


# BMJ Open Impact of COVID-19 pandemic on screening and diagnosis of patients with prostate cancer: a systematic review protocol

Seyed Mostafa Mostafavi Zadeh,<sup>1,2</sup> Fatemeh Tajik,<sup>1</sup> Yousef Moradi,<sup>3</sup> Jafar Kiani,<sup>1,2</sup> Roya Ghods,<sup>1,2</sup> Zahra Madjd <sup>1,2</sup>

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SMMZ and FT contributed equally.

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<sup>1</sup>Oncopathology Research Center, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Molecular Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Epidemiology and Biostatistics, Kurdistan University of Medical Sciences, Sanandaj, Iran

## Correspondence to

Dr Zahra Madjd;  
[Zahra.madjd@yahoo.com](mailto:Zahra.madjd@yahoo.com) and  
Dr Roya Ghods;  
[ghods.ro@iums.ac.ir](mailto:ghods.ro@iums.ac.ir)

## ABSTRACT

**Introduction** With the exponential progress of patients with COVID-19, unexpected restrictions were directed to limit SARS-CoV-2 dissemination and imposed health-system an entire reformation to diminish transmission risk. These changes likely have caused the full range of cancer screenings and diagnosis gaps. Regardless of the recommendations, prostate cancer (PCa) screening/diagnosis programmes were momentarily postponed. Prostate-specific antigen (PSA) testing has been an inexpensive, low-invasive and relatively precise means of detection for PCa screening that would improve the uncovering of any type of PCa. Unfortunately, a decrease in PSA screening would significantly decrease PCa detection, with non-negligible growth in PCa-specific death. This review is designed to improve our understanding of the impact of the COVID-19 pandemic on the screening and diagnosis of patients with PCa.

**Methods and analysis** This systematic review will be reported in accordant with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance. A comprehensive search has been executed through five main electronic databases: PubMed/MEDLINE, Web of Science, Scopus, Embase and ProQuest until 1 March 2022. Besides, grey literature, preprint studies and references of included studies will be searched. The main keywords have been used to perform the search strategy: COVID-19, prostatic neoplasms. All the relevant studies that met the inclusion criteria will be screened, selected and then extracted data by two independent authors. The quality assessment of the included studies will be performed by the Newcastle-Ottawa Scale. In case of any disagreement between the two authors in selecting, extracting data and assessing the quality of included studies, it will be resolved via consensus and checked by the third author.

**Ethics and dissemination** As this study will be a systematic review without human participants' involvement, there will be no requirement for ethics approval. Findings will be presented at conferences and in a peer-reviewed journal.

**PROSPERO registration number** CRD42021291656.

## INTRODUCTION

People have witnessed that COVID-19 has meaningfully affected the lives of millions of people and spread quickly.<sup>1–3</sup> From 1

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This review is the first qualitative systematic review evaluating the impact of COVID-19 pandemic on screening and diagnosis of patients with prostate cancer.
- ⇒ This systematic review will use the Newcastle-Ottawa Scale tool to minimise the bias of analysis and ensure the synthesis output's confidence.
- ⇒ As a qualitative systematic review, the findings will be restricted by the context and quality of the eligible included studies.

February 2022, over 252 million confirmed the cases and about 5 700 000 passing were reported in the countries and states worldwide caused by the COVID-19 outbreak.<sup>4</sup> Although the mortality rate of COVID-19 has roughly 3%, it has high transmissibility, with respiratory secretions being the predominant transmission mode for SARS-CoV-2.<sup>5 6</sup>

COVID-19 disease was identified as a significant worldwide health concern due to its different epidemiology (method of global spread, mortality rate) and patient care techniques (mechanism of action, accessible diagnostic tools, etc).<sup>3</sup> The current global pandemic of COVID-19 increased our medical and regional healthcare system's pressure<sup>7</sup> and strained economists, experts and politicians to answer the financial challenges, innovation of vaccines and referring to public worries.<sup>8–11</sup> Besides, the disease has affected maintaining the same level of healthcare as before the pandemic.<sup>12</sup>

