Guide on how to
Develop resource-appropriate prostate cancer management guidelines
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Purpose of the guide

The purpose of this guide is to outline the steps and procedures for designing resource-appropriate prostate cancer management guidelines in the context of the City Cancer Challenge Foundation (C/Can) project as it is implemented at the city level. This guide is intended to respond to the urgent need to reduce inequities in access to prostate cancer diagnosis (clinical evaluation, pathology, imaging, staging), multimodality treatment (surgery, radiotherapy, systemic therapy), genetic counselling and palliative care services in selected C/Can cities.

To create resource-appropriate prostate cancer management guidelines, the guidelines development team requires an accurate understanding of currently available resources (infrastructure, human resources, equipment, and renewable supplies) for prostate healthcare. The situation assessment required to provide this baseline information is beyond the scope of this guide but is assumed to be available to the guidelines development team.

Prostate cancer detection is necessary to improve prostate cancer outcomes at the population level (see Annex 1). However, this document focuses on providing a guide on how to obtain an accurate and prompt prostate cancer diagnosis, appropriate staging and required oncological services. Multi-modality therapy is required for the majority of these patients in order to improve overall outcomes.

The guide has been prepared through a collaboration between C/Can and Daniel Castellano, MD, PhD, Medical Oncologist, Hospital 12 de Octubre, Madrid, Spain and Ferran Ferrer, MD, PhD, Radiation Oncologist at the Catalan Institute of Oncology, Barcelona, and based on the experiences garnered from two C/Can cities that developed the resource appropriate guidelines for the clinical management of prostate cancer patients with the support of an external group of experts nominated by the partners of C/Can (listed below), with the aim of supporting the different groups that are established by the cities as they prioritise the development of prostate cancer management guidelines. These groups are tasked with interpreting, analysing, and tailoring the recommendations made in this guide, taking into account the local context and the need to build a multisectoral consultative process within their cities.

List of external experts who have supported the international consultation of the resource appropriate clinical management guideline for prostate cancer patients in Cali

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List of external experts who have supported the international consultation of the resource appropriate clinical management guideline for prostate cancer patients in Porto Alegre

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List of external experts who have supported the ASCO-C/Can Multidisciplinary Cancer Management Course in Porto Alegre

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Structure and suggested contents of the guidelines document to be produced by the guidelines development team
1. Introduction

1.1. PROSTATE CANCER IMPACT

- Current and projected prostate cancer burden (incidence, mortality, prevalence, DALYs lost) in the world, region and country.
- Economic impact of prostate cancer in the country and city as measured by lost productivity and social disruption related to prostate cancer morbidity and deaths.
- Potential for improved prostate cancer outcomes based on early detection strategies in the country and city to reduce the fraction of patients presenting with advanced stage disease requiring more extensive and costly treatments.
- Potential for improved prostate cancer outcomes as measured by lower recurrence and higher survival rates based on the implementation of proven therapeutic strategies.
- Potential for improved functional results after prostate cancer treatment with the spread of information and knowledge regarding this patient-centred objective.

1.2. PROSTATE CANCER DIAGNOSIS AND TREATMENT OVERVIEW

- Synergistic role of early detection, diagnosis and multimodality treatment to improve prostate cancer outcomes in the general population.
- Reinforce the need of accurate and timely surveillance of the high-risk population.
- Access requirements for early identification of symptoms related to prostate cancer, and appropriate diagnostic work-up at the city level.
- Diagnostic services to establish prostate cancer diagnosis and clinical staging (clinical evaluation, imaging, pathology) and Genetic counselling.
- Multimodality treatment for invasive prostate cancer [surgery, radiotherapy, androgen derivation therapy, chemotherapy].
- Requirement for supportive care to help patients get through multimodality treatment without abandonment [social workers, support groups].
- Value of supportive care after treatment in survivorship to help patients reintegrate in their community.
- Importance of palliative care for patients with untreatable metastatic disease and in end-of-life care.
1.3. PHASED IMPLEMENTATION STRATEGIC PLANNING PERSPECTIVE

- Baseline assessment provides summary of existing diagnostic and treatment services and resources in city.

- Resource-stratified framework outlines the core service gaps needing to be filled or circumvented in city.

- Resource-appropriate guidelines should be both functional (biologically predictable to improve cancer outcomes) and sustainable (realistic and affordable) in order to meet the needs of the community.

- Phased implementation strategy defines a stepwise pathway for optimising sustainable resource-utilisation while improving service delivery for prostate cancer diagnosis, treatment and palliation.
2. Aims of the prostate cancer management guidelines document

- Explain the purpose of the document and the potential interested audiences.

- Consider the clinical demand for prostate cancer diagnosis and treatment services based on epidemiological data and projected needs based on quality benchmarks within a determined timeframe (up to 10 years).

- Discuss the available material resources (infrastructure, equipment and consumable materials) for prostate cancer detection, diagnosis, treatment and supportive services.

- Reflect on the current and future training requirements to have an optimally functional work force to meet the current and projected patient demand for prostate cancer diagnosis and treatment.

