones, primarily testosterone, were responsible for the growth of prostate tumors. Over the next 5 decades, various types of chemotherapy, radiation therapy, surgical options, and hormone therapy were refined.

Breakthroughs in Prostate Cancer Treatment and Practice



10 ► ABOUT YOU AND PROSTATE CANCER

In 1994, the FDA approved the **PSA** blood test to detect prostate cancer in men without symptoms. Because cancer detected early is much easier to treat, use of the PSA test for screening has contributed to the subsequent increase in the number of patients diagnosed early enough to be cured with surgery or radiation, and has substantially contributed to a 51% reduction in deaths from prostate cancer over the past 2 decades in the U.S. However, the **PSA test** sparked concerns that it has led to over-diagnosis and over-treatment of non-aggressive, slow-growing prostate cancers that may never have caused harm to the patient if left untreated.

Since 1993, when the Prostate Cancer Foundation began funding life-prolonging advancements in research, amazing strides have been made in finding therapies for treating advanced prostate cancer that are now part of an improved standard of care. There have been tremendous advancements, including:

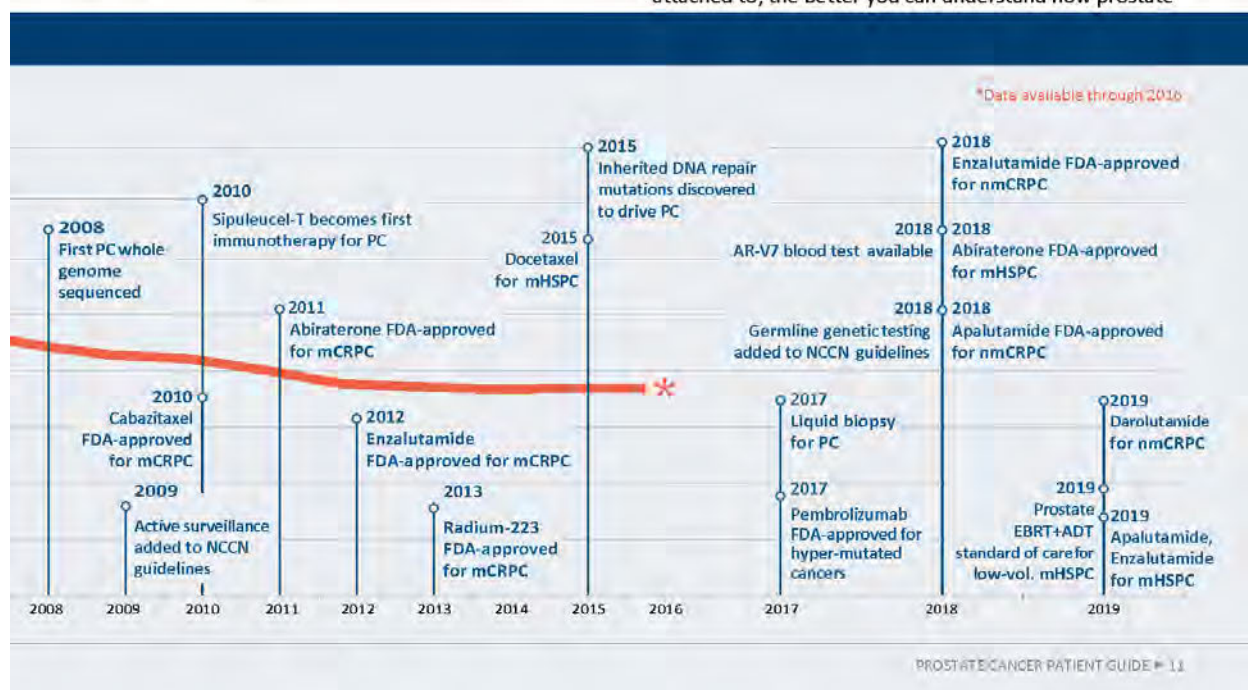
- Imaging technology to help find prostate cancer
- Precision radiation therapy
- Development of robotic surgery
- Numerous new FDA-approved therapies that help men live longer

Because of these improvements and potentially other unknown factors, **since 1993, deaths from prostate cancer have been cut in half** (from 39.3 per 100,000 men in 1993, to 19.4 per 100,000 men in 2016). A 2019 study reported that in many countries around the world, incidence and mortality rates have declined or stabilized. The U.S. has experienced the largest decline in incidence.

Today, **precision medicine**, which involves matching the right drug to the right patient at the right time, is ushering in a new era in treatment for prostate cancer including DNA testing as a gold standard in cancer care. Furthermore, in localized prostate cancer, doctors are learning that a tumor's genomic signature may help to predict which patients may be at risk for aggressive disease in the future. Scientists are also exploring how **immunotherapy**—the process of using the body's own immune system to combat disease—can be used more effectively in treating and preventing prostate cancer.

MEDICAL BASICS

The more you know about the normal development and function of the prostate, where it's located, and what it's attached to, the better you can understand how prostate



cancer develops and impacts a man's life over time—due either to cancer growth or as a result of treatment.

The Anatomy of the Prostate

The **prostate** is a small, squishy gland about the size of a ping-pong ball. It sits under the bladder and in front of the rectum. The prostate is only present in men. It is important for reproduction, because it supplies the fluids needed for sperm to survive and it helps push out semen during ejaculation. Sperm are not made in the prostate; they are made in the **testes** and travel to the prostate through the vas deferens (the tubes which are cut in a vasectomy procedure).

The prostate is divided into several anatomic regions, or zones. Most prostate cancer starts in the **peripheral zone** (the back of the prostate) near the rectum. That's why the physician's examination of the prostate via a gloved finger in the rectum, known as **digital rectal exam** (DRE), is a useful screening test.

The **seminal vesicles** are rabbit-eared structures that store and secrete a large portion of the ejaculate. These structures sit on top of the prostate.

The **neurovascular bundle** is a collection of nerves and blood vessels that run along each side of the prostate, helping to drive erectile function. They travel from the lower spine all the way across the pelvis to the penis.

Since this bundle sits very close to the prostate, it is often disturbed during prostate cancer treatment, and is sometimes directly invaded by more aggressive cancers.

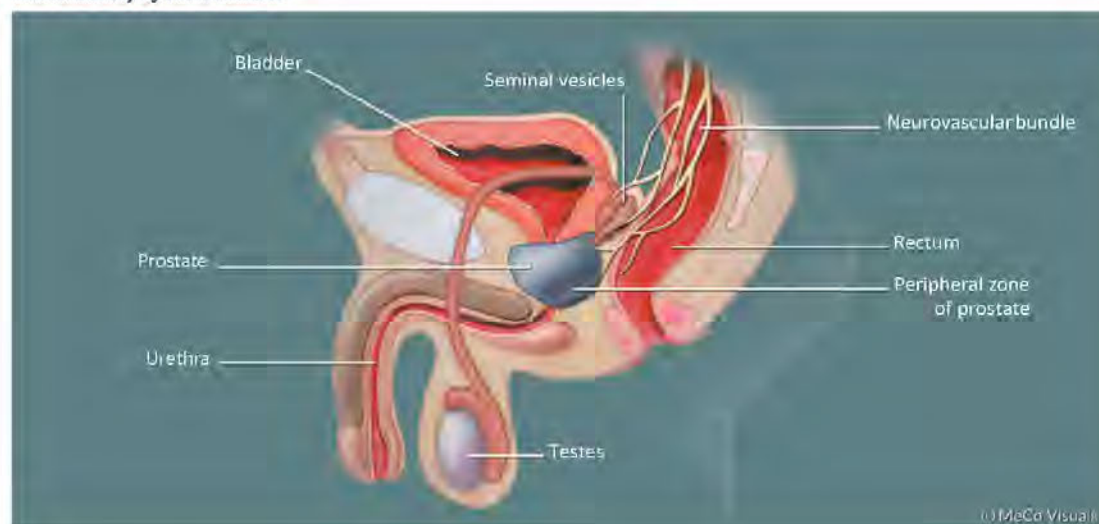
The **bladder** is like a balloon that gets larger as it fills up, holding urine until the body is ready to void. The **urethra**, a narrow tube that connects to the bladder, runs through the middle of the prostate and along the length of the penis, carrying both urine and semen out of the body. It is the hose that drains the bladder.

The **rectum** is the lower end of the intestines that connects to the anus, and it sits right behind the prostate.

The Biology of Prostate Cancer

To properly understand diagnosis and treatment options, it's important to understand how prostate cancer grows. A normal prostate processes **androgens** (including testosterone and dihydrotestosterone, or DHT) as part of its everyday function.

The Anatomy of the Prostate



ANDROGENS

Androgens are hormones that are important for many male characteristics and aspects of reproduction. A common androgen is testosterone.

GRADE

Grade is a measure of how abnormal the prostate cancer cells look under the microscope. It's used to predict how quickly they might grow or spread.

Once prostate cancer forms, the cancer feeds on these same androgens and uses them as fuel for growth. This is why one of the basic treatments for men, especially with advanced prostate cancer, is to lower a man's androgen levels with drugs collectively termed "hormone therapy" or "androgen deprivation therapy" or ADT.

Prostate cancer occurs when a normal prostate cell begins to grow out of control. In many cases, prostate cancer is a slow-growing cancer that does not progress outside of the prostate gland before the time of diagnosis.

The rate of growth and spread of prostate cancer is reflected in the [grade](#) of the cancer, measured by either the Gleason score or the ISUP (International Society of Urological Pathology) grade group classification.

"High-grade" prostate cancers are those that are composed of very abnormal cells and are more likely to both divide and spread faster from the prostate to other regions of the body. Often, prostate cancer spreads first to tissues that are near the prostate, including the seminal vesicles and nearby lymph nodes.

Researchers have identified various biological and genetic subtypes of prostate cancer. It is possible for any given prostate cancer tumor to contain multiple subtypes of prostate cancer. Doctors and researchers are only just now beginning to use subtyping to guide treatment recommendations, thanks in part to active and ongoing research funded by the Prostate Cancer Foundation. For information on different types of

tumor genetic sequencing and the scenarios in which they may be appropriate for guiding medical decisions or for contributing to research, visit pcf.org.

Understanding Metastasis

Sometimes cancer cells will escape the prostate and grow quickly, spreading to nearby tissue. Nearby lymph nodes are often the first destination for a spreading cancer. If prostate cancer has spread to your lymph nodes when it is diagnosed, it means that there is higher chance that it has spread to other areas of the body as well.

Metastasis refers to tumor cells leaving the prostate and forming tumors somewhere else in the body.

If and when prostate cancer cells gain access to the bloodstream, they can be deposited in various sites throughout the body, most commonly in bones, and sometimes in other organs such as the liver or lungs. Bone metastases are seen in 85% to 90% of metastatic cases.

Even if you are told your cancer is confined to your prostate gland, there is no way to know this with 100% certainty. New data from studies funded by the Prostate Cancer Foundation, using new types of molecular imaging, has shown that more than 10% of patients with high grade "organ-confined" prostate cancer actually have small deposits of metastatic disease. These technologies continue to be actively investigated.

"If my doctor tells me that I have prostate cancer metastases in my bones or my lungs, does that mean I have bone cancer or lung cancer?"

This does not mean you have "bone cancer" or "lung cancer," since these tumor cells came from the prostate and did not develop from bone or lung cells. Your treatment should be focused on prostate cancer rather than bone or lung cancer.

What is PSA?

PSA, or **Prostate Specific Antigen**, is a protein produced by the prostate and found mostly in the semen, with very small amounts released into the bloodstream. It is

used as a “disease marker” to represent prostate cancer. When there’s a problem with the prostate—such as the development and growth of prostate cancer—more PSA is released. PSA eventually reaches a level where it can be easily detected in the blood. This is often the first indicator of prostate cancer.

During a PSA test, a small amount of blood is drawn from the arm, and the level of PSA is measured. Doctors look at the overall level of PSA, as well as its rate of rising (velocity) compared with prior test results. As the PSA number goes up, the chance that cancer is present increases. Men whose levels go above 3 or 4 are often recommended to undergo a biopsy; however, this PSA level does not mean that prostate cancer is definitely

there, and some cancers may be present even when PSA levels are lower, particularly among younger men.

PSA screening decisions should be made in consultation with your doctor and based on a full examination of risk factors. See also, *The Genetics of Risk*, page 75.

In men who have confirmed diagnosis of prostate cancer, rising PSA is a useful test to track prostate cancer growth, since it can be detected well before any clinical signs or symptoms. The PSA is also widely accepted as an invaluable tool for monitoring prostate cancer disease activity and recurrence of prostate cancer after treatment.

The Biology of Sex Steroids

Prostate cancer cells are just like all other living organisms—they need fuel to grow and survive. The main fuel for prostate cancer growth is the sex hormone testosterone.

The term **sex steroid**, or **sex hormone**, refers to the substances secreted by the testes and ovaries (**androgens** and **estrogens**, respectively) which are responsible for the function of the reproductive organs and the development of secondary gender characteristics (such as facial hair, muscle mass, and sex drive). Androgens and estrogens are present in both men and women, though at different levels. The most important androgen for male reproduction is **testosterone**. Testosterone is primarily made in the testes, but a smaller amount is made in the adrenal glands above the kidneys. The prostate typically grows during adolescence under the control of testosterone.

Since androgens—including testosterone—fuel prostate cancer growth, prostate cancer treatment regimens may include some amount of hormone therapy, which deprives tumor cells of androgens.

The prostate is not essential for life, but it is important for reproduction. It supplies substances that facilitate fertilization, sperm transit, and sperm survival. Enzymes like PSA (the same protein that is measured in the blood test) loosen up semen to help sperm reach the egg after intercourse. Sperm is made in the testes, and it travels through the prostate during its transit, picking up seminal fluid along the way.

THE PSA DEBATE

PSA is not a perfect test to screen for prostate cancer. Elevated levels can be caused by other benign prostate diseases and problems, such as BPH (benign prostatic hyperplasia, an enlarged prostate) or prostatitis (an infection in your prostate). There is an active debate around prostate cancer screening. Some health care professionals are concerned that increased PSA screening is finding tumors that are so slow-growing as to pose no long-term threat to the patient. Some think this can lead to “overtreatment” in many men with low-risk cancers, causing unnecessary side effects and quality-of-life impact. However, there is a lot of data to suggest that PSA testing has reduced the death rate from prostate cancer, because men with aggressive cancers are diagnosed earlier—often before the cancer has spread—and can be cured and/or more effectively managed by earlier treatment. If PSA screening is done well, its value is greatly increased. It is critical to test men at the appropriate age, repeat PSA tests once the baseline level is known, and reserve treatment for those with higher risk cancers. The Prostate Cancer Foundation is actively funding new research into better prostate cancer screening tests that are more specific and sensitive than the PSA test.

The older term “medical castration” is sometimes used to describe a drug treatment regimen for controlling hormone levels. **Androgen deprivation therapy (ADT)**, in which medication is used to cut off the supply of testosterone to the prostate, is part of the treatment plan for metastatic prostate cancer and also for some patients with non-metastatic disease. ADT is associated with high rates of response, but it has *side effects*, which can be more pronounced when used for years. The side effects are typically transient when given for only a few months.

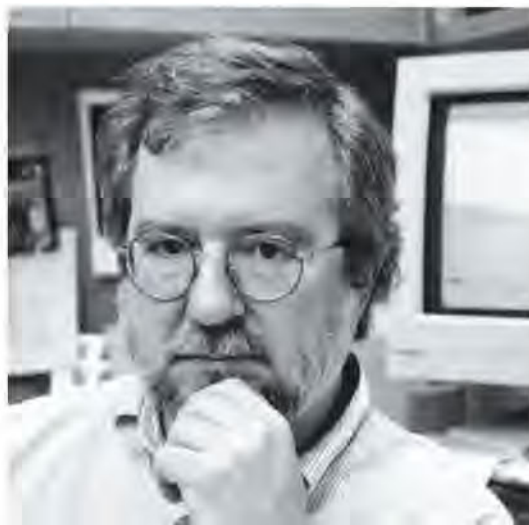
Precision Oncology

New knowledge is beginning to explain the decades-old question of why a treatment may work for one patient but not another. Cutting-edge technologies that allow clinicians to identify the mutations present in a patient’s tumor cells have resulted in the emerging field of precision medicine, or customized treatments based on the unique biology of an individual’s tumor. Precision medicine is an approach to disease treatment and prevention that takes into account individual variations in genes, immune function, environment, and lifestyle.

Doctors now know that each patient doesn’t just have prostate cancer, they have their own particular form of prostate cancer.

The hope is that someday, all treatment will start with genetic tests of the cancer, followed by custom treatments. Currently, there are multiple commercial tests that are approved by Medicare and select private insurance companies to better understand the aggressiveness of a tumor. Studies suggest that these tissue-based genetic tests outperform grade or stage in predicting whether a cancer is likely to metastasize. The tests are currently approved for use in select patient cases. Also on the horizon is the concept of “liquid biopsy,” where doctors can use blood tests to identify cancer mutations and treatment options.

How can you find out if you are a candidate for a precision therapy? Right now, precision medicine is an emerging field, so many treatments have limited availability. Still, a good start for anyone with metastatic, recurring, or treatment-resistant prostate cancer is to ask your doctor about precision medicine clinical trials that may be appropriate.



PCF was the first prostate cancer research organization to fund Jim Allison’s work in immunotherapy. Allison’s work on using the body’s own immune system to fight cancer earned him the 2018 Nobel Prize for Medicine.

Another exciting area of research in prostate cancer relates to the use of *immunotherapy*. Historically, the problem with curing cancer has been the uncanny ability of cancer cells to reprogram themselves after treatment and hide from the immune system. The promise behind immunotherapy is that doctors are able to program the body to be smarter than the tumor, and use the immune system to kill the cancer. Numerous ongoing clinical trials are being conducted around the world trying to optimize immunotherapy to treat prostate cancer.

Today, treatments for prostate cancer include many traditional forms of cancer therapy (surgery, radiation, and/or chemotherapy) and some forms that are very specific to the prostate (hormone therapy and precision medicines in clinical trials). Remember that all treatment regimens must be balanced against quality of life concerns, with consideration given to the potential side effects of each treatment, the aggressiveness of the cancer, and the overall life expectancy of the patient.

“My cell phone rang. It was the urologist. I stopped what I was doing and got the news. I still remember. He said, “There’s a little bit of cancer.”

— PATIENT



2 ► FOR THE NEWLY DIAGNOSED

See Appendix for 2020 COVID-19 Updates about Diagnosis.

UNDERSTANDING YOUR DIAGNOSIS

No matter the exact words used to describe the results of your prostate biopsy, a diagnosis of prostate cancer can change everything. It can be confusing, frightening, and overwhelming. It is important to remember that the word “cancer” can refer to an extremely wide spectrum of biology and that, when detected early, prostate cancer tends to be less aggressive than many other cancers.

As a newly diagnosed patient, you might be torn by arguments favoring one treatment plan over another or you may feel ill-equipped to make the decisions that are being required of you. For family members and loved ones, there can be an ache to help and to comfort, but without knowing what a man’s needs might be. One of the most important tools you have for managing your diagnosis, both physically and emotionally, is education. The information contained in the guide can help you feel satisfied that you have made an informed decision for you and your family.

DETECTION, DIAGNOSIS AND STAGING

The PSA blood test and digital rectal exam (DRE) can be used to detect prostate cancer when no symptoms are present. They can help catch the disease at an early stage when treatment is thought to be more effective and potentially has fewer side effects. It is recommended that you abstain from strenuous exercise and ejaculation for 48 hours preceding your PSA, since these may artificially inflate PSA test results.

After your PSA test, your health care provider may perform a DRE, in which a gloved, lubricated finger is inserted into the rectum to examine the prostate for any irregularities in size, shape, and texture.

During a PSA test, a small amount of blood is drawn, and the level of PSA (prostate specific antigen, a protein produced by the prostate) is measured. The majority of men have a PSA under 1 ng/mL. Historically, many physicians used a PSA of 4 as the borderline between “normal” and “abnormal.” We now realize this question is more complicated, and a high PSA doesn’t always mean

cancer. For example, in some cases, a high PSA may be due to infection or inflammation of the prostate. However, it is also important to understand that a PSA above 4 may suggest the need for more diagnostic studies such as imaging or biopsies.

A small but important proportion of men are at increased risk of prostate cancer due to carrying an inherited cancer risk gene or strong family history of cancer, and may consider prostate cancer screening at an earlier age. It is also important to recognize that PSA increases with age and screening PSA should be compared to normal values for the man’s age group if starting earlier. For example, the median PSA for younger men (age 40-49) is around 0.7 ng/mL, and men with a PSA above the median are at higher risk of later developing prostate cancer. Men with inherited genetic mutations (e.g., *BRCA2*) are at higher risk of aggressive prostate cancer.

Assessment of a “normal” PSA must take into account:

- The patient’s age
- Prostate size
- Previous PSA tests
- Other medical conditions, such as BPH or prostatitis
- Drugs that may artificially lower PSA, such as finasteride (Proscar® or Propecia®) or dutasteride (Avodart®)
- Infections and procedures involving the urinary tract that can elevate the PSA
- Use of various herbal supplements, such as saw palmetto

On the other hand, it is worth noting that in rare cases (<2%), men who have a normal PSA have clinically significant prostate cancer. Unfortunately, in most of these cases, disease does not present until it has progressed beyond the prostate and become symptomatic.

Making the Diagnosis via Biopsy

Although a high PSA may increase a doctor’s suspicion of prostate cancer, a biopsy is necessary to confirm a diagnosis. A PSA test is simply used to assess whether or not you should have further testing—usually in the form of imaging and/or biopsy to determine the presence of cancer.

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TALKING TO INSURANCE

At PCF, we're proud to be able to tell you about the latest & greatest research, but the American health care system is sometimes slow to catch up to make these advances accessible and affordable to all. It is important to speak with your insurance company directly about what is needed. Often, each cancer-related specialty (radiation, medical oncology, etc.) will have an expert on staff who is accustomed to dealing with cancer-related insurance claims. Be sure to find out if that person exists, and introduce yourself early on in this process.

If you need to talk to your insurance company about paying for a procedure that they consider to be non-standard, it's important to have on-hand the reasons why this test or procedure is critical for your health. It also helps if having the test or procedure could be so precise that it will save on future tests, procedures and other medical costs. In other words, when speaking to insurance, make sure to speak their language.

Let's take MRI fusion biopsy as an example. More evidence has been generated that performing MRI prior to prostate biopsy is useful for risk stratification and to allow targeting of the biopsy in patients with suspected prostate cancer. Urologists are putting this into practice in multiple countries. High-quality trials have shown that using the MRI images in combination (or "fused") with real-time ultrasound images more often detects higher-grade cancer and less often detects indolent non-aggressive low-grade cancer than just using traditional ultrasound-guided biopsy. The ultimate benefit to the patient is debatable, but most believe it will decrease the need for unnecessary biopsies, and if a biopsy is needed, it will be more accurate.

Sometimes, insurance companies are hesitant to pay for a prostate MRI. The key when speaking to your insurance company is to let them know that since your PSA or DRE indicates the likely presence of disease, MRI-targeted biopsy will provide a superior map of your cancer, and may save money on future testing, when compared with the (currently) standard TRUS biopsy. That said, things are changing fast and we are optimistic that MRI will be covered by insurance for all men with an indication for prostate biopsy.

There are 3 main ways men are initially diagnosed:

- 1. TRUS-guided biopsy:** A Trans-Rectal Ultrasound-guided biopsy using local anesthetic is the most common way that prostate cancer is diagnosed in the U.S.. An ultrasound probe is placed in the rectum to allow visualization of the prostate, then multiple needles are used to sample tissue from the prostate for cancer. If a patient had magnetic resonance imaging (MRI) before the biopsy, needles may be targeted into areas that looked suspicious on the MRI (the MRI itself provides useful information, but cannot diagnose prostate cancer).
- 2. Trans-perineal biopsy:** The prostate can also be biopsied under local or general anesthetic by placing a needle through the skin between the scrotum and anus (perineum).

- 3. Incidentally:** Some men are diagnosed when prostate cancer is found incidentally during an unrelated surgical procedure of the prostate or bladder.

Prostate tissue from the biopsy is then examined under a microscope by a pathologist to confirm the presence or absence of prostate cancer cells.

"Targeted" or "fusion" biopsies (sometimes referred to as an MRI fusion biopsy) are increasingly being offered at select centers that use MRI, in addition to the ultrasound, to better visualize tumors within the prostate and help guide biopsy needles to the areas that appear to be most suspicious. There is wide variation in quality of MRI; at this point in time, MRI and fusion biopsy should only be performed at a high-volume center with particular expertise in prostate MRI radiology. Research on the continued improvement of this technology continues.

PI-RADS (Prostate Imaging Reporting and Data System) is a structured reporting system for evaluating the prostate for prostate cancer based on an MRI scan. The PI-RADS score is for patients who have not yet undergone therapy. The scores are:

- PI-RADS 1: **very low**—clinically significant cancer is highly unlikely to be present
- PI-RADS 2: **low**—clinically significant cancer is unlikely to be present
- PI-RADS 3: **intermediate**—the chance of clinically significant cancer is equivocal
- PI-RADS 4: **high**—clinically significant cancer is likely to be present
- PI-RADS 5: **very high**—clinically significant cancer is highly likely to be present

In summary, PI-RADS 4 or 5 lesions have a **high probability** for disease that warrants targeted biopsy for confirmation. PI-RADS 1-3 are unlikely to represent clinically significant cancer.

As previously noted, prostate MRI is still a developing technology and is ideally performed and interpreted at academic centers or other prostate specialty centers.

Staging Your Disease

There are 5 main components to staging prostate cancer:

- Your PSA level
- The grade of your tumor (done via biopsy)
- The stage of your tumor (termed the “T-stage” for the prostate **tumor**)—for example, is the prostate cancer contained completely within the prostate?
- For some men, getting imaging to determine if the cancer has spread to lymph nodes (termed the “N-stage” for **nodes**) or bones or other organs (termed the “M-stage” for **metastasis**).
- The extent of the cancer revealed by the biopsy. For example, in a typical prostate biopsy which includes at least 12 needle core samples, a cancer found in 9 of the 12 cores is a higher risk than a cancer found in just 2 of the cores.

SIZE VS. GRADE

The size and grade of your tumor don't always predict its behavior over time. A small, high-grade cancer is much more likely to spread to other parts of the body than a large, low-grade cancer. In some cases, tumor DNA genetics and biomarkers may be better predictors of growth over time. Consult with your health care provider to find out if these options might be right for you.

1. PSA: A blood test.

Your doctor should have your most recent **PSA tests** and, if outdated, may order a fresh one. PSA can also be considered in relation to the size of the prostate, since a bigger prostate will normally make more PSA. Your **PSA density (PSAD)** score is calculated by taking your PSA score and dividing by the volume (size) of your prostate in grams or milliliters. PSAD values under 0.15 (e.g., a PSA of 7.5 for a 50-mL prostate) are usually considered reassuring.

2. Grade: How aggressive the cancer looks.

If prostate cancer is found when looking at biopsied tissue under a microscope, the pathologist assigns a grade to the cancer. There are 2 grading systems currently in use, which can be confusing for patients.

The original grading system for prostate cancer is called the Gleason score, which ranges from 6 to 10 (6 is low grade, 7 is intermediate grade, and a score of 8 to 10 is high grade).

In 2014, the World Health Organization replaced the Gleason score with the simpler Grade Group system ranging from 1 (low) to 5 (very high).

Many hospitals report both the Gleason score and the grade group, but there may be hospitals that still report only the old Gleason system.

Grade Group and Gleason Score Comparison

Risk Group	Grade Group	Gleason Score
Low	Grade Group 1	Gleason Score ≤6
Intermediate Favorable	Grade Group 2	Gleason Score 7 (3+4)
Intermediate Unfavorable	Grade Group 3	Gleason Score 7 (4+3)
High	Grade Group 4	Gleason Score 8
Very High	Grade Group 5	Gleason Score 9-10

3. Tumor staging (or T-stage): The extent of the prostate cancer.

The digital rectal exam (DRE) gives information on how extensive the prostate cancer is within the prostate area that can be palpated. In some cases, your practitioner may order a prostate MRI to give more information if the cancer extends outside the prostate. Staging is classified as follows:

- ▶ **T1:** The tumor was found solely by a biopsy done due to an elevated PSA (i.e. was not detectable by DRE or imaging) or was found incidentally during an unrelated procedure. T1 tumors can be divided into T1a-T1c subcategories, depending on how the tumor was found and its size.
- ▶ **T2:** The health care provider felt a nodule(s) on your prostate during the rectal exam. T2 tumors can be divided into T2a-T2c subcategories, depending on the tumor location and size.
- ▶ **T3:** The tumor extends out of the prostate capsule. If the tumor also extends into the seminal vesicles, this is referred to as T3b, if not, it's T3a.
- ▶ **T4:** The tumor invades into the rectum or bladder (advanced).