According to the guidelines, many countries initiated implementing stay-at-home in terms of the massive numbers of infected patients' globally and quickly increasing numbers of newly diagnosed patients.<sup>3</sup> It needs unparalleled strategies that influence patients' adherence to planned but postponable diagnostics,<sup>13</sup> and cancer screening programmes

were disrupted.<sup>14 15</sup> On the other hand, frequent hospital visits signify a threat of gaining infection with SARS-CoV-2. Thus, physicians and cancer patients are highly challenged with the dilemma to evaluate the advantage of routine cancer care contrary to the potential morbidity and mortality of COVID-19 infection.<sup>16</sup> Recently, studies showed that these alterations caused by COVID-19 pandemic likely had a straight and negative effect on the prostate cancer (PCa) screening by declining screening numbers and various types of cancer screenings<sup>15 17</sup> and directing to a possible hidden relationship between PCa and COVID-19.<sup>1</sup>

PCa is a leading public health problem in advanced countries that is the second most cancer in men and the fifth most prominent reason for cancer death globally.<sup>18 19</sup> Mortality has decreased in many countries as a result of PCa screening, early discovery and better treatment.<sup>18</sup> Currently, prostate-specific antigen (PSA) testing is advised as a low-cost, non-aggressive and fairly accurate method of PCa screening, according to the majority of worldwide plans.<sup>18</sup> Many urologists still follow this pattern as significant supporters of PSA testing.<sup>20</sup> Moreover, PSA screening was recently found to decrease the occurrence of PCa, and metastatic PCa meaningfully since 1992.<sup>18</sup> Furthermore, it was stressed that a reduction in PSA screening would lead to a significant decrease in PCa detection, with growth in PCa-specific mortality.<sup>21</sup>

Consequently, hospitals and clinics intensely reduced non-emergency clinical arrangements. Public avoidance of hospitals and delays to seek the routine medical care in cancer screenings and many diagnostic procedures in terms of COVID-19 are supposed to lead to loss of opportunity for timely and appropriate treatment and eventually extra excess deaths directly attributable to COVID-19 pandemic.<sup>7 15</sup>

Notwithstanding, the intensity of the association between COVID-19 and PCa remains unclear. Even though there have been different reviews which reported the effect of COVID-19 on cancers,<sup>22–24</sup> this is the first systematic review that provides comprehensive information about the effects of COVID-19 on screening and diagnosis of PCa. Therefore, we conduct this systematic review following Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols checklist guideline.<sup>25</sup>

## OBJECTIVES

The goal of the current research is to further our knowledge of how the COVID-19 pandemic affected patient with PCa screening and diagnosis, as well as to ascertain if COVID-19's continued prevalence may have an influence on regular PCa screening and diagnosis.

## METHODS AND ANALYSIS

### Eligibility criteria

The structure of the research question will be developed using PICOS; 'P' as Population, 'I' as Intervention, 'C' as Comparator/control, 'O' as Outcome and 'S' as Study

design.<sup>26</sup> According to PICOS parts, the eligibility criteria will be met the following.

### Participants/population

Inclusion criteria:

- Screening: asymptomatic people attending PCa screening programmes.
- Diagnosis: symptomatic men with suspicious lesions.

Exclusion criteria:

Studies reporting men with other cancers will be excluded (unless the data for PCa screening/diagnosis are separately reported).

### Intervention(s), exposure(s)

The intervention (exposure) of this study will be COVID-19.

### Comparator(s)/control

The comparator of this systematic review will be the period before COVID-19 pandemic and during the pandemic (initial, middle, long-term) (if comparative).

### Main outcome(s)

Screening: detection measures, such as cancer detection rate, recall rate, interval cancer rate, service usage, such as participation rate, and assessment change.

Diagnosis: number of diagnoses, stage at diagnosis, another diagnostic-oriented outcome if available.

### Studies design

Inclusion criteria:

Observation studies (cross-sectional, cohort, case-control study), grey literatures (conference papers, thesis) or any non-clinical study design related to our topic will be included.

Exclusion criteria:

- clinical studies.
- In vivo, in vitro studies.
- Reviews, case reports, case series.

### Information sources

The search of this study will be accomplished as follows:

- Electronic databases comprising PubMed/MEDLINE, Web of Science, Scopus, Embase via Emase.com and ProQuest were searched until 1 March 2022.
- Grey literature (conference papers and thesis).
- References of included papers (Manual Search).
- Key journals including Medicine and Biochemistry, Genetics and Molecular Biology.
- All preprint studies related to our topic in medRxiv and bioRxiv.