- Propose standardised guidelines for describing feasible interventions to bridge the early diagnosis and treatment gaps in terms of facilities, equipment and trained staff considering concepts like the rational use of existing resources (PSA testing, multiparametric MRI, prostate guided or systematic biopsy).
3. Objectives of the city-specific prostate cancer management guidelines

- This document should guide the users in terms of the rationale and necessity for creating prostate cancer guidelines adapted to their city's context and available resources.

- The guidelines should state the overall goal of the project to contribute to, and demonstrate its linkage with, a national or broader cancer control programme.

- The guidelines should align with the identified problems and needs, contributing to the expected impact.

- The guidelines document should describe the specific objectives and their links to expected outcomes.

- The specific objectives of the guidelines should address changes and effects expected with implementation.

- The guidelines document should expand on:
  - the increase of coverage in terms of equipment and personnel workload
  - the projected improvements in the accessibility to prostate cancer diagnosis and treatment services and in the quality and safety of treatments
  - anticipated technology requirements and the corresponding staff training and education that will be required to deliver these projected outcomes.

- The guidelines should serve as the basis for a city-wide phased implementation strategy potentially such as a four-step “APIM” (Assess, Plan, Implement, Monitor) approach to maximise the benefits of resource-stratification by permitting situation-specific adaptation.
4. Guidelines development

4.1. GUIDELINES DEVELOPMENT TEAM MEMBERSHIP

Guidelines development is a comprehensive process requiring the active involvement, input and ratification of all specialties and services involved in guidelines implementation. Those core specialties include (at least) all of the following:

- Surgery, Urology
- Radiation oncology
- Medical oncology
- Radiology (diagnostic imaging and nuclear medicine)
- Pathology

Guidelines implementation is most successful when ancillary and supportive services are directly involved in the guideline development process and have the opportunity to provide input. Key supportive services include:

- Genetic Counselling
- Nursing
- Supportive/palliative care
- Physical therapy
- Patient navigation services

Guidelines implementation is most likely to be sustained over time when their practical and financial implications are evaluated and vetted by those groups that will be required to continue and sustain their application over time. These administrative entities include:

- Hospital and clinic administration
- Health insurers
- Health services oversight (ministry of health or equivalent)
- National Societies of Surgical specialities, Medical and Radiation Oncology when available
4.2. GUIDELINES DEVELOPMENT PROCESS

A series of guidelines development meetings should be planned to permit writing, review, editing and ratification of the guidelines document:

- Creation [or designation] of a committee of experts in prostate cancer including representatives all the disciplines involved in early detection programmes (screening and early diagnosis), diagnosis and treatment of prostate cancer patients
- Clearly define datelines to avoid unnecessary delays
- Initial guidelines drafting
- Internal review to consider issues of practicality of implementation
- Guidelines revision based on internal review
- External expert (s) review to evaluate predicted efficacy
- Guidelines revision based on external review
- Administrative review to consider resource requirements and fiscal implications of implementation
- Guidelines finalisation

Principles of guidelines development include the following:

- Guidelines are most practical to apply when they follow an algorithmic approach mirroring the anticipated patient pathway (see Annex 1)
- Guidelines effectiveness depends on standardisation of care; when patients receive some but not all the essential interventions, improvement in cancer outcomes cannot be expected to occur
- Guidelines have limited utility when they are aspirational but unachievable or unaffordable

Given the complexity and rapidly evolving improvements in the diagnosis and management of prostate cancer, the guideline development team should strongly consider the use of existing resource-stratified guidelines such as the NCCN Framework for Resource Stratification of NCCN Guidelines™ (https://www.nccn.org/framework/default.aspx) as a starting point for guidelines development:

- The guidelines development team begins with a map of existing resources and services to determine how patients currently flow (or fail to flow) through the existing system and infrastructure
- The existing map of patient services permits gap analysis to identify where necessary services are missing or inadequately functional to meet service needs
- Resource-appropriate guidelines are useful for prioritising improvements to be implemented to provide an orderly progression based on existing needs that target the best predicted outcomes balanced against intervention costs
In prostate cancer diagnosis, certain questions commonly arise that need to be addressed in the guidelines to establish a prioritisation scheme for implementation, such as:

- Education of primary care physicians in identifying common clinical symptoms related to prostate cancer
- Implementation of early detection programs for the general population
- Implementation of surveillance programs in high-risk populations, such as African-Americans or who have a family history of prostate cancer
- Timeliness of diagnostic services, PSA abnormal test and urology appointment access to avoid excessive delays
- Diagnostic imaging studies to assess the local extent of the disease: Transrectal Endoscopic Ultrasound, MRI Pelvis (with/without contrast)
- Work up staging:
  - Tumour Marker: PSA
  - Imaging to detect extension of local disease: transrectal ultrasound, MRI
  - Imaging to detect regional (nodal) and/or metastatic disease: CT scan Chest – Abdomen and Pelvis with contrast; Bone Scan, PET-CT scan
- Tissue sampling methods:
  - Prostate biopsy: ultrasound-guided transrectal, ultrasound-guided transperineal with the possibility of fusion with nuclear magnetic resonance images.
- Pathology report:
  - Standard histopathological information
  - Molecular / genetic information / If available tumor testing for somatic homologous recombination gene mutations (e.g., BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51..) and/or tumour testing for MSI or dMMR
In prostate cancer treatment, certain questions commonly arise that need to be addressed in the guidelines to establish a prioritisation scheme for implementation, such as:

1. Discussion within the multidisciplinary tumour board of ALL cases prior to initiation of therapy is imperative in order to determine the most appropriate sequence of therapy.

   a. Consideration of Active Surveillance in Low Risk.
   b. Local treatment: Surgery or radiation treatment approach. Androgen deprivation for local treatment (radiation with bad prognostic features).
   c. Consideration of adjuvant or salvage radiation after radical prostatectomy.
   d. Watch and Wait approach.
   e. Local relapse diagnostic and management after radiation as primary treatment.

3. Metastatic:
   a. Systemic therapy (androgen deprivation and chemotherapy).
   b. Synchronous vs metachronous management of primary and metastatic disease.

4. Surgical Management
   a. Radical prostatectomy (open, laparoscopic, robotic).
   b. Lymph node dissection in high-risk prostate cancer.
   c. Pelvic exenteration.
   d. Resection of oligometastatic sites (i.e., nodes, bone, liver, lung)

5. Systemic Therapy:
   a. Androgen deprivation therapies.
   b. Chemotherapy protocols.
   c. Access to targeted therapy.
   d. Access to immunotherapy.

6. Radiation Therapy:
   a. Access to radiation oncology facilities
   b. Treatment modalities (external radiation, brachytherapy)
   c. Familiarity with short and long courses of RT (moderate and extreme hypofractionation)
   d. Protocols of androgen deprivation and radiotherapy
   e. Timing from RT to surgery (in case of requirement of transurethral resection for obstructive symptoms)
In *prostate cancer supportive and palliative care*, certain questions commonly arise that need to be addressed in the guidelines to establish a prioritisation scheme for implementation, such as:

a. Supportive care services during cancer treatment (especially those that help avoid treatment abandonment)

b. Supportive care following treatment in survivorship to assist patients in returning to their community

c. End-of-life palliative care for those patients in whom treatment has not been successful in eradicating the disease

In *prostate cancer surveillance* or *FOLLOW-UP* after treatments certain questions commonly arise that need to be addressed in the guidelines to establish a prioritisation scheme for implementation, such as:

a. Which tests

b. Frequency

Under each package of interventions, a distinction between *core and desirable* elements to be included should be made to account for planning with scarce resources while complying with minimal requirements, without leaving out *optimal scenarios*. 
5. Conclusions: implementation, monitoring and future guidelines revisions

Phased implementation is an evolutionary process requiring ongoing adaptation as the systems improve. As implementation takes place, ongoing monitoring is required to assess the degree to which the system is improving so that next steps in each critical phase in prostate cancer diagnosis and treatment can be recognised and re-prioritised.

Guidelines revisions should be considered episodically (one to two years), based on actual outcomes.
6. Contributors

A detailed list of all members of the city team that contributed to the drafting of the document, including the participants in the peer review meetings conducted in the city, and all the external experts that reviewed and edited the final draft.
7. References and bibliography


Annex 1. Universal prostate cancer patient pathway

**Patient interval**
- Early diagnosis
  - Low urinary tract symptom(s) or abnormal PSA test
- Screening
  - High risk population without symptoms
- Positive
- Negative
- Regular follow up

**Diagnostic interval**
- within 60 days
- Diagnostic work-up
  - Diagnosis
    - PSA + urology appointment
    - Transrectal Endoscopic Ultrasound, MRI Pelvis (with or without contrast)
  - Tissue sampling
    - Core biopsy for primary site
  - Staging
    - Tumor marker: PSA
    - CT scan chest, abdomen, and pelvis with contrast
    - Bone scan
    - PET/CT scan

**Treatment interval**
- Systemic therapy
  - Androgen deprivation therapies
  - Chemotherapy protocols
  - Access to Targeted therapy
  - Access to Immunotherapy
- Synchronous vs Metachronous management of Primary and Metastatic disease
- Supportive and palliative care
- Cancer Recurrence
  - Extent of recurrence disease
  - Goal of Therapy
  - Supportive care
  - End of life support
- Active surveillance in low risk
- Local treatment - Surgery
  - Radical prostatectomy (open, laparoscopic, robotic)
  - Pelvic Exenteration
  - Resection of Oligometastatic sites
  - Supportive service
- Local treatment - Radiotherapy
  - Short and Long courses of Radiotherapy
  - Androgen deprivation for local treatment
  - Radiation of Oligometastatic sites
- Adjuvant or salvage radiation after radical prostatectomy
- Watch and wait approach
- Local relapse diagnostic and management after radiation as primary treatment
- Supportive and palliative care

**No Evidence Of Disease (Ned)**