4. Evaluating for metastatic disease: Has the tumor spread beyond the region around the prostate?

Aggressive cancers (e.g. PSA >20, grade group 4 or 5 [Gleason score 8-10], or stage T3-4) usually warrant imaging scans to determine the presence of metastatic disease. Some men whose cancer has less aggressive features may benefit from further imaging and they should discuss this with their doctor. This is most

commonly done with a computed tomography (CT) scan or an MRI and a bone scan, although newer and more sensitive imaging technologies are in development, such as molecular PET imaging (e.g. PSMA, Axumin, Choline). It is important for your doctor to know if your cancer has spread to lymph nodes, bones or other body sites since it will influence their treatment recommendations. In the event that you are diagnosed with metastatic disease, please make sure to also read starting on page 55, [Therapies for Men with Advanced \(Recurrent or Metastatic\) Prostate Cancer](#).

5. Biopsy cores: How many were positive?

One other aspect that your physician will look at on your pathology report in addition to the grade, is the number of biopsy needle cores that contain cancer divided by the total number of cores sampled. This is referred to as **percent positive cores**. The higher the percentage, the more aggressive the disease generally. For example, if 12 biopsies were taken, and 4 were involved with cancer, then you would have 4/12, or 33% positive cores.

6. Gene expression testing

Guidelines variably support the use of testing your prostate cancer's gene expression or its RNA. Three tests exist that have been shown to potentially help provide a more accurate assessment of the aggressiveness of your cancer beyond the Gleason score, PSA, and T-stage: Decipher[®], Oncotype[®], and Prolaris[®]. Medicare usually covers the use of these tests, but private insurance payers are less likely to cover them. Ask your physician if these tests would be right for you.

GLEASON 3+3

Modern pathologists do not give a grade below Gleason 3+3 (Gleason 6, or grade group 1) when scoring prostate cancer tumors. If you have prostate cancer, the lowest Gleason score you will receive is a 6. Many, but not all, prostate cancers in this Gleason range may be slow-growing and are appropriate candidates for active surveillance. Consult your doctor or practitioner for more information.

SELECTING YOUR TREATMENT

There is no “one size fits all” approach for precise treatment of prostate cancer. For some men this feels liberating; for others, it can be confusing and frustrating.

To add to the confusion, your doctor may not recommend treatment at all (also termed observation or “watchful waiting,”) or might recommend putting you under “active surveillance,” with serial testing and a plan to offer curative treatment for the cancer only if it exhibits signs of progression. It’s important to learn as much as possible about the treatment options available and, in conjunction with your physicians, make a shared decision about what’s best for you.

Because men diagnosed with localized prostate cancer today may live for many years or decades, it is important to discuss not only cure, but also quality of life.

Your decision-making process will likely include a combination of clinical and psychological factors, including:

- ▶ The need for treatment
- ▶ Your family genetics
- ▶ Your level of risk based on biopsy and exam
- ▶ Your personal circumstances
- ▶ Your desire for a certain treatment option based on risks, benefits, and quality of life

For men who are sexually active, concerns about post-treatment potency are often top of mind. If preserving your ability to have erectile function is a priority for you, make sure to discuss this with your doctor *before* selecting a treatment plan. It is also essential to realize, however, that many interventions are available to help with sexual function both before and after prostate cancer treatment.

The vast majority of prostate cancers are diagnosed by urologists, who perform the biopsies. A urologist will typically review treatment options, and should also recommend consultation with a radiation oncologist.

FERTILITY OPTIONS

For men who are hoping to father a child in the future, it is vital to have a discussion on fertility preservation and sperm cryopreservation with your physician before you undergo any treatment. You can learn more about these issues in the Possible Side Effects: Fertility section on page 44.

For men with more aggressive disease, or metastatic disease, patients should also have a consultation with a medical oncologist and often a radiation oncologist. A multidisciplinary prostate cancer care team will give you the most comprehensive assessment of the available treatments and expected outcomes, because each physician has expertise in different areas. Many hospitals and universities have multidisciplinary prostate cancer clinics that can provide a consultation on what team of doctors might be right for you.

In general, for nearly all cases of newly diagnosed localized prostate cancer, the chance of “cure” is the same whether you have radiation therapy or surgery.

For men with metastatic disease, your doctor may now recommend genetic sequencing to determine if there is a targeted therapy for your type of disease. Talk to your doctor about whether tumor sequencing is right for you, or visit pcf.org for more information.

It is also important to remember that, often, physicians, books, blogs, and websites present only half of the story, favoring one treatment option. This leads to a great deal of misunderstanding. The best thing you can do is to read through this patient guide and make sure you seek the advice of a urologist, a radiation oncologist, and, based on the stage of your disease, a medical oncologist.

In the U.S. the 5-year survival rate for all men newly diagnosed with early stage prostate cancer is greater than 99%.

However, one treatment may be preferred for you based on the associated *side effects*. Your team of doctors will evaluate your type of prostate cancer to develop a treatment plan that may include surgery, radiation, some combination of both, or neither. The main difference between surgery and radiation therapy relates to quality of life and side effects. For many high-risk or aggressive cancers, often a combination of treatment types provides the best chance of long-term disease control. Every patient has a different cancer and different priorities in regard to what aspects of *quality of life* are the most meaningful to him, so it's important to take time to understand and process your diagnosis as well as the therapy options available to you. Remember, it is always okay to get a second opinion, whether or not treatment is needed. If possible, choose urologists, radiation oncologists, and medical oncologists at high-volume, prostate-focused cancer centers.

ASSEMBLING YOUR TEAM

Decisions about how to treat your prostate cancer can't be made in a vacuum. A new diagnosis can come with a lot of confusing information and feelings. Many aspects of this disease can affect the way you view yourself, the way you interact with others, and the way others interact with you. Yet at this chaotic time, you'll be asked to make some important decisions based on your doctors' recommendations. To help you along the way, it's prudent to work with your network of family, friends, and practitioners to align expectations and seek support as appropriate.

Doctors and Practitioners

Where possible, select a physician who specializes not just in cancer, but in the *nuances of your specific type of prostate cancer*. How do you find such a doctor? If you are newly diagnosed, start by consulting your diagnosing doctor, that is, the one who found your prostate cancer. He or she may be an expert in the field, or they may refer you to one or more doctors who are.

Other factors to consider when selecting a doctor:

- Are they affiliated with a reputable university or research hospital?

- Does their "bedside manner" align with your personality? Are they analytical? Compassionate? Do they seem interested in making you a partner in this process? Do they seem interested in what is important to you?
- Are they covered by your health insurance? If not, can you change insurance?

Remember:

- Take your time
- Get second or even third opinions if you don't feel comfortable
- Be careful of advice that seems highly opinionated, e.g. "surgery is the best" or "radiation is the best" or "eat this herb and your cancer will be cured." Avoid any health care provider who seems like he or she is "selling" something
- There are many books, websites, and blogs written by "experts" that claim their treatment is best; be cautious of these. For accurate information, use reputable websites like pcf.org and those that your doctor recommends
- Once you have committed, trust is key, but continue to be your own advocate: ask questions, do research, and remain curious

If you have a good relationship with your primary care provider, you may opt to stay in close touch about your diagnosis, treatment, and decision-making. Primary care providers can offer help to think about the big picture of your health, and can help you work through complicated decisions.

Family

Your family wants to support you. Feelings of powerlessness are a common concern around a cancer diagnosis; your loved ones want—or even need—to do something to feel like they are helping. Normally, this may feel like a fantastic offer. But after a cancer diagnosis, you may feel confused about how much support to accept, request, or reject. Keeping open channels of communication is key.

Tips for Partners, Caregivers and Adult Children

- Agree on how you will make decisions
- Get ready for changes in routine
- Understand that there could be emotions from both sides around changes in ability
- Find out how treatments may affect moods, physical ability, and urinary, bowel, or sexual function
- It is normal to experience loneliness and fear—seek out support groups for partners and caregivers, in addition to encouraging the patient to attend a support group

Tips for Young Children

- Keep children informed and treat them as part of the team
- Answer questions honestly, as age appropriate
- Be realistic but optimistic in your communications
- For older children, you might encourage them to join a support group. For younger children, consult your pediatrician or therapist for suggestions on how much information to share

Your Support Network

Outside of your immediate family, there may be many close friends and colleagues who care deeply about you, and have a strong desire to help. With friends and family who have volunteered their assistance, don't be shy about letting them know a few specific things that would be helpful to you. Examples might include rides to treatment, meals, caring for young children, or performing difficult chores during recovery. And when things feel overwhelming, don't be afraid to reach out for the support of family and friends. On the other hand, don't be shy about politely saying "no" to help you don't want, however generous. Many online resources exist for organizing volunteer resources during treatment, such as carecalendar.org or lotsahelpinghands.com.



"I needed and expected my spouse to be my advocate and help me hear the doctors. I needed my friends to listen and laugh, and not give me platitudes." – Patient

Work with your network of family, friends, and practitioners to set expectations and seek support where appropriate.

Many friends and family choose to become active in the cancer community in order to diminish the common feeling of powerlessness that can come with a loved one's cancer diagnosis. For more info on getting involved, visit pcf.org/take-action.

Doctors and Healthcare Practitioners Involved in Prostate Cancer Diagnosis and Treatment

Urologists specialize in problems affecting the urinary tract (kidney, bladder, prostate, urethra, penis, and related organs). They may treat only benign conditions (e.g. kidney stones, BPH) or may also treat cancer.

Urological Oncologists are urologists who specialize in surgery and treatments for prostate and other urological cancers.

Radiation Oncologists specialize in the use of radiation therapy to treat cancer.

Medical Oncologists specialize in treating cancer with medical therapies, such as chemotherapy, hormone therapy, and targeted therapies.

Radiologists and Nuclear Medicine Physicians specialize in interpreting imaging scans that you may have, and may also perform specialized biopsies or deliver radioactive medical therapies.

Pathologists specialize in interpreting the results from your biopsy or surgery to determine the type, extent, and grade of your cancer.

Nurse Practitioners (NPs) and Physician Associates (PA) are “physician extenders” who work closely with physicians to help you with your care. They often are the first line of response for your questions and concerns, and also manage some aspects of routine follow-up care.

Oncology Nurses administer treatment and monitor your vitals as you progress through the disease.

Dietitians and Naturopathic Doctors counsel patients on nutrition and wellness issues, including complementary medicine and mind-body awareness, related to cancer and treatment.

Physical Therapists create and execute rehabilitation programs to restore function and prevent disability following treatment.

Occupational Therapists work with patients to help them develop, recover, and improve the skills needed for daily living and working.

Genetic Counselors specialize in understanding and counseling you about inherited risks of cancer for you and your family.

Social Workers, Therapists & Counselors help patients and their families cope with the emotional, social, financial, and practical aspects of cancer.

You

Sadness, fear, sleeplessness, and anger are all normal early emotions after receiving a cancer diagnosis. Coping with these emotions isn't something you should take lightly. Seeking professional help, either from an online community, clergy, a church group, a cancer support group, or a private mental health professional isn't a sign of weakness. Taking care of your mental health is akin to the kind of psychological training that a quarterback goes through to make sure he can keep his head in the game: it's vital.

To join an online support group, please visit pcf.org/groups. For more information on counseling resources, visit cancercare.org. To find a local prostate cancer support group in your area, visit UsTOO.org.

PROCESSING YOUR DIAGNOSIS

The final decision on treatment is yours and may be informed by a variety of psychological as well as clinical factors. Sometimes this decision process can be empowering, and sometimes it can be bewildering. For example, although the first instinct may be to choose a therapy from the first provider you see who promises to eradicate the disease, you should take your time to investigate your options. Depending on the features of your cancer, and your age, overall health, and personal family circumstances, [active surveillance](#) may be the right choice for you. [Side effects](#) of each treatment are also important to consider, and only you can know what potential outcomes are acceptable to you. Regardless of which treatment you choose, it's important to observe [recommended diet and lifestyle modifications](#) from the moment you are diagnosed.



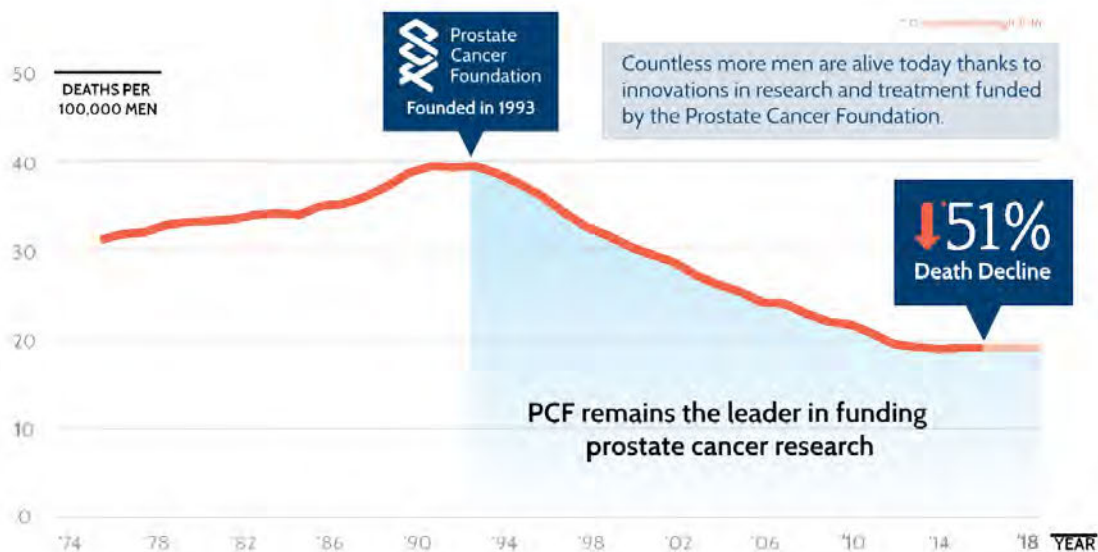
"Looking back, I wish I'd gotten more perspectives. It would have been better to really talk about all of my options." – Patient



Work with your network of family, friends, and practitioners to set expectations and seek support where appropriate.

For men who are sexually active, remember that stress can affect erectile function. In fact, a diagnosis of any type of cancer can disrupt sexual function for men and women. The maximum sexual function you could potentially regain after treatment will be based on your levels before diagnosis. Seek expert counsel for you and your partner on how to support each other through therapy and recovery.

In the end, after all of your research into different treatment types and side effects, different doctors, and different hospitals, the decision is going to come down to you. If there was one right answer that fit every man, we would tell you! The decision is very unique to each person; it may not be right for your brother, your friend, or any of the 20 other people you consulted, but it may be your best choice on the road to better health. Some people find the decision process liberating; others find it beyond their individual ability. Remember that it is okay to feel overwhelmed at first. Use this guide to begin to understand your options, but don't be afraid to rely on professionals, friends, and family to help you navigate your final treatment plan.



► TEAR-OUT SHEET: QUESTIONS TO TAKE TO YOUR DOCTOR AFTER INITIAL DIAGNOSIS

Thanks to recent advances in treatment, men who are diagnosed with prostate cancer today have many options available to them. It's important to understand the basics of prostate cancer and work with your medical team to identify what treatment options are right for you. Here are a few questions to help guide conversations with your treatment providers:

What is my PSA level? If multiple values over time have been collected, how fast has it risen, and what does this mean for me?

What is my prostate cancer grade/risk group? What does this mean in terms of our approach to my treatment?

Has my cancer spread beyond the prostate? Can it be cured?

Are there additional tests I need to have to gain the most precise understanding of the stage and aggressiveness of my cancer?

Can I avoid treatment at this time and be monitored under active surveillance? How does it work?

What treatment options exist for this stage of cancer? Which treatment do you think is better for me?

What side effects can I expect from the treatments available to me? To what extent should I worry about impotence, urinary leakage, or rectal problems, and are the risks different with different treatments?

How do my baseline urinary, sexual, or bowel function affect my treatment decisions, if at all?

When will I see a radiation oncologist and/or medical oncologist to understand all of my options? If I speak to other specialists for second opinions before making a final decision on my plan of action, how do we coordinate it?

What is the effect of the treatments on my fertility? Should I consider sperm-banking or other measures before I undergo any treatments?

What will my pre/post-surgery rehabilitation plan look like?

Is my cancer likely to come back based on what you know today?

How can I improve the success of my therapy? Are there dietary changes I need to make? What about exercise?

Should I join a clinical trial?

Remember, you want to be a partner in your own care. The more educated and proactive you are, the better. Check in at pcf.org regularly for the latest research news and changes in practice.



“A lot of men are numbers guys. They know their Gleason score down to every biopsy core. I didn’t react that way. For me, it is what it is. Every man is different.”

— PATIENT



3 ► TREATMENT OPTIONS FOR LOCALIZED OR LOCALLY ADVANCED PROSTATE CANCER

See Appendix for 2020 COVID-19 Updates about Treatment for Localized/Locally Advanced Prostate Cancer.

CHOOSING A TREATMENT OPTION

A man diagnosed with localized or locally advanced prostate cancer has 3 major treatment options: **active surveillance**, **surgery**, and **radiation therapy**. Choosing the best treatment for localized or locally advanced prostate cancer is generally based on age, the stage and grade of the cancer, the patient's general health, and an evaluation of the risks and benefits of each therapy option.

For men whose disease appears more aggressive, certain treatment combinations may be recommended. For example, radiation therapy is sometimes combined with **hormone therapy**; on the other hand, surgery is almost never combined with hormonal therapy, but may require radiation therapy after surgery.

Remember, each first-line treatment for prostate cancer carries with it different risks of **side effects**. It is critical that you ask your doctor to outline your risk for all possible outcomes of all possible treatment options before you select your path. For example, while one man might be more concerned about how fast he can get back to work, another man might be more interested in maintaining long-term erectile function or urinary continence.

THINGS TO WATCH OUT FOR

Hormonal therapy alone is not a standard treatment option for men with localized prostate cancer and should not be recommended.

Investigational treatment options for localized disease—such as **cryotherapy** and **high-intensity focused ultrasound (HIFU)**—have thus far not demonstrated the same long term success as surgery or radiation therapy in clinical trials, and both have been shown to be inferior as initial treatments. HIFU is not FDA-approved for the treatment of prostate cancer and often not covered by insurance. It is recommended that you only receive these treatments in the context of a clinical trial.

RISK GROUPS

Health care providers think about localized or locally advanced prostate cancer in terms of “risk groups,” which are assigned before the patient undergoes any treatment. There are 3 general risk groups based on the PSA, DRE, and biopsy, which can further be subdivided to better personalize treatment for each patient.

1. Low risk: Tumor confined to the prostate, the PSA is <10 and grade group 1 (Gleason 6). There is also a subset of extremely “slow-growing” tumors called “very low risk” in which fewer than 3 biopsy cores are positive, <1/50% of any core is involved with cancer, and PSA density is <0.15.

2. Intermediate risk: Tumor is confined to the prostate, the PSA is between 10 and 20, or grade group 2 or 3 (Gleason 7). This category is often divided into a “favorable” and “unfavorable” intermediate risk.

3. High risk: Tumor extends outside the prostate, the PSA is >20, or grade group 4 or 5 (Gleason 8 to 10). There is also a subset of very aggressive tumors called “very high risk” in which the tumor has extended into the seminal vesicles (T3b), or the rectum or bladder (T4), or there are multiple biopsy samples with high-grade cancer.

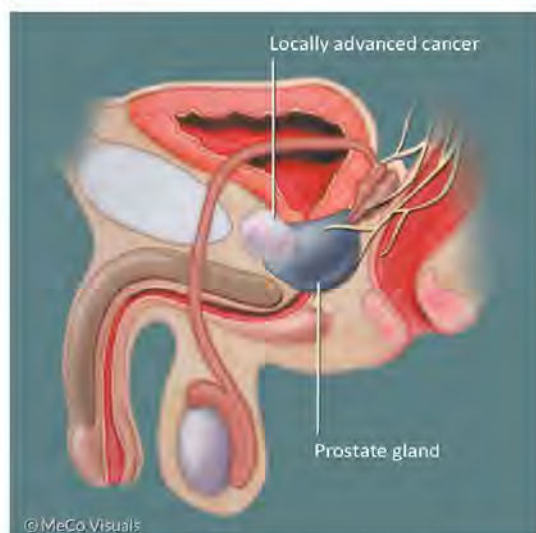
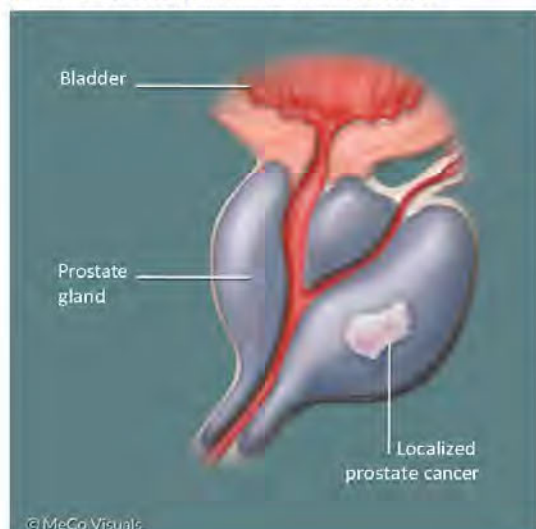
These risk groups are not perfect indicators of your risk for developing recurrent, aggressive prostate cancer. Currently, there are extensive, ongoing efforts to develop tests that can aid physicians in more accurately telling the difference between cancers that will become fatal and those that will sit in the prostate without spreading.

The treatment options for each risk group are very different and you should ask your doctor which risk group you belong to so you can better understand the most appropriate next steps.

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How are Risk Groups Determined?

Risk Group	Criteria	Treatments	Notes
Very Low			
	Grade group 1, PSAD <0.15, fewer than 3 cores are positive, and <=50% of any core is involved with cancer	Active surveillance or watchful waiting; men with a life expectancy >= 20 years may consider radiation therapy or surgery	Active surveillance is strongly recommended for nearly all men in this risk group. Immediate treatment has not been shown to help men with very low-risk disease live longer.
Low			
	T1-T2a stage Grade group 1 PSA <10 ng/mL	Active surveillance or watchful waiting, depending on age	Certain patients with higher-volume low-risk disease may be recommended definitive therapy
Intermediate			
Favorable	Any one of the following risk factors: T2b/c stage, Grade group 2, PSA 10-20 Also, must have >50% of your biopsy cores negative for cancer	Surgery Radiation therapy	Active surveillance may be appropriate for select favorable intermediate-risk men Cure rates are similar between surgery and radiation therapy
Unfavorable	Grade group 3 or Can have any two of the following risk factors: T2b/c stage, Grade group 2, PSA 10-20, >=50% of your biopsy positive for cancer	Radiation therapy + short-term hormone therapy Surgery +/- post-operative radiation therapy	Cure rates are similar between surgery +/- post-operative radiation therapy vs. radiation therapy + hormone therapy
High			
	Any one of the following risk factors: Grade group 4 or 5 T3a stage PSA >20	Radiation therapy + long-term hormone therapy Surgery +/- post-operative radiation therapy +/- hormone therapy	Cure rates appear equal between surgery + post-operative radiation therapy vs. radiation therapy + hormone therapy Post-operative radiotherapy is commonly needed after surgery for men with high-risk prostate cancer (>50% on average)
Very High			
	Any one of the following risk factors: T3b-T4 stage Primary Gleason pattern 5 >4 cores with Grade Group 4 or 5	Radiation therapy + long-term hormone therapy Surgery + post-operative radiation therapy +/- hormone therapy	The most common treatment in the U.S. and internationally for this patient subgroup is radiotherapy + hormone therapy. Very well-selected and informed men should consider surgery as part of a clinical trial, or may consider surgery in the hands of an experienced, high-volume prostate cancer surgeon with the knowledge that they likely will require additional post-operative treatment with radiotherapy and potentially hormone therapy.

Localized vs. Locally Advanced Prostate Cancer

Localized Prostate Cancer: the cancer has not spread outside the prostate.

Locally Advanced Prostate Cancer: the cancer has spread to nearby organs outside the prostate, but not to distant sites, such as lymph nodes or bones.

ACTIVE SURVEILLANCE

For men with low-risk disease who decide not to undergo immediate radical treatment for prostate cancer (radiation or surgery), active surveillance has emerged as the preferred standard of care.

Active surveillance is based on data that low-risk prostate cancer has not been shown to cause harm or decrease life expectancy. This is important because both surgery and radiation—which are the most common treatments for localized prostate cancer—can have side effects that decrease a man's quality of life.

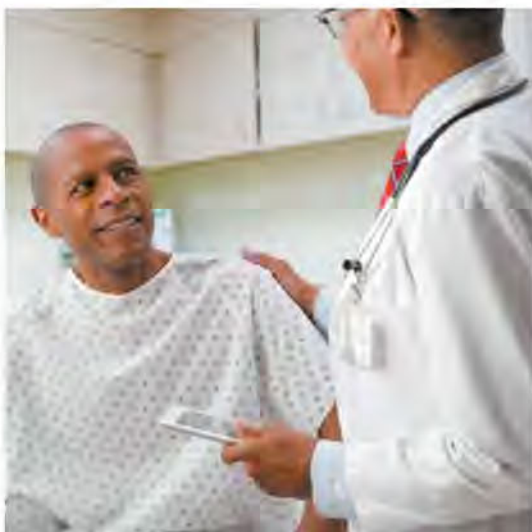
Active surveillance is not “no treatment,” but rather a strategy to follow the cancer closely so that “treatment” is deferred to only “if and when” it may be needed.

Men on active surveillance will usually have a PSA blood test done once or twice per year and a DRE annually, with repeat biopsies every 1 to 5 years. MRI is also being incorporated to help determine the timing of, and provide guidance for, the repeat biopsies.

If or when test results indicate that your cancer has begun to progress, treatment such as surgery or radiation may be warranted, and in a large majority of cases will still be curative.

Over 30% of men have prostate cancers that are so slow-growing that active surveillance is a better choice than immediate treatment because it allows them to avoid side effects from treating disease that will never cause them harm. In fact, prostate cancer is the only one of the top 10 most common types of cancer for which so many patients do not require aggressive immediate treatment.

A Johns Hopkins study found that, even after 15 years, less than 1% of men with low-risk prostate cancer who chose active surveillance developed metastatic disease. This is identical to the rate one would expect if all of these men were treated with surgery or radiation. But remember: the key to successful outcomes like these is to make sure you are monitored regularly for signs of progression.



Over 30% of men diagnosed with prostate cancer have slow-growing or “lazy” tumors that are best monitored with active surveillance vs. immediate treatment.

QUESTIONS TO ASK YOUR DOCTOR IF YOU ARE CONSIDERING ACTIVE SURVEILLANCE

- ☐ What type of testing will be required if I do active surveillance?
- ☐ How frequently will I be tested?
- ☐ What is my baseline PSA number, and what number would constitute progression?
- ☐ What are my options if a future test indicates that the disease has become aggressive?
- ☐ What are the chances that my cancer will progress in the next 10 years if I defer immediate treatment?
- ☐ How does my family history of cancer factor into this decision and the risk of progression?

The ideal candidate for active surveillance has low-risk prostate cancer.

Who Should Choose Active Surveillance?

Active surveillance may be right for you if your cancer is in grade group 1 (Gleason 3+3), PSA <10, and the cancer is confined to the prostate and/or cancer that is very low volume when biopsied (see page 30 for a full comparison of risk groups). Selected cases with low-volume grade group 2 (Gleason 3+4) tumors may also be considered for active surveillance. Sometimes commercial tests—such as Decipher[®], Oncotype DX GPS[®], and Prolaris[®]—can be used to help guide decisions about active surveillance in situations that are less clear. These tests are currently covered by Medicare and (less often) by private insurance companies, so check with your insurance provider to confirm if you are covered if your doctor recommends this test. It is always a good idea to talk with your doctor about your choices, and see if active surveillance might be right for you.

Often men wonder if they are the “right” age for active surveillance. There is no right answer to this question.

For younger men who have the potential to live for quite a long time after diagnosis, it is important to think about preserving quality of life while making sure to identify high-risk prostate cancer if it develops. A man with a less aggressive form of cancer may be able to stay on active surveillance for many years, thus delaying side effects such as urinary incontinence, erectile dysfunction and others.