### Search strategy

This study will be designed based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.<sup>27 27</sup> The main keywords were used to perform the search strategy: COVID-19, prostatic neoplasms.

**Table 1** Search strategy for PubMed/MEDLINE

Search syntax	
#1	("COVID 19"[tiab] OR "COVID-19 Virus Disease"[tiab] OR "COVID 19 Virus Disease" [tiab] OR (Disease[tiab] AND COVID-19 Virus[tiab]) OR (Virus Disease[tiab] AND COVID-19[tiab]) OR "COVID-19 Virus Infection"[tiab] OR "COVID 19 Virus Infection" [tiab] OR (Infection[tiab] AND COVID-19 Virus[tiab]) OR (Virus Infection[tiab] AND COVID-19[tiab]) OR "2019-nCoV Infection"[tiab] OR "2019 nCoV Infection" [tiab] OR (Infection[tiab] AND 2019-nCoV[tiab]) OR "Coronavirus Disease-19" [tiab] OR "Coronavirus Disease 19" [tiab] OR "2019 Novel Coronavirus Disease" [tiab] OR "2019 Novel Coronavirus Infection" [tiab] OR "2019-nCoV Disease"[tiab] OR "2019 nCoV Disease" [tiab] OR (Disease[tiab] AND 2019-nCoV[tiab]) OR "COVID19" [tiab] OR "Coronavirus Disease 2019" [tiab] OR (Disease 2019[tiab] AND Coronavirus[tiab]) OR "SARS Coronavirus 2 Infection" [tiab] OR "SARS-CoV-2 Infection" [tiab] OR (Infection[tiab] AND SARS-CoV-2[tiab]) OR "SARS CoV 2 Infection" [tiab] OR "SARS-CoV-2 Infections" [tiab] OR "COVID-19 Pandemic"[tiab] OR "COVID 19 Pandemic" [tiab] OR (Pandemic[tiab] AND COVID-19[tiab]))
#2	("Prostate Neoplasm"[tiab] OR (Neoplasm*[tiab] AND Prostate[tiab]) OR (Neoplasm*[tiab] AND Prostatic[tiab]) OR "Prostatic Neoplasm" [tiab] OR "Prostate Cancer"[tiab] OR (Cancer*[tiab] AND Prostate[tiab]) OR "Cancer of the Prostate" [tiab] OR "Prostatic Cancer"[tiab] OR (Cancer*[tiab] AND Prostatic[tiab]) OR "Cancer of Prostate" [tiab])
#3	#1 AND #2

An example of the PubMed/MEDLINE search strategy is shown in [table 1](#). The search syntax was modified in other databases. There have not been any language restrictions.

All search syntax was provided in online supplemental table S1.

### Selection process

The selection process will be executed in three steps. In the first step, we will remove duplicated studies via EndNote software (V.X9.3.3, Thomson Reuters, Philadelphia, USA) and hand searching. In the second step, two independent authors (SMMZ, FT) will screen all records by title/abstract. In the last step, two authors (SMMZ, FT) will independently select the studies by full text. In case of any disagreement between the two authors, it will be resolved via consensus then will be checked by a third author (YM).

### Data collection process

Two authors (SMMZ, FT) will be extracted data from each included study separately. The attained data will be entered into a 'Data Extraction Form'. In case of discrepancies between the two authors will be resolved by consensus, then will be checked by a third author (YM).

### Data items

Data information will be extracted from each eligible study consisting: author's name, country, year of publication, sample size, age of the target group, information related to screening of PCa: cancer detection rate, recall rate, interval cancer rate; service usage (decrease or discontinuity of services, alteration in service transference mode), screening participation rate, presentation rate, PCa screening testing (PSA or digital rectal examination) rate, information related to diagnosis of PCa: number of diagnoses, stage at diagnosis, another diagnostic-oriented outcome if available.

### Quality assessment

All studies will be evaluated based on Newcastle-Ottawa Scale (NOS) tool by two independent authors (SMMZ, FT). NOS tool comprises three sections: selection,

comparability and exposure or outcome, with a score ranging from 0 to 9.<sup>28</sup> This scoring includes four stars for selecting, two stars for comparability and three stars for exposure or outcomes.