For men who might have a shorter life expectancy, either because of older age or because of other medical problems, active surveillance may actually be too aggressive. For these men, watchful waiting may be more appropriate. **Watchful waiting** is a more passive strategy which avoids repeat biopsies and leads to non-curative or palliative treatments only if the cancer starts to cause symptoms. A man who is currently battling other serious disorders or diseases—such as very advanced heart disease or other cancers—should consult with his doctor about whether watchful waiting would help him avoid unnecessary treatment and would be recommended.

For everyone else, as with any treatment for prostate cancer, shared decision-making with a physician is necessary, and maintaining a healthy lifestyle is advised to maximize results.

SURGERY

Removing the entire prostate gland and seminal vesicles through surgery, known as a **radical prostatectomy**, is an option for men with intermediate or high-risk cancer that has not spread.

Open radical prostatectomy is the traditional way of surgically removing the prostate. In this procedure, the surgeon makes an incision in the lower abdomen in order to remove the prostate. The prostate may also be removed through the perineum, the area between the scrotum and the anus, although this technique is very uncommon.

In the last 10 years, **robot-assisted laparoscopic radical prostatectomy** has become very popular in the United States. This method requires small incisions to be made in the abdomen. A surgical robot's arms are then inserted into the incisions. With a robotic interface, the surgeon controls the robot's arms, which in turn control cameras and surgical instruments.

Compared with open surgery, robot-assisted surgery is associated with less bleeding, a bit less pain, fewer short-term complications, and equivalent cancer cure rates. Preservation of urinary and sexual function recovery depends more on the surgeon's skill and patient factors than which method of surgery is chosen.

SURGICAL MARGINS

After your doctor removes the prostate, a pathologist will examine the cells under the microscope. A final grade and stage will be determined at this point.

Your margins are **clear** if no cancer cells are seen at the outer edge of the tissue that was removed.

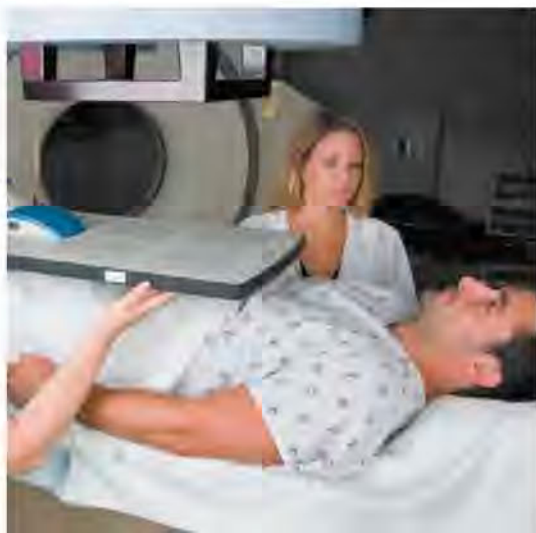
The margins are **positive** if the cancer extends all the way to the edge of the tissue that was removed.

Positive margins can imply that some cancer was left behind, and can be used to help determine the need for radiation therapy. But a positive margin isn't always a cause for alarm, especially in lower-grade cancers.

Patients with other problematic pathology features at surgery (e.g. extension of cancer beyond the capsule or invasion of the seminal vesicles or lymph nodes) may require additional treatments such as radiation and/or hormonal therapy. These decisions are usually made after the first PSA is checked 6 to 8 weeks after surgery.

Remember: make sure to request a copy of your pathology report; ask your doctor to explain it and to discuss options based on your results.

Whether open or laparoscopic/robotic surgery is chosen, patients typically go home after an overnight stay in the hospital with a bladder catheter to help drain urine for 7 to 14 days. For a full discussion of side effects including those after surgery, see page 42. Of note, men with BPH symptoms (such as urinary frequency or urgency or a weak urine stream) may experience improvement in these symptoms after surgery.



There are many different types of radiation therapy available today. Be sure to use this guide to talk to your physician about which option might be best for your prostate cancer.

There are three other second-line therapies that may be given in conjunction with surgery, based on your pathology report:

- **Adjuvant radiation therapy** may be given to men with **high-risk** prostate cancer who have cancer that has penetrated through the prostate capsule, into the seminal vesicles, and/or who have positive margins after surgery. This may reduce the risk of recurrence, but may also increase the risk of side effects. Many, but not all men, often can safely avoid adjuvant radiation therapy, and closely monitor their PSA to determine if they will need early salvage radiation therapy. You should discuss with your doctor the risks and benefits of radiation therapy once your pathology report is available.
- Another strategy is to use radiation only if PSA levels rise; this is referred to as **salvage radiation**, which should be done soon after the first PSA becomes detectable. Hormone therapy may be given along with the radiation therapy. Genomic tests have been developed that may

help you and your doctor decide if you would benefit from immediate radiation therapy instead of waiting to see if the PSA rises.

- Hormone therapy may also be recommended for men who have cancer found in their lymph nodes at the time of surgery; in this context, hormone therapy after surgery has been shown to help patients live longer.

Keep in mind that new treatment protocols are constantly improving, and you can always discuss with your doctor your eligibility to enroll in a **clinical trial** for patients who have had a prostatectomy.

RADIATION

Radiation involves the precise killing of cancer cells with ionizing radiation or photons. Radiation damages the cancer cells' **DNA** (the genetic material of the cancer cell), leaving them unable to survive, grow, or spread; subsequently, the cancer cells die. Radiation therapy, like **surgery**, is very effective at killing localized or locally advanced prostate cancer and has the same cure rate as surgery. Recent evidence suggests that radiation may also help men with metastatic disease live longer, and is discussed on page 56.

Just as surgical skill can play an important role in determining outcomes from prostatectomy, the technical skill of your radiation oncologist can play an important role in radiation outcomes. When choosing a radiation oncologist, at a minimum, make sure he or she has broad experience with an assortment of approaches and can objectively help you decide on the best course of treatment. Ideally, seek a radiation oncologist who specializes in the treatment of prostate cancer.

External Beam Radiation Therapy (EBRT)

EBRT is the most common type of radiation therapy. In EBRT, CT scans with or without MRIs are used to map out the location of the tumor cells, and X-rays are targeted to those areas. Your "mapping" scan will help your radiation oncologist to locate the precise anatomy

of your prostate, rectum, and bladder so that radiation technicians and physicists can work with sophisticated computer treatment systems to design a personalized radiation plan for you. There are many types of EBRT, each with its own advantages and disadvantages (see inset on the right).

Regardless of the form of external radiation therapy, it is done on an outpatient basis.

Since it is non-invasive, there is no down time or healing time. You can be physically and sexually active every day of treatment and in the months following. It is common to have mild increased frequency of urination or bowel movements during the weeks of treatment; 2 weeks after treatment completes, these symptoms generally begin to improve, though as with any treatment, a small percentage of men can have persistent problems with urinary and/or bowel function.

Most studies have shown that while surgery results in a more immediate loss of erectile function followed by a period of partial recovery, radiation therapy results in less erectile dysfunction, and for that those that do have erectile side effects, it develops more slowly. For more details, see [Possible Side Effects: Sexual Function](#) on page 44.

Treatment Durations

There are 3 common treatment durations, or number of treatments, that are used in EBRT:

- ▶ **Conventional:** For decades, radiation therapy has been delivered every day (Monday through Friday), for a total of 40 to 45 treatments over 8 to 9 weeks.
- ▶ **Moderate hypofractionation:** Recently, [clinical trials](#) that have shown that as few as 20 treatments in 4 weeks can have similar cure rates and side effects as conventional radiation over 8 to 9 weeks. In hypofractionation, the doses given each day are higher than conventional dose levels. This is considered by national guidelines to be the current standard of care for many men with localized prostate cancer.

EBRT Types

3D conformal radiotherapy is a form of radiation therapy that targets the tumor effectively, but also affects a small amount of healthy tissue (such as the rectum or bladder). For this reason 3D conformal radiation therapy is less favored today over more modern techniques that result in very low side effects.

Intensity-modulated radiation therapy (IMRT) uses the power of modern computers and complex computer algorithms to modulate and shape the intensity of the doses and radiation beams in order to better target the radiation delivered to the prostate, while simultaneously delivering lower doses to the bladder and rectal tissue. This treatment is usually delivered in 20 to 44 treatments.

Image-guided radiation therapy (IGRT) is a form of IMRT, but is even more accurate. IGRT utilizes multiple ways to ensure that the tumor (and not the surrounding tissue) is being treated with high doses of radiation. These methods include placing gold markers or electromagnetic beacons that track radiation into the prostate.

Stereotactic body radiation therapy (SBRT) is a form of IGRT. However, what is unique is that treatment is given in just 5 treatments instead of the usual 20 to 44 treatments with classical IMRT/IGRT. SBRT is one of the newer forms of radiation therapy and it is not yet available at all treatment centers. Studies have shown it to be safe, just as effective, and have very low side effects, similar to the longer course of 9 weeks of radiation therapy. Talk to your doctor for more information.

► **Ultra-hypofractionation:** This is another name for SBRT, or treatment delivered in about 5 treatments. These doses are even higher than hypofractionated doses. This strategy is rapidly becoming more common because it has lower side effects, equal cure rates, and increased convenience. At many centers of excellence this is the standard of care. However, not all centers can safely provide this treatment, and not all patients are good candidates, so make sure to consult your doctor. This type of radiation has been compared head-to-head with the traditional 8 to 9 week course of radiation and shown to have similar cure rates and side effects. Ongoing trials are assessing if it is superior to surgery.

Brachytherapy

Brachytherapy involves an invasive procedure under anesthesia to place radiation therapy “seeds” or temporary catheters inside the prostate that emit radiation at a very short distance.

Think of it as internal radiation therapy, rather than external radiation therapy. Radioactive seeds (LDR or low dose rate) or catheters (HDR or high dose rate) are inserted directly into the prostate while you are asleep under anesthesia. It is usually done in 1 to 4 treatment sessions depending on the method used. The seeds are permanently placed into your prostate, while the catheters are only temporarily placed inside the prostate and then removed after treatment is done. LDR brachytherapy kills the cancer over many months as the seeds give off radiation to the immediate surrounding area, thus killing the prostate cancer cells. By the end of the year, the radioactive material degrades, and the seeds that remain are harmless.

Brachytherapy by itself is usually used only for low-risk or favorable intermediate-risk patients. It is usually combined with some form of external beam radiation and often hormone therapy for higher-risk patients. The success of brachytherapy, like surgery, is dependent on the skill of your practitioner. Ask your doctor to help you find an experienced radiation oncology team who can perform brachytherapy.

As the use of IGRT and SBRT have increased, brachytherapy is now less commonly used, but some patients prefer it because it doesn’t require daily visits to the treatment center. Although brachytherapy can deliver very high doses of radiation, it also has been shown to have higher rates of side effects in recent trials compared to EBRT. Brachytherapy has been shown to increase urinary side effects by about 3-fold compared with external beam radiation therapy, and might also have worse rectal side effects. Side effects from brachytherapy can include erectile dysfunction, urinary frequency, urinary obstruction with need for catheter use, and rectal injury with bleeding. Patients who have large prostates or those patients with a lot of urinary problems are usually poor candidates for brachytherapy. Additionally, patients will need to speak with their doctor regarding restrictions for holding infants in their lap after the procedure.

Hormone Therapy with Radiation

Hormone therapy is often given together with radiation therapy for localized disease (note: it is also used alone or in combination with other treatments for men with metastatic prostate cancer).

Hormone therapy usually consists of a shot that lowers your testosterone, given every 1 to 6 months, depending on the formulation, and sometimes a daily pill that blocks testosterone from reaching the cancer cells. Clinical trials show a benefit in patients who receive hormonal treatment with radiation therapy. Hormone therapy has been shown to improve cure rates of prostate cancer for men receiving radiation therapy and is part of the standard of care for men with certain types of intermediate-risk prostate cancer and nearly all high-risk prostate cancer. It is often given for intermediate-risk cancer for 4 to 6 months (called short-term hormone therapy), and for 1.5 to 2 years in men with high-risk localized prostate cancer.

Hormone therapy should not be given to men with low-risk prostate cancer and is not a standalone treatment for localized prostate cancer in any risk category.

COMPARING SURGERY AND RADIATION

In general, for nearly all cases of newly diagnosed localized prostate cancer, the chance of “cure” is the same whether you have radiation therapy or surgery.

The main difference between surgery and radiation therapy relates to quality of life and side effects. Every patient has different priorities in regards to what aspects of quality of life mean most to them, so it's important to take time to understand and process your diagnosis as well as the therapy options available to you.

One treatment may be preferred for you based on the associated side effect profile, and your team of doctors will evaluate your type of prostate cancer and develop a treatment plan that may include radiation without surgery, surgery without radiation, some combination of both, or neither. In some cases, hormonal therapy is added.

EXPERIMENTAL THERAPIES FOR LOCALIZED PROSTATE CANCER

Surgery and radiation therapy remain the standard treatment for localized prostate cancer, but other emerging treatment options have recently become available. As time goes on and the benefits of these treatment options are better understood, it's possible that they may be reasonable alternatives for certain patients.

For now, none of these are seen as standard treatment for localized prostate cancer because they lack support from randomized clinical investigations in comparison with radiation or surgery.

FOCAL THERAPY

“Focal” therapies are treatments that target just a region of the prostate thought to have the tumor, instead of treating the entire prostate gland. None of these therapies have yet been proven to have the same long-term success as surgery or radiation therapy in clinical trials, and are still considered experimental treatments. The likelihood of recurrence is high with focal therapy due to the fact that in over 60% of cases prostate cancer is actually “multi-focal,” meaning even if the biopsy and/or MRI showed the cancer to be in only one area, there is likely tumor in many areas of the prostate.

Cryotherapy

Cryotherapy, also known as cryosurgery or cryoablation, has been around for years, but is rarely used. With this approach, probes are inserted into the prostate through the perineum (the space between the scrotum and the anus), and argon gas or liquid nitrogen is delivered to the prostate, literally freezing the prostate cells to death.

Over the years, a number of modifications were made to avoid freezing damage to the nearby structures, but the rates for both erectile and urinary dysfunction remain high when it is applied to the entire prostate, and data on long-term outcomes are still limited.

There is also investigation into treating only a portion of the prostate with cryotherapy, a type of treatment referred to as “focal therapy.”

Cryotherapy is also used as a secondary local therapy in men who underwent radiation therapy as initial treatment for localized prostate cancer. Side effects of this therapy include further urinary or sexual problems such as pain in urination (caused by scar tissue), erectile dysfunction, and an urgent need to urinate. Cryotherapy can result in injury to surrounding tissues such as the rectum or bladder, given the proximity of these structures to the prostate bed.



Be an informed patient: investigate all choices that apply to your cancer, compare treatment options and side effects, and discuss decisions with your family as appropriate.

Proton Beam Radiotherapy

Protons are similar to photons (traditional x-ray radiotherapy) in many ways. However, proton beam therapy has not been shown to improve cure rates or quality-of-life outcomes over other forms of radiation therapy, and may actually increase side effects. There have been no completed head-to-head trials comparing proton beam radiotherapy to either surgery or traditional x-ray (photon) beam radiotherapy. **Proton beam radiotherapy is often viewed as an experimental or unproven treatment for prostate cancer.** Insurance companies often do not cover it (unless you are participating in a research study) and it is typically very expensive.

High Intensity Focused Ultrasound (HIFU)

HIFU has been recently approved by the FDA for prostate tissue ablation, **but is not FDA-approved for the treatment of prostate cancer, and is thus experimental.**

HIFU works exactly the opposite of cryotherapy: with HIFU, the prostate cells are heated to death. A probe is inserted into the rectum, from which very high-intensity ultrasound waves are delivered to the target area. Although this technique remains experimental in the United States, it has been used in Europe for a number of years. Side effects of HIFU are similar to those discussed above for cryotherapy and depend on the skill and experience of the surgeon using this technique. Serious side effects have also occurred after HIFU, despite it being “focal.” Most of the published literature has demonstrated relatively high recurrence rates with HIFU, and we are still learning how best to optimize and deliver this treatment.

Using HIFU to treat only the portions of the prostate thought to be cancerous instead of the entire prostate gland is an area that is being investigated.

Primary Hormone Therapy

Since testosterone serves as the main fuel for prostate cancer cell growth, it is a common target for treatment. **Hormone therapy**, also known as **androgen-deprivation therapy or ADT**, is designed to stop testosterone from being released or to prevent it from acting on the prostate cells.

Although ADT has always played an important role in men with advanced metastatic prostate cancer, it is also increasingly being used in combination with radiation therapy because studies have shown that this combination increases long term survival.

There is data to show that **hormone therapy alone is not an effective treatment strategy for men with localized prostate cancer.** Multiple large studies with very long follow-up have shown that survival is worse with hormone therapy alone compared with hormone therapy with radiation therapy. There are certain rare situations in which the other illnesses that a patient has, a patient’s overall health status, or advanced age may make the use of ADT alone a consideration, but this is the exception rather than the rule.

► **WORKSHEET: LOCAL OR LOCALLY ADVANCED PROSTATE CANCER**

If you're a numbers guy, here's a place for you to record where you were at the time of initial diagnosis, and any notes from your doctor or outstanding questions about treatment options.

Age at diagnosis: _____

PSA #1: _____ Date: _____

PSA #2: _____ Date: _____

Grade: _____ Stage: _____

Number of positive cores in biopsy: _____

Sexual Health Inventory for Men (SHIM) score before treatment: _____
(Go to pcf.org/SHIM to find your score)

Notes/questions about treatment options:

This image shows a single page of white paper with horizontal blue lines, resembling notebook paper. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.

“I’m going to do everything I can do at
each stage. Nothing heroic. Just whatever
I can, I do.”

— PATIENT



4 ► LIVING WITH AND AFTER PROSTATE CANCER

See Appendix for 2020 COVID-19 Updates.

IN TREATMENT: WHAT TO EXPECT

Mental Health

Your state of mind has played, and will continue to play, a critical role in your cancer journey. From staying positive to controlling your diet and exercise routine, your overall mental health is a cornerstone in the ongoing treatment and control of your disease.

Just as with your diagnosis, and regardless of which treatment option you choose, you may experience difficult feelings about your situation.

New feelings about treatment are normal. Remember, you do not have to face this alone.

Living with prostate cancer can affect the way you view yourself and it can affect your interactions with the world around you. As always, it's important to check in with yourself and seek help from [your team](#) of doctors, friends and family. Many patients choose to proactively attend support groups with other patients, or begin working with a mental health practitioner. Others feel more comfortable connecting one-on-one with another prostate cancer survivor. Everyone is different in terms of what he needs and how these needs can best be met. The most important thing is to prioritize yourself and reach out in ways that will work for you. Check with the hospital or cancer center where you received treatment for referrals to counseling services, often free, for patients living with prostate cancer.

Maximizing Quality of Life

As a man with prostate cancer, you may have significant concerns about the side effects of treatment. It is important to communicate with your doctor about your questions and concerns, both when choosing between treatment options, and when undergoing treatment. Find out from your treatment team whether they have recommendations for ways to modify behavior that can reduce or help you avoid specific side effects.

There are many misunderstandings about how often side effects may occur, how severe they really are or should be, and what can be done to manage them and

counteract their occurrence. Many of the side effects that men fear most following local treatment are less frequent and severe than they have been historically. This is due to:

- Technical advances in both surgery and radiation therapy
- Researchers persistently seeking new ways to help overcome side effects
- Improvements in treatment delivery methods

It's still important to understand how and why these effects occur, and to learn how you can minimize their impact on your daily life. It is important to have frank conversations with your doctors about the complications you most want to avoid, and consider treatment options in terms of the likelihood of the risks of these complications.

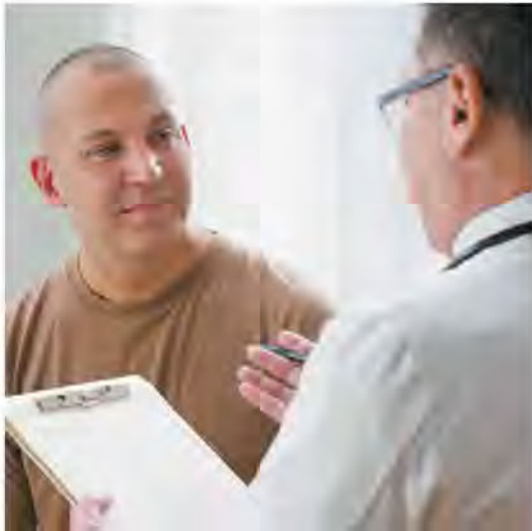
Early management of side effects has been shown to help patients live longer, better lives.

It is extremely important that you communicate with your doctors about the side effects that you are experiencing as you undergo treatment. Ongoing and proactive communication will enable your doctor to manage your side effects as early as possible to prevent worsening or development of downstream complications.

STATINS

Statins are widely used to lower cholesterol. One large longitudinal study in Denmark has concluded that men with prostate cancer who are on statins live longer than men with prostate cancer who are not on statins. If you are on a statin, you should talk to your doctor about staying on it during your prostate cancer treatment. Statins have been associated with a 17% reduction in death from prostate cancer. At present, more research is needed on the value of statins in prostate cancer survival, but the bottom line is: if you're already on statins, stay on them during treatment. Statins include: atorvastatin (Lipitor®), fluvastatin (Lescol®), lovastatin (Mevacor®, Altacor®), pravastatin (Pravachol®), rosuvastatin (Crestor®), simvastatin (Zocor®), and pitavastatin (Livalo®).

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When choosing a treatment option that is right for you, talk carefully with your doctor about which side effects are most tolerable for your lifestyle.

For resources surrounding mental and physical side effects from treatment, Us TOO is a non-profit organization providing local peer-to-peer support groups.

Monitoring for Recurrence

After initial treatment for localized or locally-advanced prostate cancer is complete, the next phase in the process is monitoring for a **recurrence**, or a regrowth of the cancer cells somewhere in your body. Monitoring for recurrence typically involves PSA testing, which is repeated every 3 to 6 months for the first 3 to 5 years, then yearly from that time on. If your PSA starts to rise, it could be a sign of your cancer returning, or it could be a sign of something else. The section on *What to Do If Your PSA Starts to Rise* (page 51) discusses all of the things that you should know about if this happens.

POSSIBLE SIDE EFFECTS

Because the prostate is close to several vital structures, prostate cancer and its treatments can disrupt normal urinary, bowel, and sexual functioning.

This section discusses side effects that might be experienced following surgery or radiation therapy for localized or locally advanced prostate cancer. For side effects related to advanced or metastatic prostate cancer, see *Side Effects from Treatments for Advanced Prostate Cancer* (page 65). Remember, before choosing any treatment, discuss worst-case possibilities of side effects with your doctor.

Prostate cancer grows over years and decades, and requires a long-term perspective when you make treatment decisions. You should focus on long-term cure and quality-of-life outcomes rather than short-term “invasiveness.”

Urinary Function

Under normal circumstances, the **urinary sphincters** (bands of muscle at the base of the bladder and at the base of the prostate) remain tightly shut, preventing urine that’s stored in the bladder from leaking out. During urination, the sphincters are relaxed and the urine flows from the bladder through the urethra and out of the body.

In **prostatectomy**—the surgical removal of the prostate—the bladder is pulled downward and connected to the urethra at the point where the prostate once sat. If the sphincter at the base of the bladder is damaged during this process, urinary incontinence or leakage may occur. Nearly all men will have some form of leakage immediately after the surgery, but this will improve over time and with strengthening exercises. The majority of men regain urinary control within a year; approximately 1 in 5 men will have mild leakage requiring the use

of one or more pads per day. This rate depends on patient factors (older age and obesity are risk factors for worse urinary incontinence) and surgeon factors (more experienced surgeons typically have better outcomes.)

Pelvic floor muscle training with a physical therapist can help. In the case that incontinence persists past a year, a **urethral sling** or **artificial urinary sphincter** can potentially correct the leakage. Men with obstruction from BPH can expect their urinary stream to improve substantially after surgery.

Radiation therapy is targeted to the prostate. Advanced technology directs the dose of radiation away from the bladder and rectum. The urethra runs through the middle of the prostate, so it will receive radiation, but fortunately the urethra is very resistant to radiation therapy, and long-term urinary leakage is rare (less than 1 in 100). However, it can become irritated during and for months after radiation therapy, which usually manifests as a mild increase in urinary frequency and urgency. This can also cause **nocturia**, or waking up more at night to urinate.

Bowel Function

Solid waste that is excreted from the body moves slowly down the intestines, and, under normal circumstances, the resultant stool passes through the rectum and then exits via the anus. Damage to the rectum can result in bowel problems, including rectal bleeding, diarrhea, or urgency.

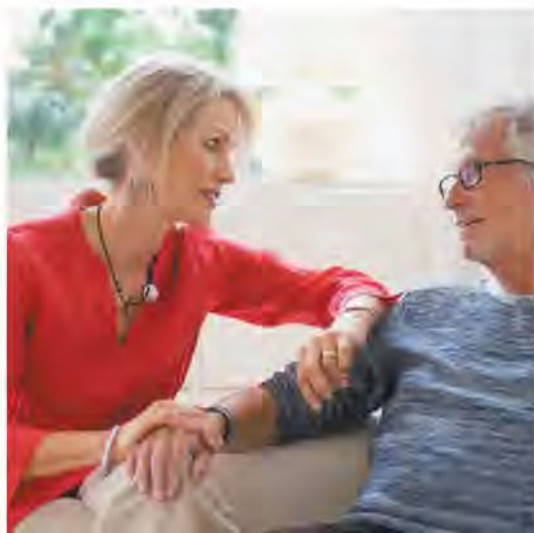
In **prostatectomy** it is very rare (less than 1%) for men to have altered bowel function after surgery. In rare cases of locally advanced prostate cancer where the cancer invades the rectum, surgery may result in rectal damage, but it isn't often used in these types of cases.

SURGERY VS. RADIATION THERAPY: MORE TO THINK ABOUT

The truth is that today, well-selected patients can expect good long-term urinary and bowel function after either surgery or radiation therapy—as long as the treatment is done by experienced, high-volume physicians working in centers of excellence. Surgery causes more urinary incontinence (leakage) than radiation, and has more early impact on erection function. Radiation causes more urinary and bowel irritation, and can have a delayed impact on erection function. Erectile function can be more variable, even in the best hands.

Since the rectum sits right behind the prostate, it may also receive some radiation during treatment. With modern **radiation therapy** (IMRT or IGRT), it is very rare to have moderate or severe bowel problems (1-3%), and with the use of a **rectal spacer** (see below) this rate is reduced to near 0%. During **radiation therapy** you may experience softer stools or diarrhea (less than 10%). These symptoms typically resolve within a few weeks of completing radiation therapy. With modern radiation, only 2% of men will have bothersome rectal bleeding that may occur months or years after treatment, and with a rectal spacer this rate is reduced to less than 1%. Be sure to discuss with your doctor the types of radiation therapy that are appropriate for you, as older forms of radiation therapy (called 3D conformal) can increase rectal side effects significantly.

Since 2016, the FDA has approved a new device, called a rectal gel or spacer (SpaceOAR) to further reduce rectal side effects of radiation therapy. In a randomized trial it was shown that the rectal spacer reduces bothersome rectal side effects to 0%. Ask your physician if they offer SpaceOAR at their practice and if your insurance covers it.



Although some erectile function may be lost in some patients during treatment, many options exist for managing side effects (see inset on page 46).

If you are hoping to father a child in the future, discuss fertility preservation and sperm cryopreservation with your physician before you undergo any treatment.

Sexual Function

Regardless of whether the nerves were spared during surgery or whether the most precise dose planning was used during radiation therapy, **erectile dysfunction** remains the most common side effect after treatment. This is because the nerves and blood vessels that control the physical aspect of an erection are incredibly delicate, and any trauma to the area can result in changes. Other less common, treatable side effects that can influence function include scarring in the penis (Peyronie syndrome) and climacturia (releasing a small amount of urine during ejaculation). Fortunately, beyond short-term side effects, there is also room for great optimism: many excellent treatments for managing erectile function (see inset on page 46) exist on the market today.

In fact, within 1 to 2 years after treatment, most men with intact nerves will see a substantial improvement. However, modern studies have shown that overall about 40% of men lose erectile function after surgery. The skill of your surgeon or physician can have a significant impact on this outcome, so it is very important to select **your team** carefully. Likewise, men with baseline erectile dysfunction and/or other diseases or disorders that impair the ability to maintain an erection, such as diabetes or vascular problems, will have a more difficult time returning to pre-treatment function. It's important to remember that your maximum functionality after treatment can only be as good as it was before treatment. The best predictor of how you will be after treatment is how healthy you were going into treatment.

Fertility

After any of the most common prostate cancer treatments—surgery, radiation therapy, or hormone therapy—you are unlikely to be fertile. As part of the surgical removal of the prostate, the seminal vesicles and part of the vas deferens are removed, disrupting the connection to the testes. Orgasm may still occur (without ejaculation) but natural conception will not be possible. Radiation similarly destroys the prostate and seminal vesicles; chemotherapy and hormone therapy are both harmful to sperm production.

Four main components of erectile function may be affected by prostate cancer treatment:

1. **Libido (sex drive)** is most commonly affected by **hormone therapy**, or treatment that decreases your testosterone. You can have a low libido and still obtain an erection, but it is usually more difficult for men who have less interest in sex. This will return once your testosterone returns to normal after completing hormone therapy. Loss of libido can be a major concern for some patients and/or their partners and much less of an issue for others. Diagnosis and treatment can bring about complex feelings that include sadness, anger, and anxiety. These are normal feelings that, when unmanaged, can likewise compromise your sex drive; don't be shy about seeking individual or couples counseling during treatment.
2. **Mechanical ability** is the ability to achieve a firm erection. It is controlled by the nerves and vessels that are intimately associated with the prostate and structures near the penis. Mechanical ability is most affected by surgery or radiation therapy.
3. **Orgasm/climax** can be more difficult after treatment, especially if libido is low or your erections are not as firm as they used to be. Also, sometimes there can be some discomfort initially after treatment when you climax. This usually is transient and will resolve. It is important to distinguish orgasm from ejaculation, as men will continue to have the pleasure sensation of orgasm without ejaculation.
4. **The quantity of ejaculate** may be minimal after treatment. The prostate and seminal vesicles which function to produce ejaculate are removed and/or irradiated during treatment, so it is common to have minimal or no ejaculate afterwards. So although you may be able to have an erection and reach an orgasm, nothing may come out. Initially, after surgery primarily, you may ejaculate blood, which will improve over time.

Prostatectomy: Since the 1980s, most men with localized disease are treated with what is termed a "nerve-sparing" prostatectomy. The goal of the procedure is to take the prostate and seminal vesicles out while sparing the nerves adjacent to the prostate. Studies have shown that approximately 50-60% of men who have the ability to have an erection before surgery will maintain this ability long-term. This number varies tremendously with surgeon expertise, and can increase or decrease based on age, obesity, and the ability to spare the nerves. In general, men with lower-risk prostate cancer have higher than average rates of erectile function, given it is easier to spare the nerves. In contrast, it is more challenging to spare the nerves in high-risk prostate cancer, since the tumor may have invaded more tissue—leading to erectile function rates that are lower than average. If you receive radiation therapy after surgery your likelihood of erectile dysfunction will increase, since you are being exposed to the cumulative side effects of both treatments.

Radiation therapy: Similar to surgery, damage to blood vessels and nerves after radiation therapy can result in decreased erectile function over time. In general, radiation therapy has less of an impact on erectile function in the first 5 to 10 years after treatment compared with surgery, and approximately 70% of men who have baseline erectile function before treatment will keep erectile function after treatment. However, radiation therapy has a slower delay in erectile function decline than surgery; within 15 years after treatment, the rates are similar to those who underwent surgery.

In the long run, these rates do not appear to be affected by the use of short-term (4 to 6 months) hormone therapy, but are more likely to be affected by the use of long-term (18 to 36 months) hormone therapy.

Newer techniques in radiation therapy, termed "vessel-sparing" radiation therapy, have shown promising results for improving the preservation of erectile function, with close to 80% of men maintaining baseline function. This technique is being tested in an ongoing randomized trial. Ask your radiation oncologist about vessel-sparing radiation therapy.

Management of Erectile Function

Oral medications such as sildenafil (Viagra®), tadalafil (Cialis®), and vardenafil (Levitra®)—a class of drugs known collectively as **PDE5 inhibitors**—relax the arteries in the penis, allowing blood to rapidly flow in. About 75% of men who undergo nerve-sparing prostatectomy or more precise forms of radiation therapy have reported successfully achieving erections after using these drugs. Consult your doctor to see if these medications might be right for you. Individuals taking medicines that contain nitrates, such as those for angina or heart problems, may not be candidates for these medications.

Alprostadil (MUSE®) is a medicated pellet about half the size of a grain of rice that is inserted into the urethra through the opening at the tip of the penis. Like oral medications, it also stimulates blood flow into the penis. About 40% of men have reported successfully achieving erections after using this drug, but the results are often inconsistent.

Alprostadil (Caverject®) uses the same drug that is in the MUSE pellets, but is delivered via an injection directly into the penis. Although nearly 90% of men using Caverject reported erections about 6 months after therapy, many men have a concern about injecting themselves regularly, so for this reason the treatment is sometimes used only after other approaches have not worked. However, it is one of the most consistently effective options after prostate cancer treatment.

Mechanical devices may be a solution for those unwilling or unable to use any form of medication to help improve erectile function, or as an adjunct to medications. The vacuum constriction device, or vacuum pump, creates an erection mechanically, by forcing blood into the penis using a vacuum seal. Because the blood starts to flow back out once the vacuum seal is broken, a rubber ring is rolled onto the base of the penis, constricting it sufficiently so that the blood does not escape. About 80% of men find this device successful, but it, too, has a high drop-out rate. Note that the constriction ring at the base of the penis is effectively cutting off fresh circulation. Because of this effect, it is crucial that the ring be removed immediately after intercourse, or the tissue can be damaged due to lack of blood flow.

A surgically inserted penile implant can be up to 100% effective, and about 90% of men remain satisfied with their implants even after 10 years. The implant consists of a narrow, flexible plastic tube, a small balloon-like structure and a release button. The penis remains flaccid until an erection is desired, at which point the release button is pressed and fluid from the balloon fills the plastic tube, pulling the penis up and creating an erection. Note that the surgical procedure is done under general anesthesia, so this option is not available to men who are not considered good candidates for surgery because of other health reasons.

WHAT'S ON THE ED TREATMENT HORIZON?

Neuro-protection therapies: We know that trauma to the body can cause tissue damage both in and around the trauma site. Fortunately, with prostate cancer surgery we know when the trauma is going to take place, and we know exactly what tissue area will be affected (unlike, say, in the case of a stroke). Therefore, researchers are looking into what preventative action we can take to strengthen and preserve the nerves around the penis before surgery.

Neuro-modulation therapy: Scientists are also using **regeneration biology**—e.g. using natural tissues like stem cells, umbilical tissues, and growth factors—to deliver protection before during and after surgery. Treatments like these have been successfully used in colorectal cancer and are now being applied to prostate cancer.

REMEMBER: ERECTILE DYSFUNCTION IS NOT A DISEASE STATE. IT'S NOT A DISEASE YOU HAVE GOTTEN. IT'S A SIDE EFFECT THAT CAN BE MANAGED.

Great strides have been made in the field of erectile dysfunction in the last 20-30 years. If you were a prostate cancer patient in the 1980s, your option was to take a single oral medication or get a penile prosthesis. Today, patients and doctors can choose between oral medications, injectable therapies, vacuum devices, penile prostheses, and erection-inducing suppositories.

In 2020, the name of the game for patients is **shared decision-making**. In 2018, the American Urological Association released 25 new guidelines for diagnosis and treatment of erectile dysfunction ranging from evaluation to diagnosis and treatment. The recommendations indicate that men should be informed of all options that are not contraindicated (e.g. harmful to their health); previously, some treatments were seen as first-line defense and others as second-line, regardless of the personal goals and characteristics of the patient.

In the recent past, oral medications such as Viagra®, Levitra®, Cialis®, or Stendra® were considered “first line of defense” for treatment. But now we appreciate that some men’s situation may dictate a better starting point. Here are two examples. If you are a man who had nerve-sparing surgery and you were potent before surgery, oral medications may be a great

starting point for you. On the other hand, if you are a man who had compromised erectile function before surgery (for any number of reasons), and your nerves were not spared during surgery, you may opt to start with a mechanical prosthesis. But here’s the thing that might be both frustrating and liberating: there’s no right answer we can give you as to which treatment fits you. It’s important to talk to your urologist to discuss your overall physical and mental health, as well as your ideal lifestyle outcomes. If you are in a long-term relationship, it could be helpful to also involve your sexual partner in these conversations.

If you have yet to go into treatment, make sure to take the SHIM (Sexual Health Inventory for Men) test. Your score from this questionnaire will provide a documented, realistic baseline to which you might return after surgery. It is important to keep in mind that while you might return to this baseline, prostate cancer treatment will never result in better erectile function than you had before. Visit pcf.org/SHIM to get your score.

With all that said, remember that one of the issues with all current ED treatments is that they are not curative—they all provide varying degrees of temporary correction to the problem.

Consult your doctor as to which of these options might be right for you. Note: it is not necessarily the case that all men should start with oral medications. If you are a man with significant vascular disease or little to no intact nerve function, ask your doctor if you should go straight to a pump or injections, which have traditionally been considered “second-line” defenses. Just as the Prostate Cancer Foundation is a strong advocate for precision medicine, we believe in precision lifestyle treatments for men to live a full life after treatment. Make sure to discuss side effects and the pros and cons of each treatment with your doctor. Beware of over-the-counter treatments, supplements, or expensive experimental treatments that promise miraculous results.

PERMANENT UPGRADES TO HEALTHY LIVING

From the moment you are diagnosed with prostate cancer, it's important to make mindful decisions about your diet and lifestyle. Your everyday choices are vital to the success of your treatment and your recovery from the disease, and it's a great way to take back some of the control that cancer and its treatment may have had on your life.

There is growing scientific evidence that suggests healthy diet and lifestyle practices may actually slow the growth and progression of prostate cancer. Cutting-edge studies are starting to unpack some unexpected data on behaviors that may increase or decrease your risk for cancer. For example, a study in Italy found that drinking 3 or more cups of European-style coffee may cut your risk of prostate cancer in half. Another study suggests that the bacteria in your gut, known as your *microbiome*, may in fact alter your immune system's ability to respond well to cancer treatment. To stay up to date on the latest in lifestyle research, subscribe to the newsletter at pcf.org.

Diet

Just a few simple changes in your daily eating habits can help support healthier living as you recover from prostate cancer, may decrease your time to return to normal function, and may even decrease risk of your cancer coming back or getting worse. All of these recommendations also apply to maintaining overall health, for you and your family. Research is ongoing, but the "anti-inflammatory" diet is heart-healthy and gives every prostate cancer survivor a better chance to maximize longevity through lifestyle.

1. Vegetables. Incorporate cooked tomatoes (preferably cooked with olive oil) and cruciferous vegetables (like broccoli and cauliflower) into many of your weekly meals. Certain fruits and vegetables contain large amounts of antioxidants. **Antioxidants** benefit the body by removing free radicals. Free radicals can attack healthy cells and permanently disrupt their operation.

2. Fat. Try to keep the amount of fat that you get from red meat and dairy products to a minimum. Several studies have reported that saturated fat intake is associated with an increased risk of developing advanced prostate cancer, while **long-chain omega-3 fatty acids** (the "good fat" found in fish such as salmon) are associated with lower risk. Avoid processed meats (lunchmeats) that contain nitrates and charred meat, which have been shown to have cancer-promoting properties. Choose fish, lean poultry, or plant-based proteins such as nuts and beans instead.

3. Vitamins. Try to get your vitamins from food sources, that is, eating a diet rich in vegetables and whole grains, rather than relying on vitamin supplements. In particular, avoid excessive calcium substitutes. Plant-based sources of calcium include dark green leafy vegetables, soy, and almonds.

For more detailed information on nutrition, visit pcf.org and download our nutrition guides.

Exercise

Exercise is part of a healthy lifestyle for everyone. For prostate cancer survivors, exercise as much as you are physically able, at a pace which is maximal for your personal fitness. More and more research studies are emerging which indicate that exercise during cancer treatment can improve long-term outcomes when combined with traditional therapies. Exercise has been proven in multiple studies to both reduce prostate cancer risk and improve survival in patients, even with the most advanced forms of disease.

For those who are able to exercise vigorously, walk as briskly as you can (3 or more miles per hour), and try to add bouts of jogging. Vigorous exercise should include when your heart beats rapidly and you are sweating. Such activity includes running, swimming, or bicycling.

Research suggests that exercise affects energy metabolism, inflammation, oxidative stress, immunity, and androgen signaling pathways, and is therefore beneficial for men with prostate cancer. Exercise reduces levels of inflammation. Several studies have shown that

vigorous exercise significantly reduced the risk of prostate cancer recurrence, compared with the same volume of exercise at an easypace.

Lifestyle Changes

In addition to diet and exercise, several other lifestyle factors may be associated with prostate cancer risk and progression.

Smoking

Quitting smoking may reduce the risk of dying from prostate cancer, and reduces the risk of dying from any cause. **The health benefits from quitting begin on the first day after smoking ceases**, so it is never too late to quit. Recent evidence further suggests that smoking is associated with more aggressive prostate cancer at the time of diagnosis. Furthermore, smokers have a higher risk of prostate cancer progression, including recurrence and metastasis, as well as an increased likelihood of death. Importantly, when compared with current smokers, men who quit smoking more than 10 years ago had prostate cancer mortality risk similar to those who had never smoked. Quitting smoking is also associated with improved penile blood flow and erections.

Body Mass Index (BMI)

Body mass index is a measure of body fat calculated by dividing an individual's weight (in kilograms) by height (in meters)-squared. A BMI of 18.5 to 24.9 is considered a healthy weight, a BMI of 25 to 29.9 is considered overweight, and a BMI of 30 or higher is considered obese. High BMI is associated with increased risk of developing lethal prostate cancer, and growing evidence suggests that obesity (either before or at the



Maintaining a positive attitude along with healthy diet and regular exercise will help during recovery, as well as for the rest of your life.

time of diagnosis) is associated with increased risk for prostate cancer recurrence, progression and mortality. This may be due to biological mechanisms that involve insulin, altered levels of male hormones (androgens), and cellular activity in fat tissue. Furthermore, obesity has been shown to increase the rates of urinary incontinence after surgery. Eating a nutritious diet and keeping up your exercise routine will go a long way towards maintaining a healthy weight.



STOP

The next 2 sections are for men with rising PSA levels after initial treatment, or with advanced/metastatic prostate cancer. If you are a newly diagnosed patient with local or locally advanced prostate cancer, we suggest skipping ahead to the section titled "For Our Sons, Daughters & Grandchildren," a discussion of the genetics of prostate cancer risk. Of course, feel free to proceed if you like.

**“Six months after hormone therapy, my
PSA started to rise. That’s when I got
choked up. This was serious.”**

— PATIENT



5 ► WHAT TO DO IF YOUR PSA STARTS TO RISE

See Appendix for 2020 COVID-19 Updates about Treatment for Advanced Prostate Cancer.

DETECTING RECURRENCE

At this point, your cancer cells have either been removed with surgery or killed with radiation.

But some prostate cancer cells might have been able to spread outside the treatment areas before they could be removed or killed. At some point these cells may begin to multiply and produce enough PSA that it can again become detectable by lab tests.

PSA monitoring after treatment is an important way of understanding whether or not all the prostate cancer cells have been destroyed. If you previously underwent surgery, your PSA should be undetectable. However, after surgery, since PSA is produced by all prostate cells, not just prostate cancer cells, there may be residual normal (benign) prostate cells that still make some PSA.

If your PSA begins to rise, your doctor will first try to determine where the cells producing PSA are located.

This involves imaging, such as a CT, MRI, or bone scan. However, in cases where PSA is still very low, imaging tests may not provide enough information to determine a further course of action. Newer **molecular imaging scans** can be done at select centers; these scans include C11-choline (performed in limited clinic centers), F18-fluciclovine (recently FDA-approved and available across the USA), F18-sodium fluoride (to evaluate for bone metastases, usually to confirm findings from bone scans) and PSMA-PET scans. It's important to note that all scans can have difficulty in finding tumors at low PSA levels. It's also important to note that some of these tests may not be covered by your insurance.

PSMA-PET is one of the new molecular imaging technologies that is more sensitive in detecting prostate cancer metastases in the body; although it is currently not FDA-approved in the USA, it is offered under research trials at select centers.

Whole body multi-parametric MRI (MP-MRI) is another emerging imaging technology for measuring sites and burden of metastatic disease that may be more sensitive than CT and bone scans. Its effectiveness is currently being tested in clinical trials.

To follow these and other evolving technologies, visit pcf.org/newsletter.

UNDERSTANDING THE NUMBERS

After prostatectomy, PSA drops to “undetectable levels,” (less than 0.1). This is effectively zero, but by definition can never get all the way to zero, given the sensitivity of the test and the fact that, at very low readings, other proteins may be misread as “PSA protein.” In contrast, because normal healthy prostate tissue isn't always completely killed during radiation therapy, the PSA level rarely drops to zero with this treatment. Rather, a different low point is seen in each individual, and that low point, called **nadir**, becomes the benchmark by which to measure a rise in PSA.

Because the starting point is different whether you had surgery or radiation therapy, there are 2 different definitions for disease recurrence as measured by PSA following initial therapy.

Following a prostatectomy, the most widely accepted definition of a **recurrence** is a confirmed PSA level ≥ 0.2 ng/mL. In the post-radiation therapy setting, the most widely accepted definition is a PSA that is seen to be rising from the lowest level (nadir) by at least 2.0 ng/mL. It's important to try to always use the same lab for all of your PSA tests because PSA values can fluctuate somewhat from lab to lab.

After radiation therapy, doctors need to look for confirmation from multiple tests because PSA can “bounce” or jump up for a short period, and will later return to its low level. If only one test was performed it's possible that it could have occurred during a bounce phase, and the results would therefore be misleading. PSA bounces typically occur between 12 months and 2 years following the end of initial therapy.

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WHEN TO BE WORRIED ABOUT RISING PSA

Surgery Patients: PSA greater than 0.2 ng/mL

Radiation Patients: if your PSA is 2.0 ng/mL above your lowest reading after treatment (referred to as your “nadir” reading), as measured on 2 consecutive tests

If your PSA is rising but doesn’t quite reach these definitions, your doctor might initiate further testing to assess the risk that cancer has come back. This is a gray area that requires a lot of input from your team, possibly including a urologist, radiation oncologist, and medical oncologist to help you decide on the best course of action.

PSA DOUBLING TIME

The rate (or velocity) at which your PSA rises (and how quickly it doubles) after prostatectomy or radiation therapy can be a very significant factor in determining how aggressive your cancer is, and can therefore be useful in determining how aggressively it might need to be treated.

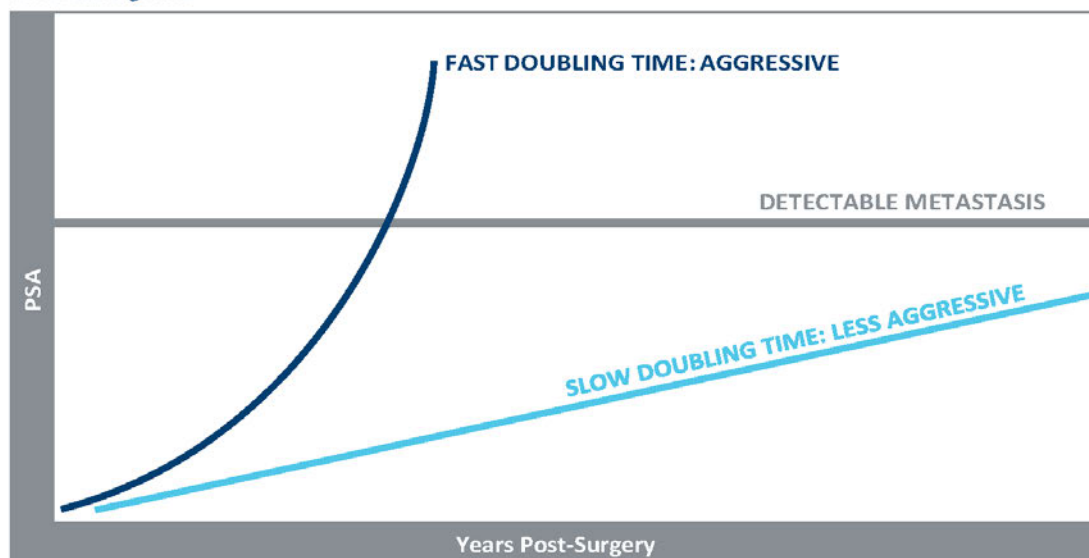
When looking at PSA doubling time in a few hundred men who had undergone either prostatectomy or radiation therapy, researchers found that men whose PSA doubled in under 3 months (fast) had the most aggressive tumors and were more likely to die from their disease, whereas those whose PSA doubled in more than 10 months (slow) had the least aggressive tumors and were less likely to die from their disease.

The faster your PSA rises, the more aggressive your disease is considered.

That said, measuring and using PSA doubling time is not an exact science. There is no set number of times that your PSA has to be tested in order to determine the rate of rise, although most researchers would agree that more frequent tests over longer periods of time will likely give a better sense of how your tumor is growing.

Ultimately, PSA is just one of many factors that can influence the decision to pursue additional treatments. You and your doctors will need to weigh all of the different factors before deciding on the course that’s right for you.

PSA Doubling Time



52 ► WHAT TO DO IF YOUR PSA STARTS TO RISE

RISING PSA AFTER INITIAL TREATMENT

Questions to ask when your PSA is rising after initial treatment.

- ▶ What does it mean that my PSA level is rising?
- ▶ What is my PSA level now and how will we monitor changes over time?
- ▶ Am I a candidate for local “salvage” prostatectomy or radiation? Why or why not?
- ▶ Should I get an imaging scan to see if the cancer has spread to my bones or other organs?
- ▶ Should we add a medical oncologist to my treatment team to gain an additional perspective on treating my disease?
- ▶ If you recommend that I initiate androgen deprivation therapy (“hormone therapy”), how will this benefit me and slow down the growth of the cancer cells? When is the optimal time to initiate this treatment?
- ▶ Should my treatment plan also include 2nd-generation anti-androgen therapy or docetaxel?
- ▶ What are the benefits and drawbacks/side effects of hormone therapy? Are there things that I can do to minimize the side effects?
- ▶ How long do the treatment effects of hormone therapy last?
- ▶ Should I consider joining a clinical trial?

LOCAL TREATMENTS FOR RECURRENT PROSTATE CANCER

In this section, we’ll look at options for what to do when PSA first starts to rise after surgery or radiation therapy, and why a secondary local treatment might be right for you.

In general, the most common site of disease recurrence after surgery or radiation therapy is **local**, meaning in or near the prostate. For this reason, re-treating the prostate region may provide a second chance at cure. This secondary treatment is often referred to as “salvage” therapy.

Whether your initial treatment was radiation or surgery, there are salvage options available for you. The chart opposite lists these options.

Secondary “Salvage” Therapy Options

If you started with <i>surgery</i> , you can follow with:	If you started with <i>radiation</i> , you can follow with:
Radiation	Surgery
ADT	Brachytherapy
	Cryotherapy
	ADT

Check with your doctor to see which option(s) might be right for you.

As with any secondary form of treatment, there is the risk of increased side effects beyond the initial treatment. While salvage brachytherapy, cryotherapy, and salvage prostatectomy appear to have similar rates of efficacy, salvage prostatectomy appears to carry the greatest risks of side effects including urinary incontinence, rectal injury, and impotence, and should only be attempted at high-volume academic medical centers.

In some men, PSA may be produced by disease outside the pelvis, such as cancer in distant lymph nodes or bone. This means that additional local therapy is not right for everyone.

The next sections provide more detail on methods of salvage treatment for local recurrence.

Salvage Radiation Therapy Following Surgery

If your PSA starts to rise after you've undergone prostatectomy, "salvage" radiation therapy might be a good option to explore and is considered part of the standard of care. With this approach, EBRT is delivered to the area immediately surrounding where the prostate used to be (called the **prostate bed**) and sometimes to the pelvis, with the goal of eradicating any remaining prostate cancer cells that have been left behind. Approximately 80% of men who have a rising PSA after surgery have residual disease in the prostate bed.

Note that this procedure is not for everyone. If there are obvious sites of metastatic disease outside of the pelvis, salvage radiation therapy is likely not the best choice, as it will only treat the prostate bed and potentially the nearby lymph nodes.

TIMING OF SALVAGE RADIATION

The best time to receive salvage radiation therapy is when your PSA first becomes detectable again, ideally when it is ≤ 0.2 ng/mL, and definitely below 0.5 ng/mL if possible. Once the PSA is above 0.5 ng/mL, cure rates with salvage radiation therapy alone start to fall off quickly. For some men whose PSA has risen above 0.5 ng/mL, hormone therapy is usually added to salvage radiation therapy, which has been shown to improve the cure rate. For men with a low PSA (0.5 ng/mL or less) at the time of recurrence, addition of hormone therapy is usually not needed.

The side effects that you suffer from salvage radiation therapy are directly related to the amount of side effects suffered from the surgery. In other words, if you had intact urinary control and erectile function after surgery, you are likely to have only mild side effects after radiation therapy. However, if you have some degree of urinary incontinence already or poor erectile function, salvage radiation therapy has the potential to worsen these to a more noticeable degree. In general, salvage radiation therapy (like all salvage therapies) is more likely to cause more side effects than upfront radiation therapy since the side effects may be additive to those previously experienced with surgery. These include rectal bleeding, incontinence (urinary leakage), strictures and difficulty urinating, diarrhea, and fatigue. Importantly, rectal spacers are not used after surgery, and thus rectal side effects with post-operative radiotherapy may be slightly higher than radiotherapy upfront. Be sure to discuss potential side effects with your doctors before deciding on a course of therapy. In some cases, hormone therapy might be given in conjunction with radiation treatment, so it is also important to discuss the impact of that with your doctor.

Salvage Prostatectomy Following Radiation

In some cases, patients who have residual cancer in the prostate after radiation therapy may have improved results with "salvage" prostatectomy.

Even under the best of circumstances, post-radiation surgery is a very difficult operation to perform and can result in significant urinary effects and erectile dysfunction, so few surgeons across the country perform it regularly and successfully. If you talk with your doctors about this treatment approach, be sure to carefully weigh all of the different factors that can play a role in determining whether this approach is right for you.

Brachytherapy Following External Beam Radiation

The use of radioactive seed implantation or high-dose-rate brachytherapy using catheters after EBRT has 5-year disease-free rates of around 50% (very similar to the success of salvage radiation therapy after surgery). Side effects from brachytherapy

following external beam radiation can sometimes be less frequent and less severe than other therapies, such as salvage prostatectomy. Because this approach delivers radiation to very localized areas, it is not an optimal treatment for men with tumors that have spread beyond the prostate.

Cryotherapy Following Radiation

Cryotherapy has been used as a secondary local therapy in men who underwent radiation therapy, and has shown 5-year disease-free rates around 40%. However, because the procedure does not completely destroy all remaining prostate cells, PSA generally does not drop to zero, so it is often difficult to determine complete success. Men with lower pre-cryotherapy PSA levels and lower-grade disease tend to fare better, while those who received hormone therapy in addition to radiation therapy tend to fare worse.

Side effects of cryotherapy tend to be milder compared with standard salvage prostatectomy. Nevertheless, rates for erectile dysfunction and urinary incontinence following this salvage procedure remain high, as do rates of pelvic or rectal pain. Because the severity of side effects tends to correlate with the amount of tissue that is frozen during therapy, better techniques are currently being studied that could improve outcomes over time.

Hormone Therapy Following Radiation or Surgery

In select men who undergo surgery or radiation therapy, the best salvage treatment option may not be more local therapy, but rather hormonal therapy, which is a systemic therapy and therefore acts on tumor sites throughout the body. This has been shown to be beneficial especially in men who have lymph node involvement that was found at time of surgery. In addition, after radiation therapy, when the PSA is rising but there is no evidence of disease within the prostate via imaging or a repeat biopsy, initiation of hormone therapy alone may be most appropriate at the time when cancer spots are first seen on a scan or with a rapidly rising PSA. The next section provides more information on hormone therapy and other treatment options for advanced disease.

THERAPIES FOR ADVANCED (RECURRENT OR METASTATIC) PROSTATE CANCER

When a man experiences PSA progression after surgery or radiation, hormone therapy is often given at some point, and often for many years. Some men will not require any therapy if their PSA doubling time is long and no disease is present on scans.

Advanced disease refers to prostate cancer that has spread beyond the prostate and is unlikely to be cured with surgery or radiation alone.

For men diagnosed with **metastatic prostate cancer** (their disease has already spread beyond the prostate by the time of diagnosis), their therapeutic journey will start in a similar way to men who were diagnosed at an earlier stage and had subsequent disease progression.