The quality assessment results are divided into three categories as follows: good (three or four stars in the selection area, one or two stars in the comparability area and two or three stars in the outcome/exposure area), fair (two stars in the selection area, one or two stars in the comparability area and two or three stars in the outcome/exposure area) and poor (0 or one star in selection area or 0 stars in comparability area or 0 or one star in outcome/exposure area).

In case of discrepancies between two authors will be resolved by consensus and then checked by a third author (YM).

### Statistical analysis

Considering the qualitative results which compare the effect of COVID-19 pandemic on PCa, and variation of data, meta-analysis and data synthesis will not apply.

### Patient and public involvement

Patients and the public are not involved in the preparation of this protocol and will not be directly involved in the final systematic review.

## DISCUSSION

Circulating biomarkers, such as phi; in association with different molecular forms of PSA, SelectMDx; based on a biomarker expression profile HOXC6 and DLX1 recommended to diminish the number of unnecessary prostate biopsies in PSA-tested men.<sup>29 30</sup> Some of these results suggest the ability of these novel biomarkers to improve PSA specificity in the detection of PCa.<sup>31</sup> Using PSA testing for PCa screening has lately been questioned, yet it remains the best available biomarker for early PCa detection.<sup>32</sup> A portion of the losses in screening in 2020 were likely attributable to cancelled or delayed screening, as well as a drop in patients' desire to undertake screening owing to the anxiety of catching COVID-19 at the doctor's office or



hospital.<sup>33</sup> The alterations in healthy-looking behaviour and the availability of and access to essential diagnostic services resulting from national pandemic processes will result in an enormous number of additional deaths from cancer.<sup>34</sup> Finally, it's crucial to ensure that patients have the ability to be continuously screened and diagnosed. It is regarded as a top priority at this time because of the overwhelming figures of COVID-19 cases and the high demand for medical supplies that many hospitals and healthcare facilities are experiencing (including personal protective equipment). It lacks healthcare suppliers in areas facing a mainly high number of cases. Moreover, the immediate consequences of COVID-19 pandemic can be considered at this time. It will take some years before the complete effect of the pandemic on cancer care can be considered.

### Ethics and dissemination

This review will retrieve published data, so it will not require ethical approval. The findings of this systematic review will be disseminated via an international peer-reviewed journal publication and several scientific conference presentations.

**Correction notice** This article has been corrected since it first published. The equally contributed statement has been added in the gutter section on the first page.

**Contributors** The search strategy developed by FT. The draft of the protocol prepared by SMMZ, FT and YM. ZM, RG and JK reviewed the manuscript and editing the final manuscript. All the authors have read, provided feedback and consented to the content of the protocol. Data screening and selecting phases of systematic review will be performed by SMMZ and FT. Quality assessment will be executed by SMMZ, FT and YM. Data extraction and preparing the draft of the manuscript will be performed by SMMZ, FT and YM. Moreover, ZM, RG and JK will be responsible for reviewing the manuscript and editing the final manuscript.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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### ORCID iD

Zahra Madjid <http://orcid.org/0000-0001-7329-2583>

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Table S1. Syntax of electronic databases