Hormone Therapy

Hormone therapy (another name for ADT) is part of the standard of care for advanced and metastatic prostate cancer. ADT is designed to stop testosterone from being produced or directly block it from acting on prostate cancer cells. Although hormone therapy is effective at controlling prostate cancer growth, the loss of testosterone has side effects in nearly all men. These side effects range from hot flashes and loss of bone density to mood swings, weight gain, and erectile dysfunction. The timing of when to start hormone therapy once the PSA begins to rise is an individual decision and one that should be discussed with your doctor.

For a man starting hormone therapy, doctor visits are usually timed with the hormone therapy injections (which lower your testosterone), along with PSA and other lab checkups such as testosterone levels and liver and kidney function tests.



"There's reason for hope. It's realistic hope, not pie-in-the-sky hope." – Patient

The majority of prostate cancer cells will die or stop growing following the removal of testosterone. This is referred to as hormone-sensitive prostate cancer (HSPC).

However, in many men, some cells gain the ability to grow in the low-testosterone environment created by hormone therapy. As these **hormone therapy resistant prostate cancer** cells continue to grow, hormone therapies have less and less of an effect on stopping the growth of the tumor over time. This state is also referred to **castration resistant prostate cancer (CRPC)**. Despite this potential pitfall, ADT remains an important step in the process of managing advanced disease, and it will likely be a part of every man's therapeutic regimen if he develops metastatic disease at some point.

Until recently, the standard-of-care first-line treatment for all patients with metastatic disease was hormone therapy alone. However, advances in medical research have generated additional options, making combination therapy the standard of care now. Recent clinical trials have found notable improvements in survival if either abiraterone acetate (a stronger form of hormone therapy) or docetaxel chemotherapy are started along with ADT. For patients with a low volume of metastatic disease at diagnosis, NCCN guidelines now recommend that treatment with radiation therapy to the primary tumor be considered in addition to hormone therapy. See *"Therapies for Metastatic Hormone-Sensitive Prostate Cancer"* on page 58. It is important to discuss these treatment options with your doctor to determine which choice is right for you.

Types of Hormone Therapy (Androgen Deprivation Therapy or ADT)

Orchiectomy: About 90% of testosterone is produced by the testicles. So orchiectomy—the surgical removal of the testicles—is an effective solution to blocking testosterone release. Because it's permanent and irreversible, most men opt for drug therapy instead. The procedure is typically done on an outpatient basis in the urologist's office. Since recovery tends to be quick and no further hormone therapy is needed, it is an option for men who prefer a low-cost, one-time procedure. It also may have a lower risk of cardiovascular complications and fractures compared with drug-based hormone therapy.

LHRH Agonist: LHRH, or luteinizing-hormone releasing hormone (also called GnRH, or gonadotropin-releasing hormone), is one of the key hormones released by the body that initiates the production of testosterone. Blocking the release of LHRH through the use of **agonists** (substances that initiate a response) is one of the most common hormone therapies used in men with prostate cancer. Drugs in this class, including leuprolide (Eligard®, Lupron Depot®, and Viadur®),

goserelin (Zoladex*), and triptorelin (Trelstar*), are given as regular shots: once a month, once every 3, 4, or 6 months, or once per year. LHRH agonists cause a “testosterone flare” reaction, which is an initial transient rise in testosterone that happens over the first week or two after the first treatment. This can result in a variety of symptoms, ranging from bone pain to urinary issues. Fortunately, this can be prevented by co-treatment with anti-androgens.

LHRH Antagonists: These are a class of medications that can block LHRH (GnRH) from stimulating testosterone production without causing an initial testosterone surge. This class includes degarelix (Firmagon*), which is given monthly to men as an alternative to orchiectomy or LHRH agonists.

Anti-Androgens: Anti-androgens such as bicalutamide (Casodex*), flutamide (Eulexin*), and nilutamide (Nilandron*) can help block the action of testosterone in prostate cancer cells. They are often added to some hormone injections to prevent a temporary rise in testosterone.

Although the sexual side effects of the anti-androgens when given alone are typically fewer compared with hormone injections, anti-androgens might not be as effective as orchiectomy or hormone injections, and they are not the optimal choice for men with documented metastatic prostate cancer. Furthermore, when given alone, more than 70% of men experience breast tenderness or the formation/growth of breast tissue, termed **gynecomastia**.

When used in combination with LHRH agonists, anti-androgens tend to increase the risk of hot flashes, and in rare occasions can result in liver injury. Your liver function should be monitored while you take these medications. Fortunately, gynecomastia is rare when LHRH agonists and anti-androgens are used together.

In addition, nilutamide is known to cause visual light-dark adaptation problems and—rarely—cause inflammation and scarring in the lungs. If you develop a persistent cough or persistent shortness of breath while on nilutamide, you should contact your doctor.

2nd Generation Anti-Androgens: Beginning in 2011, a handful of new “second-generation” hormone treatments (apalutamide, enzalutamide, and abiraterone) began gaining FDA approvals for men with certain types of advanced disease, and these approvals may be expanded. Darolutamide is an additional drug in this class that gained FDA approval in 2019 for the specific clinical state of non-metastatic CRPC. (See also “[2nd Generation FDA-Approved Anti-Androgens](#)” on page 60.) Each of these “2nd-generation” hormone treatments is associated with a unique set of side effects.

Intermittent Hormonal Therapy

Over the years, researchers have explored different ways to minimize the [side effects of testosterone loss](#) while maximizing the therapeutic effect of hormone therapy. The most commonly explored strategy is to give LHRH intermittently, meaning that the drug is taken during “on” periods and skipped during “off” periods.

It is not right for all patients, especially those who have a rising PSA shortly after stopping hormone therapy. A patient-by-patient approach should be used based on response to and tolerability of hormone therapy.

INTERACTION EFFECTS

Many plant-based and complementary medicines can have estrogen-like properties and can interact with your medications for prostate cancer or other conditions. Be sure that your doctor has a complete list of all medicines—including the “non-traditional” ones—that you are taking, so that he or she can better monitor the effects of your therapy on the progression of your disease.

Therapies for Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)

Metastatic hormone-sensitive prostate cancer (mHSPC) refers to men whose prostate cancer has spread to areas of the body outside of the prostate itself, and who are responsive to hormone therapy. This may refer to men who have had prior surgery or radiation and recurred, or to men who were initially diagnosed with disease that was already metastatic. Patients who are “hormone-sensitive” (aka, “castration-sensitive”) may have previously received hormone therapy for a certain amount of time, but their cancer has not yet developed resistance to hormone therapy.

Second-generation anti-androgens (such as abiraterone and enzalutamide) and taxane chemotherapy are therapies that were historically used after cancer becomes metastatic and resistant to hormone therapy (see [Therapies for Hormone-Resistant Prostate Cancer](#) for more information).

However, beginning in 2015, clinical trials have found that in men with mHSPC, the addition of 2nd-generation anti-androgens or docetaxel chemotherapy to ADT significantly extended survival and length of time before disease progression. While ADT alone might still be the best choice for some patients, it is now recommended that patients with mHSPC should strongly consider the use of docetaxel or an approved 2nd-generation anti-androgen in addition to ADT.

LHRH-agonists plus 2nd-generation anti-androgens

In 2018, abiraterone plus low-dose prednisone became FDA-approved for high-risk mHSPC patients who are initiating treatment with ADT. This approval was based on two large clinical trials showing that men on the abiraterone/prednisone/ADT regimen lived longer on average than those taking ADT alone. Ask your doctor to discuss this approach with you if you are starting hormonal therapy for the first time.

In 2019, results from 3 large phase 3 clinical trials demonstrated that the addition of apalutamide or enzalutamide to ADT helps men with mHSPC live longer, leading to the FDA approval of both drugs later that year.

Hormone therapy plus taxane chemotherapy

Two large trials have demonstrated that the addition of docetaxel extended overall survival in patients starting hormone therapy in men with mHSPC. While the evidence is stronger for benefit from the addition of docetaxel to ADT in men with a high burden of metastatic disease, it is possible that some men with low-burden disease may also benefit. Please discuss with your doctor.

Hormone therapy plus radiation therapy

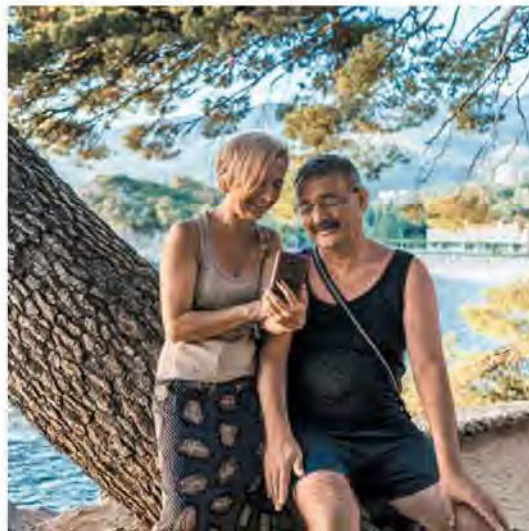
For patients with a low volume of metastatic disease at diagnosis, who have not previously received ADT, NCCN guidelines now recommend that radiation therapy to the primary tumor be considered in addition to ADT. This recommendation is based on results of the STAMPEDE phase 3 clinical trial, which showed that among men with a low disease burden, radiation + ADT was associated with a 32% lower risk of death vs ADT alone. This benefit is not seen among men with a high disease burden at diagnosis.

So which treatment is best for you? For patients with mHSPC, whether to add one of these treatments to an ADT regimen, and which treatment to add, will be based on clinical factors, including whether the cancer is high-risk, and whether there is a high or low volume of metastatic disease. Studies have clearly found that the addition of docetaxel to ADT is beneficial in patients with high-volume metastatic disease, and the addition of abiraterone to ADT is beneficial in patients with high-risk metastatic disease. Enzalutamide and apalutamide have shown benefit in both high- and low-volume disease. Benefits, risks, side effects, costs and other issues should be considered with your doctor. For instance, patients who are older or less healthy may not be able to tolerate docetaxel, and 2nd-generation anti-androgens may be the only viable choice. On the other hand, those who can tolerate docetaxel may want to consider it, as the treatment length is far shorter (6 treatments given every 3 weeks for docetaxel, versus daily treatment until disease progression for 2nd-generation drugs), and far less expensive.

THERAPIES FOR HORMONE-RESISTANT PROSTATE CANCER

It is important to note that the treatment landscape for advanced prostate cancer is rapidly changing. Treatments that were previously only given to patients after ADT has begun to fail are now being given upfront, at the time of ADT initiation. Thus, as you read the following sections, please keep in mind that optimal treatment choices are dependent on what treatments have previously been prescribed, and are best discussed with your doctor.

After a few years, prostate cancer cells often evolve ways to thrive despite the low-androgen environment produced by hormone therapy, and become “castration-resistant.” For instance, tumors may evolve to produce their own androgens, prime the pump of the androgen receptor, or acquire alterations in the androgen receptor that allow sufficient activity with little or no androgens. In these cases, because prostate cancer cells still rely on the androgen receptor pathway to survive and grow, a number of “secondary” hormone therapy approaches can be used to keep the tumor from spreading.



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TERMS TO KNOW

- ▶ Castration-resistant prostate cancer (CRPC)
- ▶ Hormone-resistant prostate cancer
- ▶ Hormone-refractory prostate cancer

All of these terms refer to the same status: the prostate cancer has learned to adapt and thrive in a low-hormone environment, thus hormone therapy is no longer an option and other treatment options should be considered, including 2nd-generation anti-androgens which are even more effective at blocking androgen activity, as well as non-hormonal therapy options and emerging near-term therapies.

For many men who were using an anti-androgen in combination with an LHRH agonist, stopping the anti-androgen is the most common first step in secondary hormone therapy. About 10% to 30% of men will respond to anti-androgen withdrawal, which lasts on average 3 to 5 months. However, inevitably, additional therapies will need to be added even if this withdrawal response occurs. Switching to a different anti-androgen might also be able to offer an extra few months of benefit before other therapeutic approaches are required.

THERAPIES FOR NON-METASTATIC CRPC

Non-metastatic CRPC (nmCRPC) is a clinical state in which men receiving ADT begin to see their PSA levels rise (indicating the cancer is developing resistance to ADT), but the sites of cancer are not yet apparent on CT or bone scans.

2ND-GENERATION FDA-APPROVED ANTI-ANDROGENS

Enzalutamide (Xtandi®) is an anti-androgen that acts by blocking the activation of the androgen receptor by testosterone, and is given orally. Side effects are mild but include fatigue, diarrhea, hot flushes, headache, frailty, falls, memory cloudiness and, very rarely, seizures. Enzalutamide has been FDA-approved for non-metastatic CRPC in combination with ADT, and for metastatic CRPC, and was most recently approved for the treatment of metastatic HSPC in combination with ADT.

Apalutamide (Erleada®) is an oral anti-androgen medication that blocks the activation of the androgen receptor by testosterone. Apalutamide is very similar in chemical structure to enzalutamide and acts through the same mechanisms. The most common side effects include fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, fall, hot flush, decreased appetite, fracture, and peripheral edema. Apalutamide is FDA-approved for the treatment of mHSPC and for nmCRPC, in combination with ADT.

Darolutamide (Nubeqa®) is also an oral anti-androgen that works in a similar fashion to the medications described above. It is FDA-approved for nmCRPC in combination with ADT. Side effects include fatigue, weakness, pain in the extremities, and laboratory abnormalities such as decreased numbers of neutrophils (a type of white blood cell) and indications of liver function. While still being evaluated in clinical trials, darolutamide may not cross the blood-brain barrier, and in some patients may lessen feelings of fatigue.

Abiraterone (Zytiga®, Yonsa®) is a pill taken by mouth that blocks the production of testosterone and other androgens, thereby stopping testosterone from stimulating prostate cancer growth. Abiraterone is administered in conjunction with prednisone, a corticosteroid, in order to minimize the adverse effects of abiraterone on other steroid pathways. Although a regimen of abiraterone + prednisone is generally well-tolerated, side effects may include fatigue, high blood pressure, and electrolyte or liver abnormalities, and patients need to be monitored regularly. Zytiga has been FDA-approved for mHSPC in combination with ADT, and for mCRPC. Yonsa is a newer formulation of abiraterone that was FDA-approved in 2018 for the treatment of mCRPC.

In 2018, the FDA approved two drugs for use in men with nmCRPC: apalutamide and enzalutamide, both of which are taken in addition to continuing ADT. In 2019, darolutamide also gained FDA approval for the treatment of nmCRPC (in addition to ADT). The men who were treated on the clinical trials that led to these FDA approvals had rapidly rising PSA levels, with a PSA doubling time of less than 10 months.

Prior to 2018, there were no FDA-approved treatments for nmCRPC, and these patients typically continued to receive ADT alone, despite evidence of a diminishing benefit. Today, thanks to research funded by the Prostate Cancer Foundation, men with nmCRPC have three treatment options which significantly delay metastatic disease.

As of press, it is still too early to know if the addition of either enzalutamide, apalutamide, or darolutamide to ADT in nmCRPC improves overall survival. If you are a man with rising PSA levels and negative CT or bone scans, talk to your doctor about whether one of these drugs may be right for you.

THERAPIES FOR METASTATIC CRPC

Metastatic castration-resistant prostate cancer (mCRPC) is a clinical state in which men who have previously received hormone therapy see their tumors begin to grow, and sites of metastatic disease can be found on imaging scans.

2nd-Generation Anti-Androgens

There are 2 major androgen pathway blockers that are used for the treatment of mCRPC: abiraterone and enzalutamide. These therapies have exhibited similar survival benefits in similar clinical settings. Therefore, which one is initially prescribed is often driven by its side effect profile combined with other medical issues the patient may have. For example, enzalutamide is preferred if a patient has diabetes to avoid the prednisone that is given alongside abiraterone, and abiraterone is preferred if a patient has memory concerns, seizure disorders, or frailty related to age. Often when there is no medical necessity, insurance coverage and clinical trial options can help inform which agent is used first.

When treatment with either 2nd-generation anti-androgen begins to fail, patients may be switched to the other drug. However, recent studies have indicated that patients who stop responding to abiraterone will have poor responses to enzalutamide and vice versa.

Researchers are actively investigating optimal strategies for patients whose cancer has become resistant to enzalutamide or abiraterone—for example, whether the next treatment should be chemotherapy or an investigational therapy. Clinically available blood tests which determine the presence of AR-V7, a biomarker, can help to indicate whether a patient is more likely to benefit from a 2nd-generation anti-androgen (abiraterone or enzalutamide) versus docetaxel chemotherapy.

NON-HORMONAL THERAPY OPTIONS

The therapies described in this section are typically used in patients whose cancer has progressed after treatment with hormonal therapy (ADT). However, clinical trials are continuing to test whether it is useful to introduce each of these treatments even earlier in the course of disease progression.

Taxane Chemotherapy

Currently, taxane chemotherapy, given with prednisone, is a standard of care for men with metastatic prostate cancer that has spread and is progressing despite hormone therapy. Taxane chemotherapy agents



Although chemotherapy has a historically “bad rap,” prostate cancer chemotherapy drugs can actually help manage pain in patients with metastatic disease.

approved for the treatment of advanced prostate cancer include docetaxel (Taxotere®) and cabazitaxel (Jevtana®).

Taxane chemotherapy is also effective in prolonging life in patients who have a high burden of cancer on scans when starting hormonal therapy for the first time for metastatic disease. Taxanes kill rapidly dividing prostate cells by disrupting the protein structures required for cells to divide.

The decision on when to start chemotherapy is difficult and highly individualized based on several factors:

- What other treatment options or clinical trials are available
- How well chemotherapy is likely to be tolerated
- What prior therapies you have received and how you responded to them
- If radiation is needed prior to chemotherapy to relieve pain quickly

Often chemotherapy is given before pain starts, with the goal of preventing the cancer from spreading further to other sites. Discuss the use of chemotherapy with your medical oncologist early and often, and keep an open mind despite your concerns about chemotherapy's "bad reputation." Docetaxel can extend life, reduce pain, and improve quality of life. Clinical trials of docetaxel combinations and other promising therapies are a high priority for researchers.

Many men who are suffering from their cancer will experience symptomatic improvement after starting chemotherapy. For example, pain is often reduced in men starting docetaxel, and quality of life is generally better for men with cancer-related symptoms who receive chemotherapy as compared with no therapy.

For patients who have already been treated with both docetaxel chemotherapy and a 2nd-generation anti-androgen (enzalutamide or abiraterone), results from the CARD trial reported in late 2019 suggest that cabazitaxel should be the new standard of care third-line treatment, if patients meet certain criteria and are fit enough to tolerate chemotherapy (as opposed to another 2nd-generation anti-androgen).

Platinum Chemotherapy

Platinum-based chemotherapy agents including carboplatin (Paraplatin[®]), cisplatin (Platinol[®]), and oxaliplatin (Eloxatin[®]), are used for the treatment of various cancer types. Platinum chemotherapy is not yet FDA-approved for the treatment of prostate cancer; however, it is sometimes used in very advanced prostate cancer patients who have exhausted all other treatment options or in patients who have certain genetic subtypes of prostate cancer. Patients with advanced disease who are not responding to standard therapy can talk with their doctor about whether they may be candidates for platinum chemotherapy.

Results from a phase 2 clinical trial have demonstrated that in a subset of patients with very aggressive and atypical cancer features (termed "aggressive variant prostate cancer," AVPC), the addition of carboplatin to taxane chemotherapy may be of benefit.

Sipuleucel-T Immunotherapy

The immune system has the remarkable ability to kills cells considered dangerous, such as infected cells or cancer cells. However, in most patients with progressing cancer, anti-cancer immune responses either never developed or have been turned off by the cancer. One way to turn on anti-cancer immune responses is the use of **therapeutic cancer vaccines**, which stimulate the immune system to recognize and fight cancer cells.

Sipuleucel-T (Provenge[®]) is a cell-based prostate cancer vaccine that has been approved by the FDA for men with metastatic hormone-resistant prostate cancer. This treatment is meant for men with minimal or no pain, and is most commonly given before chemotherapy, although it appears to be effective in some men even after chemotherapy. Some data suggest that the greatest benefit from sipuleucel-T is realized when it is used early (i.e., at a lower PSA level).

The treatment process involves drawing blood, filtering out your immune cells, stimulating them in a lab to fight prostate cancer, and then reinfusing those cells back into you intravenously (IV). This process is repeated every 2 weeks for a total of 3 treatments. The goal is to stimulate your own immune system to fight the cancer cells. This immunotherapy does not typically lower PSA, treat symptoms, or delay disease progression—however, it has been shown to prolong life. There are ongoing studies attempting to clarify exactly how this treatment works. Sipuleucel-T should only be considered in cases where the patient has a slow-growing tumor and does not need urgent cancer shrinkage (which can be achieved more effectively with other agents).

This treatment can only be given in certain centers, and you should discuss with your doctor whether this treatment is appropriate for you.

The side effects of sipuleucel-T are usually limited to the few days after infusion of the stimulated cells. You can sometimes experience a flu-like illness with fever, chills, nausea, and bone/muscle aches. This generally resolves within 3 days and can be treated with acetaminophen.

Pembrolizumab

Pembrolizumab (Keytruda®) is a type of “immune checkpoint inhibitor,” which are a class of immunotherapies that block immune-suppressive signals and activate tumor-killing immune cells. Pembrolizumab was approved by the FDA in 2017 for the treatment of all solid tumors, including prostate cancer, that have mutations in **mismatch repair genes** (MMR) and/or exhibit **microsatellite instability** (MSI) in the tumor. Patients who qualify for this therapy must have progressed on prior treatment and have no satisfactory alternative treatment options. Hence, pembrolizumab would typically be considered after other available effective treatments (such as sipuleucel-T, abiraterone, enzalutamide, docetaxel, cabazitaxel, radium-223, etc.) have been used or deemed inappropriate.

Studies suggest that about 5% of metastatic prostate cancer patients have evidence of MMR mutations and/or MSI in their tumors. Some of these mutations may be inherited, and may be associated with **Lynch syndrome**, a condition which predisposes individuals to higher risks of developing certain cancers such as colorectal cancer. At present, regardless of **family history**, MMR deficiency and MSI are identified by **genetic tests** performed on biopsies or tumor material from prostate surgery. Pembrolizumab is delivered intravenously once every 3 weeks. The most common side effects are fatigue, cough, shortness of breath, nausea, constipation, itching, rash, and decreased appetite. Because it works by modifying the immune system, there are rare but serious side effects related to overactive immune responses which are typically treated by stopping the drug and, in some cases, starting steroid medications to suppress the immune reactions.

Radium-223

Radium-223 (Xofigo®) is a radiopharmaceutical chemically similar to calcium that is used to treat men with castration-resistant prostate cancer that has metastasized to the bones. Because of its calcium-like chemical properties, radium-223 is absorbed in areas where bone is actively growing and

healing, in place of calcium, the mineral that would typically be absorbed in these areas of bone to build and repair them. Radium-223 is more likely to be taken up in places where the bone is damaged and is undergoing repair, particularly sites of growing metastases.

Treatment with radium-223 both prolongs survival and improves quality of life, with more time free of the debilitating complications of advanced prostate cancer (such as pain, bone fractures or spinal cord compression).

It is important to discuss with your doctor the proper sequence of available therapies. Studies have shown that patients with predominantly bone-only metastatic disease do better when radium-223 is given earlier in the course of the disease than when it is given after many lines of therapy (enzalutamide, chemotherapy, abiraterone, etc.), likely because men with more advanced disease often have cancer that has spread beyond the bones by that time. Radium-223 is delivered intravenously once every 4 weeks. The most common side effects are nausea, vomiting, diarrhea, and swelling of the lower legs and hands (peripheral edema). Your white and red blood cells and platelet counts may temporarily decrease as well.

Radium-223 should not be given in combination with abiraterone acetate and prednisone/prednisolone, as this combination has been found to increase risk for bone fractures and a concern for higher rates of death. It is unknown if this applies to other forms of hormone therapy.

A recent study has indicated that risk of fracture is almost entirely eliminated when a bone health agent such as zoledronic acid or denosumab is added to the combination therapy regime of radium-223 and enzalutamide. However, no trial has yet to demonstrate a survival benefit from using the two treatments together. You should talk with your doctor about whether you should also receive a bone health agent when you are starting treatment with radium.

External Beam Radiation Therapy (EBRT)

Radiation therapy can be used in multiple ways in men with metastatic prostate cancer. Recent guidelines now recommend that EBRT to the primary tumor be used in combination with ADT to treat men with low-volume metastatic disease who have not previously received hormone therapy. Early results of the phase 2 ORIOLE trial suggest that some patients with oligometastatic disease (about 3 or fewer metastases) may benefit from highly-focused spot radiation (SBRT) to the metastatic lesions, but more data are needed. Another very common reason to receive radiation therapy is to manage pain from prostate cancer spreading to bone. Radiation therapy is very effective at reducing cancer-related pain and about 70% to 80% of patients will experience some degree of pain relief after palliative radiation therapy. Usually the radiation therapy is delivered across 1, 5, or 10 treatments.

Since this is a pain relief strategy, a low/moderate dose of radiation therapy is used and there are usually very few side effects.

Another indication for radiation therapy is progressive disease within the prostate causing urinary obstruction or bleeding. Radiation therapy is usually given over 1 to 4 weeks in these settings, and is highly dependent on whether you have had previous radiation therapy to the prostate. Less common indications include relieving pain from spinal cord compression. Sometimes radiation therapy may be recommended if there is an area of the bone (typically in the hip or leg) that looks like it may easily break, even if it is not currently painful. The goal in that case is to reduce the risk of developing a fracture. This kind of radiation targeted to sites of painful metastases can usually be safely given, even if you received radiation to treat your initial prostate cancer. More recently, stereotactic body radiation therapy (SBRT) has been used (high-dose, ultra-precise radiation therapy, sometimes using only 1 dose).

Given the many uses of radiation therapy in advanced prostate cancer, talk to your medical oncologist and consult with a radiation oncologist to see if radiation therapy may be an option for you.

Other Bone-Targeting Treatments

Bones are the most common site of prostate cancer metastasis, occurring in 85%–90% of patients with metastatic prostate cancer. Bone metastases interfere with the bone's normal health and strength, and if they grow large enough can lead to bone pain, fracture, or other complications that can significantly impair a man's health.

Early detection of bone metastases can help determine the best treatment strategy. It can also help ward off complications. Because men with prostate cancer bone metastases often experience painful episodes, pain management and improving quality of life are important aspects of all treatment strategies.

Treatment with bisphosphonates or denosumab (Xgeva® and Prolia®) can help prevent complications related to bone metastases, like fractures.

Bisphosphonates are drugs that are designed to help reset the balance in the bone between bone growth and bone destruction that is disrupted by the prostate cancer metastases.

Zoledronic acid (Zometa®) is a bisphosphonate that can delay the onset of complications associated with prostate cancer bone metastases and relieve pain. It is typically given once every 3 weeks as a 15-minute infusion. Less frequent schedules are sometimes used as well, depending on your individual circumstance and risk.

Denosumab is a different type of bone-targeting drug which is given as an injection, rather than an infusion, and may be used instead of a bisphosphonate.

There are some risks with both classes of bone-targeted agents, including something called osteonecrosis of the jaw, that can occur after deep dental procedures and extractions or sometimes spontaneously. This can result in jaw pain and poor healing of your teeth. Certain laboratory assessments must be monitored with regular use of either medication. Daily calcium and vitamin D supplements are needed, and you should discuss this with your doctor.

Current Treatment Options for Advanced Prostate Cancer

Disease Stage	Treatments to Consider Once This Stage is Reached
Rising PSA but no detectable tumors on imaging (No previous hormone therapy or adjuvant radiotherapy after surgery)	The standard of care is the use of salvage radiotherapy with or without hormone therapy An alternative option for patients with a slow PSA doubling time and/or limited life expectancy is surveillance Clinical trials
Hormone-sensitive metastatic disease (Cancer has spread outside the prostate and is responsive to hormone therapy)	Hormone therapy Hormone therapy + radiation to prostate bed (newly diagnosed and with low-volume metastatic disease) Hormone therapy + 2 nd -generation anti-androgen* Hormone therapy + docetaxel Clinical trials
Non-metastatic castration-resistant prostate cancer (Rising PSA but no detectable tumors on imaging in patients who had previous hormone therapy)	Hormone therapy + 2 nd -generation anti-androgen* Clinical trials
Metastatic disease; resistant to hormone therapy	Sipuleucel-T (if minimal symptoms) Abiraterone or enzalutamide Radium-223 (for treatment of symptomatic bone metastases) Taxane chemotherapy (docetaxel or cabazitaxel) Clinical trials
Patient has exhausted all therapeutic options	Platinum chemotherapy Pembrolizumab (if MMR-deficient or MSI-high) Clinical trials
Bone protection	Denosumab Zoledronic acid Clinical trials

*Discuss the options in this medication class with your doctor.