<b>PubMed/MEDLINE</b>
<p>(“COVID 19”[tiab] OR “COVID-19 Virus Disease*”[tiab] OR “COVID 19 Virus Disease” [tiab] OR (Disease[tiab] AND COVID-19 Virus[tiab]) OR (Virus Disease[tiab] AND COVID-19[tiab]) OR “COVID-19 Virus Infection*”[tiab] OR “COVID 19 Virus Infection” [tiab] OR (Infection[tiab] AND COVID-19 Virus[tiab]) OR (Virus Infection[tiab] AND COVID-19[tiab]) OR “2019-nCoV Infection*”[tiab] OR “2019 nCoV Infection” [tiab] OR (Infection[tiab] AND 2019-nCoV[tiab]) OR “Coronavirus Disease-19” [tiab] OR “Coronavirus Disease 19” [tiab] OR “2019 Novel Coronavirus Disease” [tiab] OR “2019 Novel Coronavirus Infection” [tiab] OR “2019-nCoV Disease*”[tiab] OR “2019 nCoV Disease” [tiab] OR (Disease[tiab] AND 2019-nCoV[tiab]) OR “COVID19” [tiab] OR “Coronavirus Disease 2019” [tiab] OR (Disease 2019[tiab] AND Coronavirus[tiab]) OR “SARS Coronavirus 2 Infection” [tiab] OR “SARS-CoV-2 Infection” [tiab] OR (Infection[tiab] AND SARS-CoV-2[tiab]) OR “SARS CoV 2 Infection” [tiab] OR “SARS-CoV-2 Infections” [tiab] OR “COVID-19 Pandemic*”[tiab] OR “COVID 19 Pandemic” [tiab] OR (Pandemic[tiab] AND COVID-19[tiab]))</p> <p>AND</p> <p>(“Prostate Neoplasm*”[tiab] OR (Neoplasm*[tiab] AND Prostate[tiab]) OR (Neoplasm*[tiab] AND Prostatic[tiab]) OR “Prostatic Neoplasm” [tiab] OR “Prostate Cancer*”[tiab] OR (Cancer*[tiab] AND Prostate[tiab]) OR “Cancer of the Prostate” [tiab] OR “Prostatic Cancer*”[tiab] OR (Cancer*[tiab] AND Prostatic[tiab]) OR “Cancer of Prostate” [tiab])</p>
<b>Embase</b>
<p>(‘COVID 19’:ti,ab OR ‘COVID-19 Virus Disease*’:ti,ab OR ‘COVID 19 Virus Disease’:ti,ab OR (Disease:ti,ab AND COVID-19 Virus:ti,ab) OR (Virus Disease:ti,ab AND COVID-19:ti,ab) OR ‘COVID-19 Virus Infection*’:ti,ab OR ‘COVID 19 Virus Infection’:ti,ab OR (Infection:ti,ab AND COVID-19 Virus:ti,ab) OR (Virus Infection:ti,ab AND COVID-19:ti,ab) OR ‘2019-nCoV Infection*’:ti,ab OR ‘2019 nCoV Infection’:ti,ab OR (Infection:ti,ab AND 2019-nCoV:ti,ab) OR ‘Coronavirus Disease-19’:ti,ab OR ‘Coronavirus Disease 19’:ti,ab OR ‘2019 Novel Coronavirus Disease’:ti,ab OR ‘2019 Novel Coronavirus Infection’:ti,ab OR ‘2019-nCoV Disease*’:ti,ab OR ‘2019 nCoV Disease’:ti,ab OR (Disease:ti,ab AND 2019-nCoV:ti,ab) OR ‘COVID19’:ti,ab OR ‘Coronavirus Disease 2019’:ti,ab OR (Disease 2019:ti,ab AND Coronavirus:ti,ab) OR ‘SARS Coronavirus 2 Infection’:ti,ab OR ‘SARS-CoV-2 Infection’:ti,ab OR (Infection:ti,ab AND SARS-CoV-2:ti,ab) OR ‘SARS CoV 2 Infection’:ti,ab OR ‘SARS-CoV-2 Infections’:ti,ab OR ‘COVID-19 Pandemic*’:ti,ab OR ‘COVID 19 Pandemic’:ti,ab OR (Pandemic:ti,ab AND COVID-19:ti,ab))</p> <p>AND</p> <p>(‘Prostate Neoplasm*’:ti,ab OR (Neoplasm*:ti,ab AND Prostate:ti,ab) OR (Neoplasm*:ti,ab AND Prostatic:ti,ab) OR ‘Prostatic Neoplasm’:ti,ab OR ‘Prostate Cancer*’:ti,ab OR (Cancer*:ti,ab AND Prostate:ti,ab) OR ‘Cancer of the Prostate’:ti,ab OR ‘Prostatic Cancer*’:ti,ab OR (Cancer*:ti,ab AND Prostatic:ti,ab) OR ‘Cancer of Prostate’:ti,ab)</p>

scopus
<p>(TITLE-ABS-KEY(("COVID 19" OR "COVID-19 Virus Disease*" OR "COVID 19 Virus Disease" OR (Disease, AND COVID-19 Virus) OR (Virus Disease AND COVID-19) OR "COVID-19 Virus Infection*" OR "COVID 19 Virus Infection" OR (Infection AND COVID-19 Virus) OR (Virus Infection AND COVID-19) OR "2019-nCoV Infection*" OR "2019 nCoV Infection" OR (Infection AND 2019-nCoV) OR "Coronavirus Disease-19" OR "Coronavirus Disease 19" OR "2019 Novel Coronavirus Disease" OR "2019 Novel Coronavirus Infection" OR "2019-nCoV Disease*" OR "2019 nCoV Disease" OR (Disease AND 2019-nCoV) OR "COVID19" OR "Coronavirus Disease 2019" OR (Disease 2019 AND Coronavirus) OR "SARS Coronavirus 2 Infection" OR "SARS-CoV-2 Infection" OR (Infection AND SARS-CoV-2) OR "SARS CoV 2 Infection" OR "SARS-CoV-2 Infections" OR "COVID-19 Pandemic*" OR "COVID 19 Pandemic" OR (Pandemic AND COVID-19)))</p> <p>AND</p> <p>(TITLE-ABS-KEY(("Prostate Neoplasm*" OR (Neoplasm* AND Prostate) OR (Neoplasm* AND Prostatic) OR "Prostatic Neoplasm" OR "Prostate Cancer*" OR (Cancer* AND Prostate) OR "Cancer of the Prostate" OR "Prostatic Cancer*" OR (Cancer* AND Prostatic) OR "Cancer of Prostate"))</p>
WOS
<p>(TS=("COVID 19" OR "COVID-19 Virus Disease*" OR "COVID 19 Virus Disease" OR (Disease, AND COVID-19 Virus) OR (Virus Disease AND COVID-19) OR "COVID-19 Virus Infection*" OR "COVID 19 Virus Infection" OR (Infection AND COVID-19 Virus) OR (Virus Infection AND COVID-19) OR "2019-nCoV Infection*" OR "2019 nCoV Infection" OR (Infection AND 2019-nCoV) OR "Coronavirus Disease-19" OR "Coronavirus Disease 19" OR "2019 Novel Coronavirus Disease" OR "2019 Novel Coronavirus Infection" OR "2019-nCoV Disease*" OR "2019 nCoV Disease" OR (Disease AND 2019-nCoV) OR "COVID19" OR "Coronavirus Disease 2019" OR (Disease 2019 AND Coronavirus) OR "SARS Coronavirus 2 Infection" OR "SARS-CoV-2 Infection" OR (Infection AND SARS-CoV-2) OR "SARS CoV 2 Infection" OR "SARS-CoV-2 Infections" OR "COVID-19 Pandemic*" OR "COVID 19 Pandemic" OR (Pandemic AND COVID-19)))</p> <p>AND</p> <p>(TS=("Prostate Neoplasm*" OR (Neoplasm* AND Prostate) OR (Neoplasm* AND Prostatic) OR "Prostatic Neoplasm" OR "Prostate Cancer*" OR (Cancer* AND Prostate) OR "Cancer of the Prostate" OR "Prostatic Cancer*" OR (Cancer* AND Prostatic) OR "Cancer of Prostate"))</p>
ProQuest
<p>(AB, TI(("COVID 19" OR "COVID-19 Virus Disease*" OR "COVID 19 Virus Disease" OR (Disease, AND COVID-19 Virus) OR (Virus Disease AND COVID-19) OR "COVID-19 Virus Infection*" OR "COVID 19 Virus Infection" OR (Infection AND COVID-19 Virus) OR (Virus Infection AND COVID-19) OR "2019-nCoV Infection*" OR "2019 nCoV Infection" OR (Infection AND 2019-nCoV) OR "Coronavirus Disease-19" OR "Coronavirus Disease 19" OR "2019 Novel Coronavirus Disease" OR "2019 Novel Coronavirus Infection" OR "2019-nCoV Disease*" OR "2019 nCoV Disease" OR (Disease AND 2019-nCoV) OR "COVID19" OR "Coronavirus Disease 2019" OR (Disease 2019 AND Coronavirus) OR "SARS Coronavirus 2 Infection" OR "SARS-CoV-2 Infection" OR (Infection AND SARS-CoV-2) OR "SARS CoV 2</p>

Infection” OR “SARS-CoV-2 Infections” OR “COVID-19 Pandemic\*” OR “COVID 19 Pandemic” OR (Pandemic AND COVID-19)))

AND (AB, TI (“Prostate Neoplasm\*” OR (Neoplasm\* AND Prostate) OR (Neoplasm\* AND Prostatic) OR “Prostatic Neoplasm” OR “Prostate Cancer\*” OR (Cancer\* AND Prostate) OR “Cancer of the Prostate” OR “Prostatic Cancer\*” OR (Cancer\* AND Prostatic) OR “Cancer of Prostate”))