SIDE EFFECTS FROM TREATMENTS FOR ADVANCED PROSTATE CANCER

This section will discuss the side effects of common therapies used to treat patients with advanced prostate cancer, including hormone therapy and chemotherapy. For a review of side effects from therapies for localized disease, such as surgery and radiation therapy, please refer to [Possible Side Effects](#) on page 42. And remember, **early management of side effects has been shown to help patients live longer, better lives.** Communicate with your doctor as soon as you experience any side effect of treatment.

It is important to understand how and why these side effects occur, so you can minimize their impact on your daily life.

Side Effects of Hormone Therapy

Testosterone is the primary male hormone, and plays an important role in establishing and maintaining typical male characteristics, such as body hair growth, muscle mass, sexual desire, and erectile function, and contributes to a host of other normal physiologic processes in the body. The primary systemic treatment for prostate cancer, androgen deprivation therapy (ADT), lowers testosterone and causes side effects related to reversing all of the normal functions of testosterone.

Although most men may experience only a few of these symptoms, the list of potential effects of testosterone loss is long: hot flashes, decreased sexual desire, loss of bone density and increased fracture risk (osteoporosis), erectile dysfunction, fatigue, increased risk of diabetes and heart attacks, weight gain, decreased muscle mass, anemia, and memory loss. "Bad" cholesterol levels rise, particularly LDL and total cholesterol, and muscle tends to get replaced by fat, especially around the abdomen.

Current research indicates a weak link between prolonged ADT and increased risk of dementia; in a subsequent study, no increased risk was shown between ADT and Alzheimer's. While substitute therapies for ADT are an active area of research for the [Prostate Cancer Foundation](#), ADT is currently a part of the standard of care. While it's important to be aware of the possible side effects, it should not affect your decision to receive life-extending care.

At this time, it is not possible to predict how severely any individual will be affected by lowering testosterone with hormone therapy, but work is being done to find ways to help predict who might be affected by which effects.

Changes in diet and exercise have been shown to relieve many of the side effects of ADT. Before beginning hormone therapy, every man should discuss the effects of testosterone loss with his doctor and nutritionist, so he can alter his lifestyle to accommodate or head off the changes.

Because hormone therapy is used to treat nearly every man with advanced prostate cancer, it is important to think about ways to prevent, reverse, or identify these effects so that men can live their best lives.

One important approach is considering lifestyle measures that can reduce some of these effects. Eating a heart-healthy diet low in red meat and high in vegetables and fiber, and maintaining physical activity through daily weight-bearing exercise can

reduce weight gain and maintain bone and muscle mass. Men should also discuss the increased risk of diabetes, heart disease, weight gain, and high cholesterol with their primary care physicians so that they can undergo screening and, if necessary, treatment for these other illnesses throughout the course of treatment for prostate cancer. When making these changes, it is important to talk with a doctor to ensure that you are planning lifestyle modifications that are safe for you. There are also some strategies that can decrease the hot flashes, including medications and acupuncture.

It is important to check bone mineral density around the time of starting hormonal therapy and every 1 or 2 years following, to assess for loss of bone density. There are medications that can be used to reduce the risk of fracture if early signs of bone loss are found.

Side Effects of 2nd-Generation Anti-Androgens

The newer anti-androgen drugs (abiraterone, apalutamide, enzalutamide, and, most recently darolutamide) are used when prostate cancer has become resistant to traditional ADT and, increasingly, earlier in the management of advanced disease. They each have their own side effect profile (see page 60). You and your doctor will need to consider your disease status and other medical conditions when choosing among these agents. For example, men with a cardiovascular disease history should be monitored closely when using these therapies, and consider management of any risk factors or disease with a cardiologist. Because abiraterone is given with prednisone, patients and doctors must be aware of possible side effects associated with steroid treatment as well.

Side Effects of Chemotherapy

Reactions to drugs can vary widely from patient to patient, so it's important to pay attention to any side effects that you experience, expected or otherwise.

The chemotherapy drug docetaxel is well tolerated, and many men are surprised to find that disease-related symptoms (pain, fatigue, loss of energy) are improved

after starting this therapy. However, docetaxel does have some side effects to be aware of. For example, between 5% and 10% of men will experience a fever with a low white blood cell count that will require medical attention and can be life threatening. The risk can be reduced through the use of **white blood cell growth factors** (Neulasta®); note that the use of this supportive medication is at the discretion of the physician who must weigh the benefits of Neulasta against its side effects. Despite use of Neulasta, there is still a risk of serious infection. About 50% of men will experience significant fatigue at some point in their therapy, usually for the first week of each cycle. About one-third of men will experience numbness or weakness in their toes or fingers that may interfere with function (**neuropathy**). This side effect is not always reversible, but in most cases resolves slowly over time. There are no treatments available to prevent neuropathy, but reducing the dose of docetaxel, delaying the next dose, or stopping treatment can slow neuropathy and potentially prevent it from progressing. It is important to talk with your doctor if you are developing neuropathy so that you can speak together about how to best handle further cycles of docetaxel.

Other side effects of docetaxel include low platelets which can result in bleeding (1%), anemia (5%), reduced heart function (10%), hair loss (65%), diarrhea (32%), nail changes (30%), loss of appetite (20%), shortness of breath (15%), and fluid retention (10% to 20%). Most of these are mild, reversible, and treatable, and should not be a reason to avoid chemotherapy if you need it.

Cabazitaxel, which affects blood counts, is almost always given with Neulasta to boost infection-fighting white blood cells because life-threatening infection due to a depressed immune system is the most serious side effect associated with this medication. A blood transfusion is sometimes necessary to treat anemia to combat the fatigue and shortness of breath related to low blood counts. Other possible side effects include: fatigue (37%), neuropathy (13%), shortness of breath (12%), headache (8%), hair loss



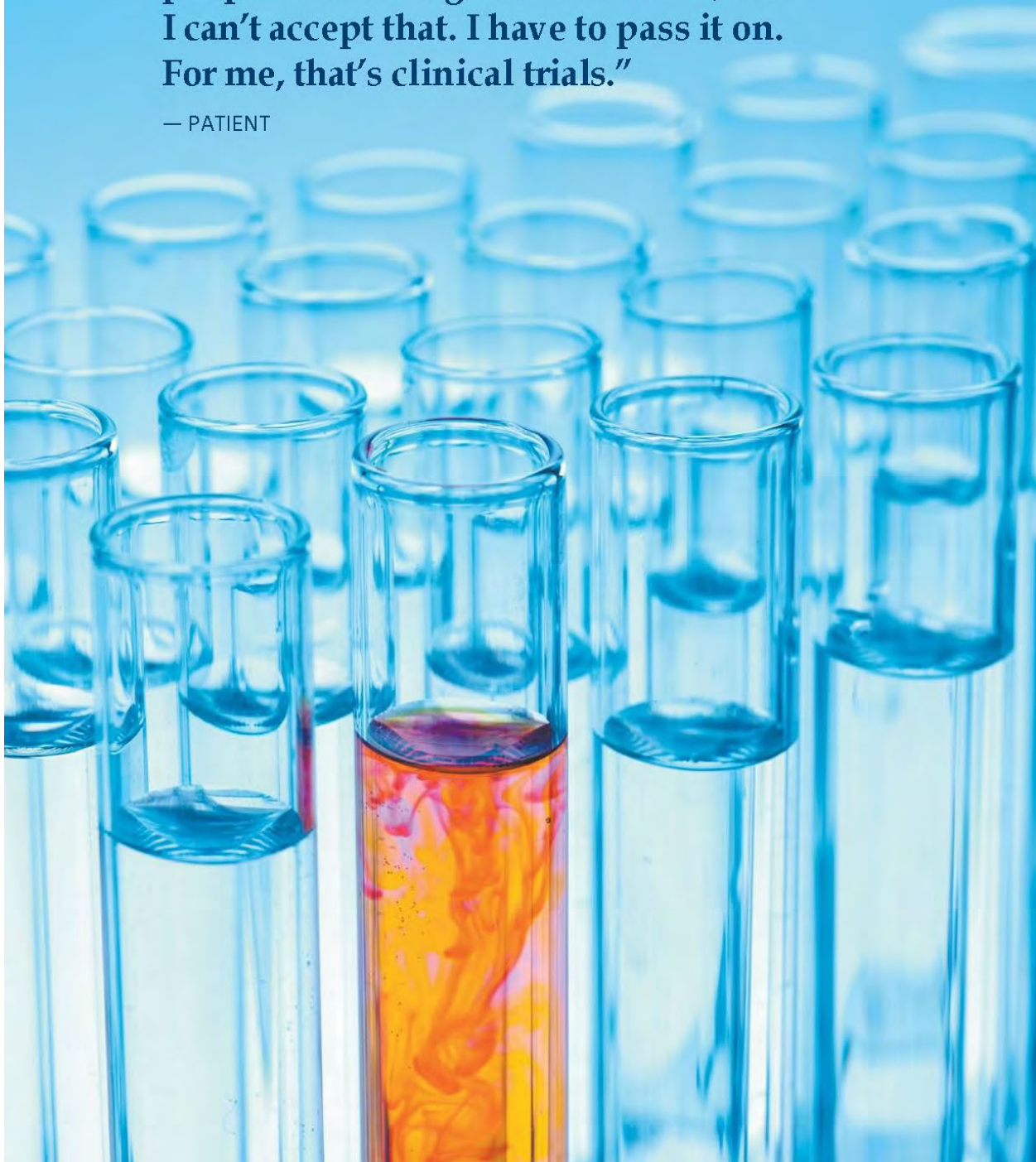
Reducing red meat and increasing daily consumption of cruciferous vegetables (such as broccoli, cauliflower, and Brussels sprouts) can help during ADT and beyond.

(10%), abdominal pain (17%), diarrhea (6%), and low blood pressure (5%). Based on trial results, the FDA now recommends a lower dose than was initially approved to improve tolerability for most patients; the dose can be increased in select patients.

Regardless of the type of chemotherapy you are receiving, you will be monitored very closely by doctors, nurses, and pharmacists to make sure that all side effects are being addressed. Many of these side effects, especially fever and inability to keep food/drink down, need to be addressed right away—don't wait until your next appointment to tell your provider.

“There’s no way for me to pay back the people who have gotten us this far, and I can’t accept that. I have to pass it on. For me, that’s clinical trials.”

— PATIENT



6 ► CUTTING-EDGE DEVELOPMENTS IN PROSTATE CANCER RESEARCH

See Appendix for 2020 COVID-19 Updates.

WHAT IS PRECISION MEDICINE?

Precision medicine uses new diagnostic tests to treat the right patient with the right medicine at the right time based on the unique biology of that patient's cancer. **The promise of precision medicine is this: someday, there will be no trial and error for prostate cancer drugs.**

Precision diagnosis is the process of looking at the genetic and molecular characteristics of your unique tumor (uniquely mutated genes and uniquely expressed proteins), and using this information to identify the tumor's weaknesses—think of it like taking your cancer's fingerprint. Once that level of identification is possible, custom selected treatments have the potential to be effective with less guess work. Since cancer is a “genomic” disease, that is, most cancers involve mutations of various genes, it makes precision oncology one of the most exciting fields in research today.

Because every cancer fingerprint can be different, each cancer needs a custom treatment.

By example, if you have advanced prostate cancer and conventional hormonal therapy is no longer working, you might be helped by a new treatment regime—but you might not. Now, instead of wasting precious time and money, and experiencing the side effects of therapies that will not benefit you, you can find out ahead of time if you should take one of these drugs by tests that use either tumor biopsies or your blood to analyze the genome and molecular make-up of your cancer.

DID YOU KNOW?

25-30% of metastatic prostate cancer patients have been found to have mutations in genes that repair damaged DNA (known as DDRs or DNA damage repair genes). These mutations have likely contributed to the tumor's development by allowing cells to accumulate more and more mutations, until they become cancer. New drug development for patients with DNA repair mutations is an active area of research for the Prostate Cancer Foundation.

Here's one example of just how precise the right treatment can be. Thanks to research funded by PCF, scientists have discovered a simple test to indicate whether your prostate cancer may be fueled by hormones produced outside of the testes, therefore decreasing the effectiveness of hormone therapy alone for you. About half of all men have a genetic variation called HSD3B1(1245C) that allows prostate cancer to make its own dihydrotestosterone from non-testicular sources. If you have low-volume advanced prostate cancer that is being treated with ADT or orchiectomy (so that testicular sources alone are blocked), your tumor may be more likely to become resistant more quickly if you have the more active HSD3B1(1245C) gene. You may want to talk to your doctor ordering genetic testing of your tumor to find out if you qualify, and about adding another hormonal therapy that might block the effects of the HSD3B1(1245C) gene and early progression.

Every day, more and more precision therapies are coming to [clinical trials](#), and hopefully, soon to market. Someday, the hope is that your cancer treatment will be 100% designed for your cancer, and it will be 100% effective. Unfortunately, some treatments may be so new that even your doctor isn't up to date on their availability. For the very latest information on emerging precision therapies, please visit pcf.org.

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EMERGING NEAR-TERM THERAPIES

There are nearly 1,000 ongoing clinical trials in prostate cancer just in the U.S. that are testing new therapies and therapeutic strategies. Worldwide, there are many more emerging therapies being tested in patients. Only a few of these will lead to practice-changing solutions for prostate cancer patients, new therapies, or improved ways to use therapies that have already been FDA-approved. There are however, several emerging therapies that have demonstrated highly promising results in clinical trials for the treatment of prostate cancer and should be noted. Consult your doctor to find out about getting into a clinical trial or to check the status of FDA approval.

PARP Inhibitors

PARP inhibitors, which include rucaparib (Rubraca[®]), olaparib (Lynparza[®]), niraparib (Zejula[®]), talazoparib (Talzenna[®]) and others, are a class of precision medicine treatments that are effective against breast and ovarian cancers with mutations in genes that repair damaged DNA and are now being tested in prostate cancer. These “DNA damage repair” (DDR) genes include the breast and ovarian cancer risk genes *BRCA1* and *BRCA2*. 25-30% of metastatic prostate cancer patients have these mutations in their tumors and may be candidates for treatment with PARP inhibitors.

PARP inhibitors are not yet FDA-approved for the treatment of prostate cancer, but several are now being tested in phase 3 trials (for more information on trial phases see [Clinical Trials](#) on page 72). In late 2019, a phase 3 clinical trial testing the PARP inhibitor olaparib (Lynparza) in patients with mCRPC and certain DDR mutations (particularly in the *BRCA2* gene) reported positive results, which may lead to FDA approval in the near future. Screening of metastatic prostate cancer patients to identify those who have DDR mutations and may benefit from treatment with PARP inhibitors will likely soon become a standard of care.

In addition to olaparib, three other PARP inhibitor drugs are currently in phase 3 clinical trials in

prostate cancer: rucaparib, talazoparib, and niraparib. Trials are also testing PARP inhibitors in all prostate cancer patients (regardless of the presence or absence of DDR gene mutations) and in combination with other treatments, including immunotherapies and radionuclide therapies.

Notably, about 12% of men with metastatic prostate cancer have inherited DDR gene mutations. Men with metastatic prostate cancer should strongly consider [genetic testing](#) and counseling, as inherited DDR mutations may have treatment implications, and may be associated with an increased risk of other cancers.

There are options for early detection and prevention for some cancers including prostate, breast, ovarian, pancreatic, and colon.

In addition, this information may be critically important for blood relatives, because they may also have inherited the same cancer risk gene mutation.

Inherited gene mutations can cross many forms of cancer—including but not limited to prostate, breast, ovarian, colon and pancreatic. For this reason, it is very important to both learn and share with your doctor what cancers have occurred in other members of your family. It is also important to talk with your family about your own diagnosis, if you feel comfortable. See also the section on [Prostate Cancer Genes in Families](#) on page 77.

PSMA Radionuclide Therapy

PSMA, prostate membrane-specific antigen, is a protein that is found at high levels on the surface of prostate and prostate cancer cells. PSMA radionuclide therapy is a new type of treatment consisting of radioactive molecules injected into your bloodstream that specifically seek out and destroy prostate cancer cells using PSMA to target the cancer. These agents (referred to as “radiopharmaceuticals”) are available in clinical trials. For instance, ¹⁷⁷Lu-PSMA-617, the agent in this class which is furthest along in clinical development, is currently being tested in an international phase 3 trial.

CASE STUDY: HOW GENES AND TREATMENTS ARE BEGINNING TO WORK ACROSS CANCER TYPES

In prostate cancer, we currently have experimental treatments in the works for dozens of genes, but only one treatment that is FDA-approved based on a mutation found in tumors—pembrolizumab (Keytruda®) for microsatellite instability (MSI) or mutations in a mismatch repair (MMR) gene. MMR genes are proteins that work to proofread and edit DNA to prevent mistakes that can lead to mutations and cancer. Defects in MMR gene function can be detected through laboratory-based tumor testing of MSI or special marker stains of tumor material. While only about 5% of advanced prostate cancer patients have MSI, approximately 15% of colon cancer patients do. Because testing for MSI was first developed and optimized for colon cancer, not all MSI tests may detect all prostate cancer with MSI; talk to your doctor about more precise testing.



Everything about you—from your cancer to your immune system to the bacteria that inhabit your body—is unique. More and more, scientists are thinking of cancer treatment as a personalized plan.

THE FUTURE LANDSCAPE OF PROSTATE CANCER PRECISION THERAPY

A few of the most exciting emerging therapies, which are currently being tested in clinical trials, are discussed below.

Precision Screening

The advent of precision medicine will enable patients to have their tumors profiled for mutations that render them sensitive to certain therapies. Clinical trials are being conducted to test therapies that target mutations in genes including PTEN, PIK3C, AKT, RAF, Wnt, CDK12, IDH1, RB, and others. Investigations into the efficacy of therapies targeting these mutations are only just getting started, and many of these investigational agents will only be offered at select treatment centers—typically academic institutions.

All men with metastatic prostate cancer are now encouraged to speak with their physician about genetic screening to determine whether they may carry any actionable inherited or acquired mutations.

Immune Checkpoint Inhibitors

Immune checkpoint inhibitors are a class of immunotherapy that activate tumor-killing immune cells. Checkpoint immunotherapy alone (not in combination with other treatments) may only work for a subset of prostate cancer patients, and studies are underway to determine how best to identify these men. In 2017, the FDA approved the checkpoint inhibitor pembrolizumab (Keytruda®), for patients with solid tumors that have mutations in mismatch repair genes (MMR) and/or exhibit microsatellite instability (MSI). Recent studies suggest that advanced prostate cancer patients whose tumors have lost both copies of the *CDK12* gene may respond to checkpoint immunotherapy.

Many studies are underway in prostate cancer to test other checkpoint inhibitors, including pembrolizumab, ipilimumab (Yervoy®), nivolumab (Opdivo®), durvalumab (Imfinzi®), atezolizumab (Tecentriq®), and avelumab (Bavencio®) alone and in combination with various

therapies including PARP inhibitors, cancer vaccines, and radiation therapy.

CAR T Cells

CAR T cells (“chimeric antigen receptor”) are T cells taken from a patient and genetically engineered to target and kill tumor cells. CAR T cells targeting prostate cancer began testing in phase 1 clinical trials in 2017.

PROSTVAC

There are many strategies to activate the immune system to target and kill prostate cancer. One strategy is the use of **cancer vaccines**, which instruct immune cells to identify and kill cells that express certain prostate cancer-associated proteins. PROSTVAC is a vaccine that activates the immune system to target prostate specific antigen (PSA), a protein specifically expressed by prostate cancer cells (same PSA as in the PSA test). PROSTVAC has not shown efficacy as a single agent in clinical trials, but is currently being tested in combination with other therapies.

Microbiome

The microbiome is the collection of microorganisms living in your body and, in particular, your gut. So, what’s that got to do with cancer? New research is revealing that it could be a lot. Studies suggest that the gut microbiota can affect the immune system and may influence how well patients respond to certain cancer treatments. Doctors now think that for your body to stay healthy and cancer-fighting, it’s important to have the right diversity of bacteria in your gut, but there’s still a lot to learn about how this translates to improved patient outcomes. Exploring the relationship between your microbiome and cancer is an active area of research for the [Prostate Cancer Foundation](#).

CLINICAL TRIALS: HOW TO GET INVOLVED

Finding new treatments, and how to best use new treatments, is the work of clinical trials. As just one example, the first 500 men cured of what was thought to be incurable advanced prostate cancer are likely to be cured on a new clinical trial, even before it is FDA-approved.

Clinical trials are the place where patients go to “be there for a cure.”

In clinical trials, researchers test the hypothesis that a certain treatment may be effective for patients, under certain conditions. Clinical trials bring life-extending and curative new treatments to cancer patients. Clinical drug trials play a vital role in moving new treatments to patients who need them most, securing data so that FDA approval can be obtained and new drugs can move into widespread clinical practice.

Moreover, for all the promising treatments that have emerged in cancer research in the last several years, there’s still a huge task of figuring out exactly the right way to use them. For example, what are the best doses for optimum response? At what time during disease progression and treatment do we insert a drug into the regimen?

There are currently over 140 phase 3 trials and more than 650 phase 1 and 2 trials related to prostate cancer treatment in progress in the United States alone. These trials focus on the full breadth of the prostate cancer experience, looking at everything from better treatments for localized prostate cancer, to life-prolonging drugs for advanced disease, to lifestyle and prevention changes which can improve the lives of patients and their families. Treatments that are approved will further improve outcomes for patients and join the multiple life-extending and life-improving therapies that are already in use.

Drugs for Advanced Prostate Cancer

There are currently more than 20 drugs FDA-approved for the treatment of advanced prostate cancer. As an example of the efficacy of clinical trials, remember that all of them had to go through phase 1, 2, and 3 clinical trials in order to receive FDA-approved designation. Of these drugs, 9 were developed with direct early-stage support from the Prostate Cancer Foundation. To support life-saving cancer research, you can make a donation at [pcf.org](#).

Treatment	Approved for Treatment of Prostate Cancer
Estramustine	1981
Leuprolide acetate	1985
Flutamide	1989
Bicalutamide	1995
Mitoxantrone + prednisone	1996
Nilutamide	1996
Goserelin acetate	1998
Triptorelin	2001
*Zoledronic acid	2002
*Docetaxel	2004
Histreltin acetate	2004
Degarelix	2008
Cabazitaxel	2010
*Sipuleucel-T	2010
*Denosumab	2010
*Abiraterone	2011
*Enzalutamide	2012
*Radium-223	2013
Pembrolizumab	2017
*Apalutamide	2018
*Darolutamide	2019

*PCF supported

In 1996, in response to a critical unmet need for clinical trials in prostate cancer research, PCF created the Therapy Consortium. In 2005, PCF partnered with the Department of Defense to transform this organization into the Prostate Cancer Clinical Trials Consortium. Since 2006, consortium members have enrolled more than 8600 men with prostate cancer in over 230 trials. To find out what clinical trials are available specifically for prostate cancer, go to pcf.org/trialfinder.

GET INVOLVED!

Patients who participate in clinical trials become citizen scientists, providing an invaluable service both to treatment science and fellow patients.

If you are considering a clinical trial, speak to your doctor about the potential benefits of participating in a trial so you can make an informed decision that is best for you. **Remember: A common misconception about clinical trials is that the “placebo” group gets no treatment at all; in fact, they often still receive the minimum standard of care.**

Clinical Trials

To achieve FDA approval, all new treatments must typically pass through 3 phases of testing.

Phase 1: Test a new agent on a small number of subjects for overall safety and to find the appropriate dose that can be safely given with acceptable side effects.

Phase 2: Determine if a therapy has any activity against the cancer and can prevent tumor growth, progression, extend a patient's life, or relieve symptoms.

Phase 3: Compare promising treatments from phase 2 against standard treatments to determine if the test treatment works better and has fewer or more manageable side effects. Phase 3 trials are typically large (hundreds of patients), randomized (each patient is randomly assigned to the standard treatment or the test treatment), and sometimes blinded (the patient and/or doctors are not told which treatment the patient is getting as a way to control for the “placebo effect”).

Phase 4: Approved drugs are continually monitored for safety and efficacy.

**"I needed my children to be well and
live their lives happily, while at the same
time being aware of what was going on."**

— PATIENT



7 ► FOR OUR SONS, DAUGHTERS & GRANDCHILDREN

See Appendix for 2020 COVID-19 Updates about Prostate Cancer Screening.

THE GENETICS OF RISK

In the last 25 years, several **hereditary mutations** (genetic mutations that run in families) have been discovered that may increase the risk of developing certain cancers. The most famous that you may have heard of are the *BRCA1* and *BRCA2* mutations that increase risk for breast and ovarian cancer.

Prostate cancer has long been recognized to have a familial component. In fact, of all human cancers, prostate cancer is the most common among family members, with 40% of prostate cancer attributable to genes that run in families. If you have received a prostate cancer diagnosis, it's important to speak with your family about risk, prevention, and screening. Having a father or brother with prostate cancer increases a man's risk of developing prostate cancer. The genes that cause this risk have been extensively studied and are complex.

SCREENING FOR PROSTATE CANCER

If you're reading this guide, it's probably because you've already been diagnosed with prostate cancer.

Because we now know so much about the relationship between genetics and risk, it is our hope that readers will immediately consider these issues in consultation with their extended family.

Should My Family Members Be Screened?

The question of screening is a personal and complex one, which may be further complicated by family history. It's important for each man to talk with his doctor to assess at what age prostate cancer screening might be appropriate.

Revisiting Family Risk

If a family history of prostate cancer or genetic predisposition exists, it is all the more important that your family understands the full picture of risk related to prostate cancer. There are 4 major factors that influence one's risk for developing prostate cancer. Since prevention can hinge on appropriate screening—neither too early, nor too late—it's important to understand your personal risk profile.

Age: The risk of prostate cancer increases with age. The average age at diagnosis of prostate cancer in the United States is 69 years, which is likely reflective of recommended screening patterns.

Race: African Americans are more likely to develop prostate cancer and have more than twice the risk of dying from it.

Family history and germline (inherited) genetic mutations: A man with a father or brother who developed prostate cancer may have a twofold-increased risk for developing it. This risk is further increased if the cancer was diagnosed at a younger age (less than 60 years of age) or affected 3 or more family members. You should discuss with your doctor if you have a family history of not only prostate cancer, but also breast cancer, ovarian cancer, colon cancer, or pancreatic cancer. Certain inherited gene mutations may be associated with the development of prostate and other cancers. See Prostate Cancer Genes in Families on page 77.

Where you live: Consider this: Men who live north of 40 degrees latitude (north of Philadelphia, Pennsylvania, Columbus, Ohio, and Provo, Utah) have the highest risk for dying from prostate cancer of any men in the United States—this effect may be mediated by inadequate sunlight, which reduces vitamin D levels. Similar results were found in Sweden, which is also a high-risk country for prostate cancer: Immigrants to Sweden had a lower risk compared with native-born Swedes but, interestingly, the difference diminished the longer they were in Sweden.

Prostate cancer is over 8 times more common in Western culture than in Asia; moreover, when Asian men migrate to western countries the risk of prostate cancer increases over time. Why? Genetics, environment and lifestyle factors, and screening protocols may all play a role. Researchers are now looking at prevention strategies which may shed light on this mystery.

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There is ongoing debate about the risks and benefits of prostate cancer screening. Benefits include early detection that could offer a better chance to cure the disease if your cancer warrants treatment. It also may inform you that you don't need your prostate cancer treated at all.

On the other side of the argument is concern with overtreatment. Because most prostate cancers grow very slowly, the side effects of diagnosis (a prostate biopsy) and treatment of low-risk prostate cancers could outweigh any benefit that might be gained.

The U.S. Preventative Services Task Force (USPSTF) is an independent panel of experts that issues recommendations on disease screening. In 2018 the USPSTF issued an updated recommendation for prostate cancer screening, which recommends shared decision-making about PSA screening. Since the potential benefits and harms of PSA-based screening are closely balanced in men ages 55 to 69 years, the decision to screen should be an individual one. For men age 70 years and older, USPSTF continues to recommend against screening for prostate cancer, with the rationale that potential benefits do not outweigh the harms. For more info on the latest U.S. Preventative Services Task Force recommendations visit pcf.org/uspstf-faqs.

Other professional organizations, such as the American Society of Clinical Oncology, National Comprehensive Cancer Network, and the American Urological Association, also recommend shared decision-making about PSA screening. They maintain that PSA screening should be considered in the context of a man's life expectancy, family history, ethnicity, and other medical conditions. Experts agree that there is no role for PSA screening in men expected to live less than 10 years, since the rigor of some treatments and side effects can actually lessen life expectancy as well as quality of life.

BEGIN TO TALK TO YOUR DOCTOR ABOUT SCREENING AT AGE

40 ▶ If you have a family history of prostate or other cancers in a first-degree relative, are African American, or have known *BRCA 1/2* mutations

45 ▶ If you have no history and you are not African American

When to Start—and Stop—Screening

Regardless of your age, the Prostate Cancer Foundation recommends that you practice “precision screening,” and consult with your doctor to come up with a personal screening plan that’s right for you. Go to pcf.org/screen and use the screening tool as a guide to start a conversation with your doctor.

Be proactive: there is no “one-size-fits-all” approach to screening,

For men with a family history of prostate, breast, ovarian, pancreatic, or colon cancer in a first-degree relative, begin a conversation with your doctor at age 40. Because African American men are more likely to have aggressive disease, it is recommended that they begin the conversation at age 40 as well. Lastly, because we now know that genes that run in families can affect prostate cancer risk, if you have a personal or family history of *BRCA1* or *BRCA2* mutation (most infamously responsible for hereditary breast cancer), begin discussions about screening at age 40, or, better yet, consider a clinical trial for early detection of prostate cancer. For average-risk men, the National Comprehensive Cancer Network recommends starting this discussion at age 45. Shared decision-making (or a discussion of the pros and cons of screening) is an important part of the process. For most men over the age of 70, the USPSTF recommendation to discontinue screening may be appropriate. Research is ongoing to further illuminate the benefits and harms associated with screening in men above the age of 70.

If you are a healthy man over 70, be sure to discuss continued screening with your doctor.

Screening and Biopsy Decisions

PSA screening may reveal results that prompt a doctor to recommend a biopsy. However, the result may create more confusion if the PSA is mildly elevated. Fortunately, there are many other supplementary tests and considerations that can help a man who is undergoing screening decide whether a biopsy is necessary, including:

- Digital rectal exam results
- Free PSA test (<10% Free PSA indicates greater risk of having cancer)
- PSA velocity or the rate of rise over time (faster increases mean more risk)
- PSA density, or the PSA per volume of prostate (higher density means more risk)
- PSA-based markers (for instance the Prostate Health Index, 4K score)
- EPI test score >15.6
- Other markers, a urinary PCA3 or SelectMDx test
- MRI of the prostate

It should be noted that these recommendations apply only to screening—testing of healthy men without symptoms. Once the diagnosis of prostate cancer is confirmed by biopsy, PSA is used for monitoring the status of the cancer, and the interpretation of results depends on how the cancer is managed. Discuss these individual tests with your doctor to make screening decisions that are best for you.

PROSTATE CANCER GENES IN FAMILIES

For most patients, it is thought that multiple genes together lead to the highest risk. However, we have recently learned that there are certain relatively rare genes that run in some families that, when present, may increase a man's risk of developing prostate cancer; in some cases, these genes lead to the more aggressive forms of prostate cancer. In 2016, a PCF-supported study of men with metastatic prostate cancer found that more than 10% have inherited mutations in cancer risk genes such as *BRCA1*, *BRCA2* and at least 18 other newly-discovered genes that may be important to risk of prostate cancer and other types of cancer.



We now know: some of the same genes that are responsible for prostate cancer are also responsible for cancers in daughters.

Over 20 different genes have been identified that run in families with prostate cancer (hereditary prostate cancer).

Because many of the genes and cancer pathways that drive prostate cancer occur across other cancers, PCF's work now has overlap in at least 70 other cancers (see chart on page 80). This is important because it highlights that men should be aware of their family history of all cancer—i.e. not just prostate cancer, but also breast, ovarian, pancreatic, leukemia, and other cancers. Having a sister with breast cancer diagnosed at an early age (for example, in her 40s or younger) may be valuable information for a man to know and share with his doctor. Conversely, your prostate cancer may imply a high cancer risk for both your male and female family members.

There can also be other mutations that occur after birth which drive cancer development and progression. Scientists have identified over 97 of these “somatic mutations” implicated in prostate cancer.

Do You Carry A Genetic Mutation?

All men with metastatic prostate cancer are now encouraged to speak with their physician about determining whether they carry an inherited cancer risk mutation. Talk to your doctor about a referral to a genetic counselor if you have any of the following risk factors that may indicate the possible presence of a hereditary cancer-risk mutation:

- ▶ Personal history of metastatic prostate cancer
- ▶ Lymph node-positive prostate cancer or intraductal carcinoma on biopsy
- ▶ Blood relative with a known cancer risk gene (eg, *BRCA1*, *BRCA2*, Lynch syndrome)
- ▶ Two or more family members with prostate cancer at Gleason ≥ 7 (Grade Group ≥ 2)
- ▶ One male relative with metastatic prostate cancer and/or who died from prostate cancer
- ▶ Ashkenazi Jewish ancestry
- ▶ Three or more family members on the same side of the family with one or more of the following cancers: breast cancer, ovarian cancer, pancreatic cancer, colon cancer, melanoma, or multiple other cancers

“CASCADE” GENETIC TESTING

Different from standard PSA screening for prostate cancer, cascade genetic testing is a form of screening that identifies whether family members share a genetic mutation. For example, if a man discovers that he is a carrier of an inherited mutation in the *BRCA1*, *BRCA2*, or other genes that increase risk for prostate cancer, this has critical implications for all his family members. If male family members have inherited the same mutation, they may be at increased risk for prostate cancer and other cancers such as male breast and pancreatic cancer. And if female family members have inherited these mutations, they may be at increased risk for pancreatic, breast, ovarian, and endometrial cancer. These mutations may also increase risk for other cancers, depending on the gene.

Men who find they are gene mutation carriers should talk with a genetic counselor to encourage “cascade”

WHAT DO WE KNOW ABOUT PROSTATE CANCER GENES?

Researchers are beginning to categorize genes for prostate cancer by whether they increase your risk of getting the disease or they increase the aggressiveness of advanced disease.

(i.e. setting off a cascade of events) genetic counseling and testing for male and female family members, to assess whether they, too, are carriers of the mutation and are at increased risk for certain cancers.

Family members who learn that they are carriers need to discuss their findings with genetic counselors and their doctors to better understand their cancer risks, options for early detection, and how to reduce risk for various other forms of cancer.

There may be sufficient information about certain gene mutations to recommend more frequent screening for specific cancers in family members. However, the information about other gene mutations may be less well-established, or tests may identify variants of uncertain significance. These may require further discussion with a genetic counselor. Patients and families with these types of mutations may consider participating in research registries to help doctors and researchers learn more about those specific variants.

For some genes which are better studied, there may be clear screening recommendations and risk-reduction strategies. However, these decisions must be made with a well-informed genetic counselor and physician. While this information can have important benefits, it can also cause unnecessary worry and/or medical procedures if the family members or doctors are not fully informed. Early detection and management of cancer risk is a very specialized field. It is strongly recommended that families consider consulting doctors at a top-tier or academic medical center that is actively engaged in the latest research and treatments to get the most updated information, recommendations and the best medical plan if they are found to have a cancer risk mutation.

THE NUANCES OF GENETIC SCREENING

Many genetic testing companies are offering services to find hereditary mutations in cancer-associated genes. It is critical to be aware that **the risk for any given cancer associated with any given mutation is not always clear.** There are several well-studied mutations that researchers believe are more often present in patients with cancer. However, there are many more mutations that are less well studied, but have been observed in cancer patients, and therefore have some association with risk that is not yet well understood. Importantly, there are many more variants of “unknown significance,” where we do not yet know whether they confer a change in the gene that is sufficient to increase cancer risk or is simply a neutral variant.

WHAT'S THE DIFFERENCE BETWEEN GENETIC SEQUENCING AND TUMOR SEQUENCING?

Genetic sequencing (also known as germline genetic testing) uses a blood test or saliva test to look only for hereditary or inherited cancer risk mutations—those that you inherited from your mother or father that may increase your risk for developing cancer.

Tumor sequencing (also known as somatic sequencing) is performed on cancer samples obtained from biopsies, surgery, or blood tests. Your tumor may contain mutations that are inherited or have been acquired during disease progression. This test is usually performed for the purpose of treatment decision-making.

Because both kinds of testing have the potential to suggest presence of inherited mutations, it is important to consider whether knowing more about inherited cancer risk is important to you and your family.



The same gene errors that PCF is researching for prostate cancer apply to 7 of the top 10 pediatric cancers (so far).

How To Get Genetic Counseling and Testing

If you or someone in your family has been treated for prostate cancer, your family's urologist or oncologist may have a recommendation for a local genetic counselor and testing center. You can also find a list at the National Society for Genetic Counselors: www.nsgc.org. There are also telehealth genetic counseling services available.

If your genetic testing returns a result with a pathogenic variant—that is, you have an inherited gene mutation implicated in prostate cancer risk or growth—it is important to consult with your doctor and seek genetic counseling. Remember, new clinical trials and studies are emerging regularly to find new treatments that might be relevant for you. Go to pcf.org/news for more information on the latest research and drug approvals.

COMMERCIALLY AVAILABLE GENETIC TESTING SERVICES

Whenever possible, we encourage discussion with a genetic counselor and/or your doctor to help you understand which tests are most appropriate for you, what they mean, and how they affect your care—ideally before you take such a test. There are also telehealth genetic counseling services increasingly available. After gathering information and understanding benefits, risks and limitations of testing, you may ultimately choose to proceed with commercially available clinical testing. Several companies offer germline genetic testing for cancer-related inherited genetic mutations, which have the benefit of accessibility. Out-of-pocket costs vary (often in the range of \$250-\$350, depending on the number of genes in the panel). Consumers use a kit to submit a saliva sample. However, more genes is not always better, and can sometimes lead to more questions than answers, so we encourage discussion with your providers before choosing a test. Whether the test is covered by insurance depends on your insurance benefits. Consumers receive a report with their results and are encouraged to discuss with their healthcare provider, if they have not done so already. Access to a genetic counselor by telephone before or after the test may be included in the fee. Three such companies are:

Color: Offers panels (in 3 different sizes) of genes involved in hereditary cancers, including at least 11 genes implicated in prostate cancer.

Invitae: Offers a Cancer Screen panel of at least 61 genes to assess the risk of hereditary cancer, including prostate cancer.

Ambry: Offers panels for several specific cancers, including prostate cancer, as well as larger, more comprehensive panels.

Of note, recreational tests (such as 23andme) should not be considered an adequate substitute for comprehensive genetic testing for inherited cancer risk mutations.

PCF'S IMPACT ACROSS ALL CANCERS

Particularly for men with advanced or aggressive disease—that is, whose disease is most resistant to standard treatment—biomarker- or gene mutation-directed therapies may be unusually effective. PCF believes that gene targets and pathways may be the bridge to unlocking treatments for all cancer, not just prostate cancer. PCF research in prostate cancer has been able to add to the conversation on tumor mutations in more than 70 other forms of cancer.

- | | | | | |
|-------------|---------------|-----------|------------|---------------------------|
| ▶ Brain | ▶ Thymus | ▶ Kidney | ▶ Blood | ▶ Ovary |
| ▶ Eye | ▶ Lung | ▶ Colon | ▶ Sarcoma | ▶ Uterus |
| ▶ Lip | ▶ Liver | ▶ Bladder | ▶ Prostate | ▶ Childhood brain cancer |
| ▶ Neck | ▶ Stomach | ▶ Rectum | ▶ Testicle | ▶ Childhood blood cancer |
| ▶ Thyroid | ▶ Gallbladder | ▶ Skin | ▶ Breast | ▶ Childhood kidney cancer |
| ▶ Esophagus | ▶ Pancreas | ▶ Nerve | ▶ Cervix | |

THE FUTURE LANDSCAPE OF CANCER

For years, doctors focused on cancer as an organ-site disease, e.g. you had breast cancer, or colon cancer, or prostate cancer, etc. Thanks to some significant discoveries funded by PCF, we now know cancer is too complex to be studied in a single site in the body. Cutting-edge research is now targeting the mechanisms cancer uses to grow, which may be shared across many cancer types. In treating prostate cancer, PCF will likely impact hundreds of forms of disease, including most major forms of cancer in children.

For more information visit impact.pcf.org.

PREVENTION

The ultimate goal is to prevent men from ever developing prostate cancer. Although significant progress has been made, the evidence is not strong enough to form conclusive recommendations on how to prevent prostate cancer. Note that screening does not lead to prevention, but only to earlier detection.

DIET AND EXERCISE

Improvements in diet and exercise are among the most commonly accepted strategies for prevention. This remains an active area of investigation with numerous ongoing studies examining the impact of medications, supplements, diet and exercise on prostate cancer risk.

As a critical prevention strategy, it is important to share these diet and exercise tips with family members who may be at risk.

For those with a family history of prostate cancer, it's important to make some preemptive, permanent lifestyle changes to maintain the best possible health.

Beyond genetics, diet and exercise are believed to be two of the major risk factors for prostate cancer. There is much hope on the horizon for men with prostate cancer and their families. Continuing to be prudent with regard to risk factors, screening recommendations, and diet



Fish, berries, cooked tomatoes, and broccoli may act as anti-inflammatory foods to help protect your prostate health.

and exercise changes can help men with prostate cancer live longer and better lives. For more information, download PCF's cancer prevention and wellness guide at pcf.org/guides.

In closing, although living a healthy lifestyle and eating right are good for you, they will not eliminate your risk of prostate cancer, nor will they cure you by themselves if you are diagnosed with prostate cancer. If you are age 45 or over, or if you are age 40 or over and African American or have a family history of prostate cancer, regular exercise and a good diet are even more critical for reducing risk; consider regular PSA tests, and, if indicated, rectal examinations, and discuss the risks and benefits of these screening procedures with your doctor.

Remember: Every patient is unique. Be sure to take these general guidelines and discuss all available options, information, and questions with your physician.

► CHECKLIST: LIFESTYLE CHANGES FOR PROSTATE CANCER PREVENTION

- ☐ Adopt an “anti-inflammatory diet,” low in red meat, sugar, processed foods, and dairy products, and high in foods that fight inflammation, like some of those listed below.
- ☐ Eat fewer calories AND exercise more to maintain a healthy weight. Vigorous exercise, within the bounds of safety for your personal physical fitness level, has been shown to reduce a man’s chance of developing lethal forms of prostate cancer.
- ☐ Watch your calcium intake. Do not take supplemental doses far above the recommended daily allowance. Some calcium is okay, but avoid taking more than 1200 mg of calcium a day.
- ☐ Eat more fish—evidence from several studies suggest that fish can help protect against prostate cancer because they have “good fat,” particularly omega-3 fatty acids. Avoid trans fatty acids (for example, margarine, microwave popcorn, packaged baked goods).
- ☐ Try to incorporate cooked tomatoes, whose high lycopene content may help to protect against the cellular damage associated with cancer.
- ☐ Cook with extra virgin olive oil. Consider 1-3 tablespoons per day, depending on your size. Make sure you use the first pressed “extra virgin” oil.
- ☐ Incorporate cruciferous vegetables (like broccoli and cauliflower) into many of your weekly meals. Recently, a study found that eating broccoli can help shift your intestinal flora away from the types of bacteria that are related to prostate cancer.
- ☐ Soy has been a topic of some health debate, but recent research suggests that eating soy is associated with a lower risk of prostate cancer.
- ☐ Green tea’s high antioxidant properties may be beneficial in warding off cancer.
- ☐ Avoid smoking for many reasons. In particular, a recent study revealed that men who smoked during prostate cancer treatment had a higher likelihood of metastasis.
- ☐ Drink alcohol in moderation. If you do drink, try one glass of red wine per day. Red wine contains resveratrol, which has been shown to possibly have cancer-fighting properties.
- ☐ Enjoy coffee, if you drink it. A recent study has shown that drinking 3 cups per day of unfiltered “Italian style” coffee may lower your risk for prostate cancer.
- ☐ Seek medical treatment for stress-related conditions, high blood pressure, diabetes, high cholesterol, and depression. Treating these conditions may save your life and will improve your survivorship with prostate cancer.
- ☐ Avoid over-the-counter supplements. While a multivitamin is not likely to be harmful, you probably don’t need it if you follow a healthy diet with lots of vegetables, whole grains, fish, and healthy oils. Ask your doctor about herbal supplements, as some may harm you or interfere with treatment.
- ☐ Relax and enjoy life. Studies have shown that the stress hormone cortisol can interfere with cancer cell death. Reducing stress in the workplace and home will improve your survivorship and lead to a longer, happier life.

Basic Sofrito Recipe

Sofrito is a tomato-based sauce that is used as a base in cooking in many cultures. The lycopene in cooked tomatoes may act as a protective antioxidant. Add that to the latest research on olive oil and you’ve got a great cancer-fighting food.

This base recipe can be multiplied or modified with different herbs and spices, to transport it across the globe.

- 1 pound of tomatoes
- 1 medium onion
- 1 red pepper
- 3 cloves of garlic
- 1/3 cup of extra-virgin olive oil
- Fresh herbs to taste
- Salt, to taste

Finely chop all ingredients. Heat oil and add everything at once to the pan. Cook 20-30 minutes. Let cool, and refrigerate or freeze.





APPENDIX: YOUR CARE DURING THE COVID-19 PANDEMIC

In the past couple of years, updates to this guide have included everything from PSA screening, to active surveillance, to genetic testing, to new drug approvals for patients with advanced prostate cancer. No one could have predicted that our 2020 update would need to cover cancer care during a global pandemic.

There are currently several factors affecting the care of cancer patients. First, doctors are concerned about inviting patients to appointments and treatments in a healthcare setting where they may be exposed to the coronavirus. This goes double for patients whose immune system is weak for any reason, whether they have prostate cancer or not. Some of the biggest risk factors for COVID-19-related suffering often overlap with men who have prostate cancer, which include older age, male gender, having cancer, and comorbid conditions, such as high blood pressure, heart disease, diabetes, and obesity.

As if that wasn't enough, a shortage of personal protective equipment (PPE) for both doctors and patients compounds the issue. Medical centers have had to reallocate resources—from providers to PPE to hospital beds—to care for infected patients, resulting in delays of less-urgent care.

This situation has undoubtedly caused some anxiety for men with prostate cancer and their families. Depending on where you live in the country, everything from routine PSA screenings to advanced treatment may have been delayed. The Prostate Cancer Foundation (PCF) immediately adapted our patient materials and research priorities to help patients and doctors make the best choices possible in unusual times.

This Appendix addresses possible changes to your prostate cancer treatment during the pandemic. Please remember that these are general principles. Resource availability and the impact of COVID-19 on prostate cancer care may be highly variable depending on your location. Some medical offices and cancer centers may be open and relatively unaffected, while others are limiting procedures and in-person appointments. You should contact your doctor—by telephone or email, if an in-person appointment is not possible—to discuss your particular situation. As the situation is rapidly evolving, we suggest you also check back frequently at pcf.org/COVID-19 for updated resources as well as subscribing to our [newsletter](#) for breaking updates.

WHAT COVID-19 RESEARCH IS LEARNING FROM PROSTATE CANCER

Men are 2-3 times more likely to die of COVID-19 than women. A recent PCF-funded study found that men with prostate cancer who were taking ADT were 4 times less likely to be infected, and 5 times less likely to die. What's the connection? It may be a protein called TMPRSS2, which naturally occurs on the surface of cells in the prostate, lungs, and elsewhere. The virus uses this protein to help enter lung cells, leading to infection.

PCF has funded millions of dollars of research into TMPRSS2 and prostate cancer over the past 2 decades. Because of this work, we know that TMPRSS2 is regulated by male hormones such as testosterone, and that in about half of all prostate cancer patients, TMPRSS2 is a key factor that drives prostate cancer. Higher testosterone levels may lead to more TMPRSS2 on cells, leaving men at greater risk.

As the pandemic unfolded, PCF researchers began applying their years of collective knowledge about TMPRSS2 and collaborating with infectious disease experts. One strategy to combat the virus may be to give a single dose of ADT to men—without prostate cancer—who are infected with COVID-19. Temporarily lowering testosterone levels may decrease the amount of virus entering lung cells. Thanks in part to the longstanding partnership between PCF and the VA, clinical trials are quickly getting underway at VA hospitals in LA, Seattle, and New York City.

SCREENING AND DIAGNOSIS

In April, the National Comprehensive Cancer Network (NCCN) updated their guidelines to suggest avoiding routine prostate cancer screening in men with no symptoms. Routine screening includes a PSA blood test and digital rectal exam (DRE). Check with your doctor; he or she may recommend waiting several months until there is more public health coronavirus testing and the local risk of coronavirus transmission is lower. If your screening is postponed, don't forget to revisit this later—put a reminder on your calendar to call your doctor in a few months.

If your PSA is high or your DRE is abnormal, NCCN recommends postponing further testing for a few months. However, if your doctor suspects that your cancer is particularly aggressive, they may opt to continue with imaging and/or a biopsy, and you should follow that advice.

TREATMENT

NCCN also released guidelines on prostate cancer treatment that consider the risk of COVID-19 infection to patients as well as the new demands on healthcare systems. These guidelines are based on published studies and input from experts at many nationally-recognized cancer centers.

In a nutshell, guidelines say that a relatively brief delay (less than 4 months) in treatment is unlikely to make prostate cancer worse. Remember, in most cases, prostate cancer is slow-growing. Until there is more information about how to protect prostate cancer patients from infection, the safest thing to do may be to stay distant from health care facilities that are treating large volumes of COVID-19 patients.

In the following sections we break down these recommendations based on the stage of your cancer journey.

Localized/Locally Advanced Prostate Cancer

If you have been diagnosed with localized or locally advanced prostate cancer (cancer that has not spread outside the prostate or the region around it), your risk of infection with COVID-19 is not higher. Risks at this stage of prostate cancer are the same as they are for the general population.

Treatment options for localized prostate cancer include:

- ▶ Active surveillance (scheduled monitoring, with treatment only if the cancer starts to progress)
- ▶ Surgery
- ▶ Radiation therapy
- ▶ Androgen deprivation therapy (ADT, also known as hormone therapy)
- ▶ A combination of these methods

The choice of therapy often depends on your risk group, which ranges from very low to very high risk. At this time, for low, very low, and favorable intermediate-risk patients, NCCN recommends deferring further staging, monitoring, active surveillance, or treatment. Studies have not shown a risk in delaying treatment for this patient population, to date. As mentioned, prostate cancer is generally slow growing but it is *possible* for prostate cancer cells to become more aggressive, start to grow, and spread more quickly.

If you and your doctor decide to delay treatment, talk to them about any warning signs to look out for. This might include pain in your lower back or legs, pain or pressure in the rectum, difficulty urinating, blood in the urine, or new difficulty getting an erection. Make a plan for how to contact your doctor if you notice new or concerning symptoms. If possible, make it a *proactive* plan: request to have regularly scheduled telemedicine check-in appointments with your doctor or nurse about any symptoms you may be experiencing.

Active Surveillance

Under normal circumstances, active surveillance is appropriate for many very low-, low-, and certain favorable-intermediate risk patients who qualify. This may be an even more attractive option now, in an effort to minimize health care visits. If you are already scheduled for surgery or radiation, check with your doctor about whether active surveillance is an option.

Active surveillance involves using PSA checks—usually done once or twice per year—to monitor your cancer. If you are in a COVID-19 hotspot, some health care centers may also be deferring PSA testing, depending on volume of emergencies.

If you are already on active surveillance, and you and your doctor decide that you should continue monitoring, the procedures for getting your PSA test may change. Whereas before you might have had your blood drawn at a medical center and returned to discuss the results with your doctor, now you may get blood drawn at a local lab and have a scheduled follow-up appointment with your doctor only by phone or video call. Discuss the timing of any scheduled MRI or biopsy with your provider. In some situations, it is clinically appropriate to stretch out time between MRI tests but keep routinely checking the PSA on schedule.

Surgery

Depending on the volume of COVID-19 in your local community, surgery to treat prostate cancer may be delayed. During this time of national emergency, some non-essential surgeries are being postponed to minimize exposing patients to the virus and to reserve healthcare resources—providers, PPE, hospital beds, ventilators—for the sickest patients. Luckily, in prostate cancer, this is unlikely to cause significant harm. Research has shown that delaying surgery even in high-risk patients is unlikely to affect long-term outcomes. Importantly, data has shown that patients who undergo surgery are at increased risk of contracting COVID-19, likely given the increased exposure to the healthcare environment. This must be weighed against the benefit of alternative treatment options (such as radiation therapy, discussed in the next section).

Follow-up visits after surgery may occur through telehealth or a home nurse visit to avoid bringing you into the clinic. If you are recovering from recent surgery, be sure to check in with your doctor about any possible changes to your follow-up plan. And if you are having new or severe pain, bleeding, changes in urination, fever, or other warning signs, call your doctor's emergency number.

Radiation Therapy

Radiation therapy is a very common treatment for localized prostate cancer, and the pandemic may affect this care option as well. In general, most radiotherapy facilities have been less impacted (as compared to surgery) given that radiation does not require intubation, hospitalization, and substantial PPE use.

A team of experts, led by PCF-funded investigator Dr. Dan Spratt, has developed a framework for doctors to consider how and when to modify radiation treatments during COVID-19. The goal is to help doctors safely care for their

patients—balancing concerns of prostate cancer with COVID-19 infection risk—while conserving healthcare resources. This new framework is called RADS (which, coincidentally, is also a pun: it is the term used to describe a “dose” of radiation therapy). It stands for:

R = Remote Visits. Use phone or video instead of in-person visits.

A = Avoid Radiation. Do not treat with radiation therapy where there may be little or no benefit based on clinical trials.

D = Defer Radiation. Defer the start of treatment to maintain safety.

S = Shorten Radiation. If radiation is used, use the shortest safe form possible.

How will this affect you if you were considering radiation therapy? If you are newly diagnosed, your first visit may be delayed weeks to months, depending on your risk level and whether you live in a COVID-19 hotspot. Men with very low- and low-risk prostate cancer (see Table below) may be advised to delay until the risk of COVID-19 is low in your area. If delay is not possible (e.g., with high-risk, high-Gleason grade tumors), your provider will consider how to give safe and effective radiation therapy with the fewest possible number of visits. It is important to make COVID-19 prevention a top priority from when you arrive at the clinic to when you return home. Fortunately, hormone therapy is often combined with radiation as part of the standard of care, and hormone therapy can safely be used to delay the start of radiation by up to 6 months without any jeopardy in long-term outcomes.

If you have already had a prostatectomy and are planning radiation afterwards, you and your provider may consider following your PSA (via telehealth as much as possible) and starting radiation only if your PSA starts to rise. In general, the more treatments you have, the more exposure you will have to the healthcare environment, which may increase your risk of contracting COVID-19. Thus, the shortest-course treatment is preferred, which often can be done in as few as 5 treatments, termed SBRT.

Risk Groups for Localized Prostate Cancer

Risk Group	Criteria
Very Low	All of the following: T1c stage, Grade group 1, PSA < 10 ng/mL, PSA density <0.15, fewer than 3 biopsy cores are positive, and <=50% of any core is involved with cancer
Low	All of the following: T1-T2a stage, Grade group 1, PSA <10 ng/mL
Intermediate - Favorable	Any one of the following risk factors: T2b/c stage, Grade group 2, PSA 10-20, Also must have >50% of your biopsy cores negative for cancer
Intermediate - Unfavorable	Grade group 3 - or - Any two of the following risk factors: T2b/c stage, Grade group 2, PSA 10-20, >=50% of your biopsy positive for cancer
High	Any one of the following risk factors: Grade group 4 or 5, T3a stage, PSA >20
Very High	Any one of the following risk factors: T3b-T4 stage, Primary Gleason pattern 5, >4 cores with Grade Group 4 or 5, or at least 2 high-risk features

See the Prostate Cancer Patient Guide, Chapter 2, “Detection, Diagnosis, and Staging” for more details on how risk groups are defined.

Talk to your doctor about when and how to proceed with radiation therapy to ensure that you have the best cancer outcome possible, while minimizing your risk of COVID-19.

Hormone Therapy (ADT)

Hormone therapy does not put men at additional risk of infection with COVID-19. In fact, clinical trials are beginning to test whether a very short course of ADT may actually be beneficial in men (without prostate cancer!) who are already infected with COVID-19. However, there is no data to recommend starting ADT in men with prostate cancer as a way to prevent COVID-19.

If you have unfavorable intermediate, high, or very-high risk prostate cancer and are planning to have radiation therapy as your primary treatment, you and your doctor may choose to begin ADT in order to delay radiation for 4-6 months. A major advantage of ADT is that it can be given as a long-acting injection, minimizing the number of clinic visits.

Advanced or Metastatic Prostate Cancer

Men with advanced disease may be especially worried about delays or changes in their treatment plan. In general, cancer centers are continuing to treat patients with advanced cancer during the pandemic, and patients who need chemotherapy can still come in for infusions, using COVID-19 prevention protocols for patient flow door-to-door. Many clinics are screening patients for COVID-19 symptoms upon arrival, ensuring that patients and staff wear masks and other PPE, and limiting visitors. Soon, centers may begin doing nose, throat, or saliva testing for coronavirus prior to commencing treatment.

Taxane chemotherapy (for example, docetaxel) is part of the standard of care for metastatic prostate cancer. However, it is important to know that, in general, chemotherapy weakens the immune system—it lowers your white blood cell count and reduce your body's ability to fight off infections. For some men, the risk of prostate cancer progression outweighs any increased risk of COVID-19 infection while on chemotherapy. Another option may be to increase the time between infusions to allow your immune system to more fully recover. If you are currently undergoing chemotherapy, or are scheduled to begin, call your doctor and make a plan for how you will be protected during your infusion—starting from the time you get out of your car to when you return home.

If you are on docetaxel, your doctor will have given you a list of warning signs of infection, such as fever or inability to keep food and drink down. Especially during this pandemic, be vigilant about these symptoms and call right away if you notice them. More research is needed to show how chemotherapy directly affects prostate cancer patients' risk of COVID-19 infection.

Your provider may also consider treatments that do not weaken your immune system in the same way as chemotherapy. For example, 2nd-generation anti-androgen medications such as enzalutamide, apalutamide, darolutamide, or abiraterone may be appropriate for treating advanced or metastatic disease, and do not affect your infection-fighting cells. However, abiraterone is given with prednisone, which can cause immunosuppression. Abiraterone also requires more frequent lab tests when starting therapy. Your doctor may consider these factors when choosing among the 2nd-generation anti-androgens. To monitor your labs, your doctor may have you go to a local lab to get blood drawn and then follow up with you by phone or email.

If you have been newly diagnosed with low-volume metastatic or oligometastatic prostate cancer, radiation therapy may be part of your treatment plan. As mentioned above, your doctor may recommend that ADT be used to safely

delay starting radiation for 4-6 months. However, longer delays of radiation therapy for men with advanced disease and excessive use of ADT are not recommended.

Under normal circumstances, clinical trials are an important option for men with advanced disease. However, be aware that many clinical trials are on hold or are enrolling fewer patients during the pandemic.

Post-Treatment: Prostate Cancer Survivors

Men who have completed their prostate cancer treatment are not thought to be at higher risk of infection with COVID-19, but more information is needed. If you had surgery or radiation therapy several months ago, and you are feeling well, you're probably at the same risk as any man of your same age and with the same other health conditions who's never been diagnosed with prostate cancer. But if you are over age 60 and being treated for conditions such as diabetes, coronary artery disease, high blood pressure, or lung disease, take extra precautions to maintain your health. It's especially important to follow any local public health recommendations to stay home, wear a face covering when going out, and continue to wash your hands and disinfect surfaces in your home. Check out pcf.org/COVID-19 for updates.

Your doctor may postpone any post-treatment monitoring until it is deemed safe for you to come to the clinic, or you and your doctor may choose to do this via telehealth.

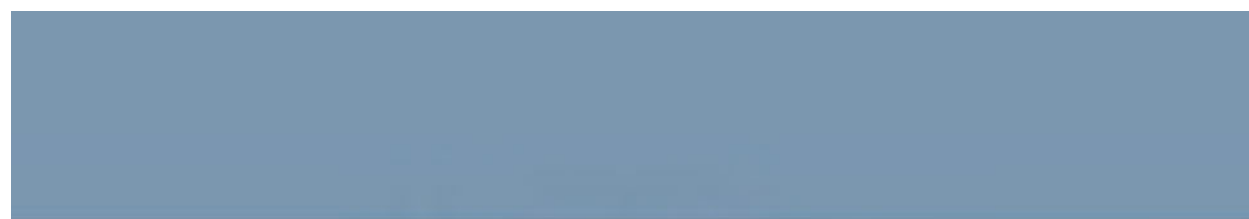
WHAT YOU CAN DO: KEEP YOURSELF AND YOUR LOVED ONES HEALTHY

It may be frustrating to read that all you can do is "hurry up and wait." But there is a LOT you can—and must—do for yourself now to keep yourself and your family well and to prepare for any treatment that you may have in the future. **It is important that you keep yourself and your caregivers well.** COVID-19 is an immediate threat for everyone, regardless of prostate cancer, and if you or someone you live with becomes infected, this may put you at risk for severe illness. Rather than stress about delays or changes in treatment, use this time to ensure that you are in the best shape possible for when you do begin treatment. Being sick with COVID-19 could set you back and even endanger your life.

1. The basics: Wash your hands frequently with soap and especially after being outside or touching surfaces that others have touched such as packages, takeout containers, or groceries. Keep your fingers away from your face. Clean surfaces in your home. Check the CDC website for more details.
2. Follow local public health guidelines for "social distancing." Many communities are urged to stay at home as much as possible and to wear cloth face protection when going on necessary errands. It is important that you adhere to local guidelines. This will change over time, so check reliable local sources of information, such as your public health department website. You may be able to sign up for alerts on your smartphone from your local government.
3. Maintain your wellness to be in the best shape possible for treatment. This includes physical (diet, exercise) and mental (engaged mind, virtual social connections). [PCF.org](https://pcf.org) has a [blog](#) with suggestions, and this [article](#) notes how losing weight before surgery, if that applies to you, may improve surgical outcomes.

SUBSCRIBE AT [PCF.ORG](https://pcf.org) FOR THE LATEST UPDATES ►89

- 
4. Plan for your every move to and from treatment. You may have already arranged who will help you after surgery or who will drive you to your appointments. Check back with those family and friends, as they may have been impacted by COVID-19 in terms of health, finances, or living situation. Wash your hands frequently before, during, and after your clinic visit.
 5. Be physically distant but socially present. While this may not be a great time to see friends and family in person, it's a critical time to stay connected. Research suggests that people's amount of social connection is related to health outcomes, including cancer. Use videoconferencing to stay in touch; replace in-person card games with online apps that allow you to play with friends and family that you can't meet out; take a walk with neighbors, maintaining 6-10 feet of social distance between households, and respecting local government requirements.



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**Prostate Cancer
Foundation**
Curing Together.

www.pcf.org

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ATTACHMENT 13 - ALTERNATIVES

Alternative #1: Maintain the Status Quo (do not purchase a new linear accelerator)

This alternative has no capital costs associated with it, but also yields no benefit to the community. The current linear accelerator is not yet obsolete, but inevitably it will be at some point in time. Taking no action now ensures a significant disruption in the ongoing care necessary for patients reliant upon this physician group for treatment. It also will result in a notable gap in available care and would reflect poor healthcare planning. Hospitals and other centers would be unlikely to be capable of filling this avoidable gap in care, thus meaning that patients would go without necessary cancer treatments. For these reasons, this alternative was not selected.

Alternative #2: Wait to Replace Linear Accelerator until Failure

Whether this alternative would have greater or lesser cost is unpredictable, ultimately, and unknown. It would likely result in increased cost because the additional expense associated with maintaining the current equipment would likely exceed any potential cost savings that could result from delay. More importantly, it would ensure patient disruption and result in a notable gap in available care because the applicants would have to proceed through the CON process upon the current equipment becoming obsolete. This would result in an unacceptably long period where necessary care and treatment would be unnecessarily unavailable. For these reasons, this alternative was not selected.

Alternative #3: Project as Proposed

The project, as proposed, is the most responsible from a health planning perspective as well as from a patient care delivery perspective. More importantly, since the group does envision requiring the acquisition of additional linear accelerators in the future (those projects requiring CON Board approval will obtain such approval) they are able to utilize this unique market position to negotiate the lowest possible costs available for such a project. Accordingly, this project enables the applicant to fulfil the CON principle of pursuing the most effective increase in access to care at the lowest appropriate cost. More importantly, it will ensure those patients reliant upon this exceptional practice group for their care will continue to have access to necessary life-improving and life-sustaining care. For those reasons, and given the deficiencies of the alternatives identified above, this is the alternative that was selected and is being presented to the Board for consideration and approval.

ATTACHMENT 14 - SIZE OF PROJECT

SIZE OF PROJECT				
DEPARTMENT/SERVICE	PROPOSED BGSF/DGSF	STATE STANDARD	DIFFERENCE	MET STANDARD?
Radiation Therapy (Linear Accelerator)	1350 GSF	2400 GSF maximum	-1050	YES

The linear accelerator that is the subject of this application will be installed at an existing physician office building operated by UroPartners. The equipment itself must be installed in vault structure. The vault in which a linear accelerator is housed is either designed as having a maze or direct shielded door, with each design having its own advantages. The applicants are working with their contractor to determine which type of vault would be most efficient for the existing space. A maze structure has the advantage of a door that will be significantly lighter and less expensive than a direct shielded door vault. The disadvantage of the maze vault is access to the room for therapists takes longer, which for busy cancer centers impacts patient flow. A direct shielded door is heavy and expensive and typically needs to be controlled by a motor. The ultimate decision will be made based on the specific treatment program needs and the configuration of the maze and vault, and the types and thicknesses of shielding materials shall be as prescribed by a registered radiological physicist approved by the American Board of Radiology in accordance with the National Council of Radiation Protection standards and regulations.

ATTACHMENT 15 - PROJECT SERVICES UTILIZATION

UTILIZATION					
	DEPT./ SERVICE	HISTORICAL UTILIZATION (PATIENT DAYS) (TREATMENTS) ETC.	PROJECTED UTILIZATION	STATE STANDARD	MEET STANDARD?
YEAR 1	Linear Accelerator	12,180 Treatments	6,500	7,500 Treatments	YES
YEAR 2	Linear Accelerator	12,180 Treatments	7,280	7,500 Treatments	YES

Pursuant to 77 Illinois Admin. Code Section 1110 Appendix B, the applicant is required to provide project utilization to determine if the new equipment will meet Board target utilization standards for applicable clinical service areas. As the linear accelerator will be utilized to provide Radiation Therapy that is the only applicable clinical service. To determine the project utilization of the new linear accelerator the applicants reviewed their historical utilization of the existing machine.

For radiation treatments to be effective patients must receive consecutive treatments as prescribed by the radiation oncologist, typically 5 days on followed by two days off. The current linear is now over 10 years old. The acquisition of a second linear accelerator prior to serious issues with the existing machine will allow UroPartners the ability to continue providing services to patients as prescribed in their individualized treatment plans. The new linear accelerator would allow for an orderly transition of patients to the new machine.

The current linear accelerator, Varian 21iX, began treating patients in February of 2009. The center has shown growth every year since opening. Below is a chart illustrating the year over year growth of the linear accelerator and the number of treatments delivered each year.

Year	Number of Treatments
2014	9,372
2015	11,710
2016	11,024
2017	11,950
2018	11,936

The chart above illustrates the amount the applicants have historically utilized their existing equipment. Because of the equipment's age, the applicants would propose to lower utilization of the existing machine and phase in the new machine over time. In year 1 the applicants will only shift just over 53% of their procedures to the new machine, and the following year they will increase that percentage to just over 59%. This will allow the practice to gradually retire the existing machine while still ensuring that it is fully utilized through the end of its life cycle. The applicants purpose to retire the existing machine as the new machine accommodates additional volume over the 2 years of initial operation.

On average during calendar year 2019, UroPartners treated 46 patients per day. During November of 2019 the practice treated as many as 56 patients per day. Because of the capacity of the existing machine, the practice was unable to schedule additional procedures in excess of 56. UroPartners projects that given their patient volume and with an increased capacity that they can expect to average approximately 60 patients treated per day. They would propose to perform 35 procedures on the new linear accelerator and 25 on the existing accelerator during the phase in of the new machine. This would result in 15,600 annual treatments for the first year using both machines. Projections for the second year are to treat an additional 5 patients per day. This would result in 16,900 treatments for the second year.

According to the Health Facilities and Services Review Board Annual Surveys data, there were a total of 32 linear accelerators operating in Health Service Area 7 during 2018 and those machines provided 115,227 treatments to patients. Additionally, there are ASTCs in Health Service Area 7 that perform procedures using linear accelerators, such as the UroPartners Surgery Center in DesPlaines. However, the

HFSRB does not maintain data on the number of linear accelerators in ASTCs and the number of treatments provided.

ILLINOIS HOSPITALS DATA SUMMARY - Calendar Year 2018

HSA 7

Page 1

Number of Hospitals:	38	Emergency Services		Patients by Race			Patients by Ethnicity			
Number of Critical Access Hospitals:	0	Classifications		White:	64.4%	Hispanic or Latino:	12.5%			
Number of Long-Term Acute Care Hospitals:	0	Comprehensive:	29	Black:	20.5%	Not Hispanic or Latino:	84.1%			
Number of General Hospitals:	30	Basic:	1	American Indian:	0.4%	Unknown Ethnicity:	3.4%			
Number of Psychiatric Hospitals:	5	Stand-By:	4	Asian:	3.5%	Trauma Care Hospitals				
Number of Rehabilitation Hospitals:	1			Hawaiian/Pacific:	0.1%	Adult	Pediatric			
Number of Children's Specialty Care Hospitals:	0			Unknown Race:	11.1%	Level 1:	4			
						Level 2:	6			
							0			
							0			
Facility Utilization Data by Category of Service										
	Authorized CON Beds 12/31/2018	Peak Beds Setup and Staffed	Peak Census	Admissions	Inpatient Days	Observation Days	Average Length of Stay	Average Daily Census	CON Occupancy Rate %	Staffed Bed Occupancy Rate %
Clinical Service										
Medical/Surgical	5,747	4,882	4,856	263,301	1,197,254	170,897	5.2	3,748.4	65.2	76.8
0-14 Years				904	1,481					
15-44 Years				37,633	141,893					
45-64 Years				75,586	336,910					
65-74 Years				57,584	274,502					
75 Years +				91,594	442,468					
Pediatric	291	275	236	10,905	35,272	11,766	4.3	128.9	44.3	46.9
Intensive Care	1,117	945	923	50,736	237,506	2,359	4.7	657.2	58.8	69.5
Direct Admission				50,736	175,834					
Transfers					61,672					
Obstetric/Gynecology	714	644	610	47,061	128,413	6,097	2.9	368.5	51.6	57.2
Maternity				44,602	122,673					
Clean Gynecology				2,459	5,740					
Neonatal	288	281	297	4,569	74,312	16	16.3	203.6	70.7	72.5
Long Term Care	159	120	111	3,667	66,673	0	18.2	182.7	114.9	152.2
Swing Beds			0	0	0		0.0	0.0		
Acute Mental Illness	1,420	1,386	1,254	43,684	342,779	267	7.9	937.3	66.0	67.6
Adolescent		333	295	9,255	80,186	0	8.7	219.1		65.8
Adult		1,053	959	34,429	262,593	267	7.6	718.2		68.2
Rehabilitation	460	333	335	8,900	119,449	17	13.4	327.3	71.2	98.3
Long Term Acute Care	338	319	277	1,281	43,144	0	13.4	118.2	35.0	37.1
Dedicated Observation	119					18,953				
Total Utilization	10,534			434,104	2,244,802	210,372	5.7	6,708.1	63.7	
Inpatient and Outpatients Served by Payor Source										
	Medicare	Medicaid	Other Public	Private Insurance	Private Pay	Charity Care	Totals			
Inpatients	43.3%	16.3%	0.3%	35.4%	2.3%	2.4%				
	188,841	71,011	1,525	154,546	9,977	10,426	436,326			
Outpatients	31.8%	13.6%	0.8%	50.2%	2.3%	1.2%				
	2,949,891	1,264,673	69,943	4,656,670	215,051	114,413	9,270,641			
Inpatient and Outpatient Net Revenue by Payor Source (Fiscal Year Data)										
	Medicare	Medicaid	Other Public	Private Insurance	Private Pay	Totals	Charity Care Expense	Total Charity Care		
Inpatient Revenue	40.4%	14.5%	0.4%	42.1%	2.6%	100.0%		150.2		
(\$ in Millions)	2,438.3	871.9	25.6	2,538.0	159.7	6,033.4	64.7	Total Charity Care as % of Total Net Revenue		
Outpatient Revenue	24.2%	8.5%	0.8%	62.3%	4.3%	100.0%				
(\$ in Millions)	1,313.7	460.2	43.7	3,382.6	232.8	5,433.0	85.5	1.3%		
Birth Data										
Number of Total Births:	42,872	Newborn Nursery Utilization				Organ Transplantation				
Number of Live Births:	42,809		Level I	Level II	Level II +	Kidney:	136			
Birthing Rooms:	0	Beds	589	199	62	Heart:	59			
Labor Rooms:	23	Patient Days	69,035	20,281	16,934	Lung:	55			
Delivery Rooms:	0	Total Newborn Patient Days			106,250	Heart/Lung:	0			
Labor-Delivery-Recovery Rooms:	199					Pancreas:	5			
Labor-Delivery-Recovery-Postpartum	89					Liver:	63			
C-Section Rooms:	51					Total:	318			
CSessions Performed:	13,558									

Source: 2018 Annual Hospital Questionnaire, Illinois Department of Public Health, Division of Health Systems Development

ATTACHMENT 30 - 1110.270 (c)(1) DETERIORATED FACILITIES

Linear accelerators are utilized by the UroPartners practice to provide various radiotherapy procedures. Because UroPartners is the largest urology group in the Midwest, they have an equally large patient base. This has resulted in consistent use of their existing linear accelerator over time. These machines like any other have a finite life expectancy, and the length of their life depends on number of hours of clinical use.

For example, a linear accelerator that is used for 40 hours per week can be expected to have a working life of between 10-12 years. This means that practices like UroPartners who regularly utilize their machine must be cognizant of the machine's life span. Because use of the equipment can decrease the life span of a linear accelerators, factors like an aging population and increased incidences of cancer will require more use of the machine and in this case replacement in advance of complete deterioration of existing equipment. By filing this application UroPartners is undertaking the most prudent course of action by ensuring the replacement machine is installed and functioning before the existing machine is unusable. This ensures continuity of care for their practice and the patients suffering from various urological cancers.

The Varian Linear Accelerator utilized by UroPartners is an advanced radiation therapy device that is utilized for the delivery of Intensity Modulated Radiation Therapy (IMRT) and Image Guided Radiation Therapy (IGRT) radiation. The existing linear accelerator was acquired on December 1, 2008, it is manufactured Varian, model number 21iX, and its serial number is 4194. Pursuant to 32 Illinois Admin. Code Section 320 the equipment maintains a registration with Illinois Emergency Management Agency.

The current linear accelerator, Varian 21iX, began treating patients in February of 2009. Below is a chart illustrating the year over year growth of the linear accelerator and the number of treatments delivered each year.

Year	Number of Treatments
2014	9,372
2015	11,710
2016	11,024
2017	11,950
2018	11,936

On average during calendar year 2019, UroPartners treated 46 patients per day. During November of 2019 the practice treated as many as 56 patients per day. Because of the capacity of the existing machine the practice was unable to schedule additional procedures in excess of 56. UroPartners has noticed an increase in service interruptions due to machine problems over the last few years. As it continues to age the reliability will decrease according to service engineers. The likelihood of a major part failure rises and depending on the part that fails the resulting down time could be up to 2 weeks. This combination could adversely affect patient service and access to care.

The annual maintenance costs for the existing machine exceeds \$400,000 per year. As of the filing of the application, the expenses paid are approximately \$380,000. There have been no issues with existing registration with the Illinois Emergency Management Agency, nor have there been any fire code deficiency citations involving the current equipment or the future site.



Facility Profile for Uropartners Prostate Center at the Glen

[Return to Facility Search](#)**Name:** Uropartners Prostate Center at the Glen**Status:** Open**Category:** Therapy Clinic**Administrator:** Paul Levan, PhD, RSO**Physical Address:** 2600 Patriot Blvd Ste J, Glenview, IL, 60026-8024**Facility Contact:** Par Mehta, M.D., Medical Director**County:** Cook**Phone:** (224) 260-3100**Facility ID:** 9258748

Active X-Ray Equipment

Equip ID	Class	Manufacturer	Model #	Location	Serial #	Acquired	Registered
9000	Ct Scanner	General Electric	2377708-555	CT	206844HM3	12/22/2008	1/29/2009
9500	Linear Accel	Varian	21 iX	Therapy Vault	4194	12/1/2008	2/10/2009

Copyright 2020 Illinois Emergency Management Agency

ATTACHMENT 30 - 1110.270 (c)(3)(A) UTILIZATION MAJOR MEDICAL EQUIPMENT

The applicants propose to acquire a new linear accelerator to meet the growing need to perform radiotherapy treatments at their Prostate Center-Glenview. After reviewing historical data on treatments performed using their existing machine, the applicants are confident that a second machine is needed and will meet the state's target utilization for this clinical service.

The current linear accelerator, Varian 21iX, began treating patients in February of 2009. The center has shown growth every year since opening. Below is a chart illustrating the year over year growth of the linear accelerator and the number of treatments delivered each year.

Year	Number of Treatments
2014	9,372
2015	11,710
2016	11,024
2017	11,950
2018	11,936

The chart above illustrates the amount they applicants have historically utilized their existing equipment. Because of the equipment's age, the applicants would propose to lower utilization of the existing machine and phase in the new machine over time. In year 1 the applicants will only shift just over 53% of their procedures to the new machine, and the following year they will increase that percentage to just over 59%. This will allow the practice to gradually retire the existing machine while still ensuring that it is fully utilized through the end of its life cycle. The applicants purpose to retire the existing machine as the new machine accommodates additional volume over the 2 years of initial operation. The new machine will meet the state's target utilization rate within its initial year of operation.

On average during calendar year 2019, UroPartners treated 46 patients per day. During November of 2019 the practice treated as many as 56 patients per day. Because of the capacity of the existing machine the practice was unable to schedule additional procedures in excess of 56. UroPartners projects that given their patient volume and with an increased capacity that they can expect to average approximately 60 patients treated per day. They would propose to perform 35 procedures on the new linear accelerator and 25 on the existing accelerator during the phase in of the new machine. This would result in 15,600 annual treatments for the first year on both machines. Projections for the second year are to treat an additional 5 patients per day. This would result in 16,900 treatments for the second year.

ATTACHMENT 33 - AVAILABILITY OF FUNDS

The applicants have sufficient resources to fund the cash portion of this project. Attached as evidence, is a screen shot of the multiple bank accounts maintained by the applicant. This screen shot was taken Friday, July 10, 2020.

UROPARTNERS LLC

[REDACTED] | USD

Ledger Balance \$211,819.28

Available Balance \$211,819.28

UroPartners LLC

[REDACTED] | USD

Ledger Balance \$5,682,542.19

Available Balance \$5,388,602.64

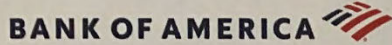
Uropartners LLC

[REDACTED] | 081904808 | USD

Ledger Balance \$10,067.98

Available Balance \$10,067.98

ATTACHMENT 33 – FINANCING LETTER



July 6, 2020

Uropartners, LLC
Attn: Nick Radonjic
2245 Enterprise Drive, Suite 4506
Westchester, IL 60154

Dear Nick:

Based upon our 15-year banking relationship and history of successfully financing your previous capital projects, we are excited to share a potential financing structure for the Glenview IMRT project. We would envision an interest only draw period for up to 1-year for both the Construction and Linear Accelerator loans. The Equipment loan (Linear Accelerator) would potentially amortize up to 7 years from conversion and the Construction loan would potentially amortize up to 5 years from conversion. I also note that as of today, Uropartners has sufficient cash on hand and availability under existing loan facilities to support the project.

Borrower: Uropartners, LLC

Facility 1: \$1,650,000 Equipment Loan

- Interest only during the draw period priced at Prime, floating (currently 3.25%).
- At maturity the outstanding balance would convert to a term loan with a projected amortization of up to 7 years. We used an estimated fixed rate of 3.80%. Projected monthly principal and interest payments would be \$22,401.94.

Facility 2: \$2,450,000 Construction Loan

- Interest only during the draw period priced at Prime, floating (currently 3.25%).
- At maturity the outstanding balance would convert to a 5 year term loan. We used an estimated fixed rate of 3.62%. Projected monthly principal and interest payments would be \$44,701.56.

The information contained herein does not represent a commitment to lend by Bank of America or any of its affiliates and is presented for discussion purposes only. Bank of America may withdraw or amend this information at any time at its sole discretion. The actual terms and conditions (including pricing and financial covenants) upon which Bank of America might extend credit is subject to satisfactory completion of due diligence, necessary credit approval and such other terms and conditions as determined by Bank of America in its sole discretion.

Sincerely,

A handwritten signature in black ink, appearing to read "Edward J. Brennan", followed by a horizontal line.

Edward J Brennan
Market Executive

ATTACHMENT 35 -FINANCIAL VIABILITY

Uropartners, LLC											
Viability Ratios											
</											

ATTACHMENT 36 - Total Effect of the Project on Capital Costs

The applicants have calculated that the capital cost per treatment over the expected 12 year life span of the equipment is \$13.51 per treatment. While we expect to perform more than 12,180 per year on the new equipment, we used that number to conservatively estimate the capital cost per treatment. In the event we provide procedures in excess of 12,180 during years 7-12 of operation the capital cost per treatment would be even lower than \$13.51 per treatment.

	Expected Procedures
Year 1	6,500
Year 2	7,280
Year 3	8,154
Year 4	9,132
Year 5	10,228
Year 6	11,455
Year 7	12,180
Year 8	12,180
Year 9	12,180
Year 10	12,180
Year 11	12,180
Year 12	12,180
Total number of treatments	125,829
Cost of linear accelerator	\$ 1,700,000
Capital cost per treatment	\$ 13.51

ATTACHMENT 36 - ECONOMIC FEASIBILITY



2345 Enterprise Drive, Suite 4500 | Westchester, IL 60154 | Phone: 708.422.8502 | Fax: 708.422.8503

July 2, 2020

Courtney Avery
Board Administrator
Illinois Health Facilities and Services Review Board
525 W. Jefferson Street, 2nd Floor
Springfield, IL 62761

RE: Reasonableness of Financing Letter

Dear Ms. Avery:

I hereby attest that the terms and conditions of the proposed debt financing associated with the establishment of UroPartners, LLC are reasonable. Borrowing is less costly than the liquidation of existing investments, and the existing investments being retained may be converted to cash or used to retire debt within a 60 day period. The project will be funded through a combination of cash resources acquired through existing capital of UroPartners, LLC and debt financing through Bank of America.

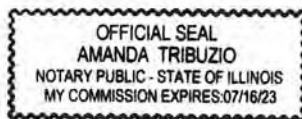
Furthermore, I certify that, as this project will require debt financing, the selected form of debt financing will be at the lowest net cost available. The project does not involve the leasing of equipment.

Sincerely,

Richard G. Harris, M.D.
CEO
UroPartners, LLC

Notarization:

Subscribed and sworn to before me this 8 day of July, 2020.



13562560 v1

ATTACHMENT 36 - ECONOMIC FEASIBILITY

COST AND GROSS SQUARE FEET BY DEPARTMENT OR SERVICE									
Department (list below)	A	B	C	D	E	F	G	H	Total Cost (G + H)
	Cost/Sq. Ft		Gross Sq. Ft.		Gross Sq. Ft.		Const. \$	Mod. \$	
	New	Mod.	New	Circ.*	Mod.	Circ.*	(A x C)	(B x E)	
Linear Accelerator		\$1,640.85			1350			\$2,215,149	\$2,215,149
Contingency		\$162.96			0			\$220,000	\$220,000
TOTALS		\$1,803.81			1350			\$2,435,149	\$2,435,149
* Include the percentage (%) of space for circulation									

ATTACHMENT 37 - SAFETY NET IMPACT STUDY

Pursuant to 77 Ill. Admin Code Section 1110.20 the acquisition of major medical equipment is classified as a non-substantive project. As a non-substantive project for the acquisition of major medical equipment the submission of a safety net impact study is not required by the applicants pursuant to 77 Illinois Admin. Code Section 1110.10(c).

ATTACHMENT 38 - CHARITY CARE

The applicant, UroPartners, LLC is a physician practice group. The applicant is providing charity care data for UroPartners Surgery Center, LLC (a wholly owned subsidiary) of UroPartners Investments, LLC which operates the ASC, UroPartners Surgery Center and has identical ownership as the applicant.

CHARITY CARE			
	2016	2017	2018
Net Patient Revenue	N/A	0	0
Amount of Charity Care (charges)	N/A	0	0
Cost of Charity Care	N/A	0	0

After paginating the entire completed application indicate, in the chart below, the page numbers for the included attachments:

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