astellas

When their first antimuscarinic has failed, why not take a different path?

Prescribing another antimuscarinic may be of minimal benefit after the first has failed.[1] So why not choose another route? BETMIGA is in a different class, relaxing the bladder via β_3-adrenoceptors.[2] It can be just as effective as an antimuscarinic, but it doesn't have the same side-effect profile.[3]

BETMIGA is indicated for symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.[2]

Prescribing information: BETMIGA™ (mirabegron)

For full prescribing information, refer to the Summary of Product Characteristics (SPC)

Presentation: BETMIGA prolonged-release tablets containing 25 mg or 50 mg mirabegron.

Indication: Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.

Posology and administration: The recommended dose is 50 mg orally once daily in adults (including elderly patients). Mirabegron should not be used in paediatrics. A reduced dose of 25 mg once daily is recommended for special populations (please see the full SPC for information on special populations). The tablet should be taken with liquids, swallowed whole and is not to be chewed, divided, or crushed. The tablet may be taken with or without food.

Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SPC. Severe uncontrolled hypertension defined as systolic blood pressure ≥ 180 mm Hg and/or diastolic blood pressure ≥ 110 mm Hg.

Warnings and Precautions: Renal impairment: BETMIGA has not been studied in patients with end stage renal disease (GFR < 15 mL/min/1.73 m^2 or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m^2); based on a pharmacokinetic study (see section 5.2 of the SPC) a dose reduction to 25 mg is recommended in this population. This medicinal product is not recommended for use in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m^2) concomitantly receiving strong CYP3A inhibitors (see section 4.5 of the SPC). Hepatic impairment: BETMIGA has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. This medicinal product is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors (see section 4.5 of the SPC). Hypertension: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with mirabegron, especially in hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg). Patients with congenital or acquired QT prolongation: BETMIGA, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies (see section 5.1 of the SPC). However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinics medicinal products for OAB: Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medicinal products for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with BETMIGA; however, BETMIGA should be administered with caution to patients with clinically significant BOO. BETMIGA should also be administered with caution to patients taking antimuscarinic medicinal products for the treatment of OAB.

Interactions: Caution is advised if mirabegron is co-administered with medicinal products with a narrow therapeutic index and significantly metabolised by CYP2D6. Caution is also advised if mirabegron is co-administered with CYP2D6 substrates that are individually dose titrated. In patients with mild to moderate renal impairment or mild hepatic impairment, concomitantly receiving strong CYP3A inhibitors, the recommended dose is 25 mg once daily. For patients who are initiating a combination of mirabegron and digoxin (P-gp substrate), the lowest dose for digoxin should be prescribed initially (see the SPC for full prescribing information). The potential for inhibition of P-gp by mirabegron should be considered when BETMIGA is combined with sensitive P-gp substrates. Increases in mirabegron exposure due to drug-drug interactions may be associated with increases in pulse rate.

Pregnancy and lactation: BETMIGA is not recommended in women of childbearing potential not using contraception. This medicinal product is not recommended during pregnancy. BETMIGA should not be administered during breast-feeding.

Undesirable effects: Summary of the safety profile: The safety of BETMIGA was evaluated in 8433 patients with OAB, of which 5648 received at least one dose of mirabegron in the phase 2/3 clinical program, and 622 patients received BETMIGA for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with this medicinal product, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for patients treated with BETMIGA 50 mg during the three 12-week phase 3 double blind, placebo controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 1.2% in patients receiving BETMIGA 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving BETMIGA 50 mg. The frequency of urinary tract infections was 2.9% in patients receiving BETMIGA 50 mg. Urinary tract infections led to discontinuation in none of the patients receiving BETMIGA 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies. Adverse reactions: The following list reflects the adverse reactions observed with mirabegron in the three 12-week phase 3 double blind, placebo controlled studies. The frequency of adverse reactions is defined as follows: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000) and not known (cannot be established from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The adverse events are grouped by MedDRA system organ class. *Infections and infestations:* Common: Urinary tract infection, Uncommon: Vaginal infection, Cystitis. *Psychiatric disorders:* Not known (cannot be estimated from the available data): Insomnia*, Confusional state*. *Nervous system disorders:* Common: Headache*, Dizziness*. *Eye disorders:* Rare: Eyelid oedema. *Cardiac disorders:* Common: Tachycardia, Uncommon: Palpitation, Atrial fibrillation. *Vascular disorders:* Very rare: Hypertensive crisis*. *Gastrointestinal disorders:* Common: Nausea*, Constipation*, Diarrhoea*, Uncommon: Dyspepsia, Gastritis, Rare: Lip oedema. *Skin and subcutaneous tissue disorders:* Uncommon: Urticaria, Rash, Rash macular, Rash papular, Pruritus, Rare: Leukocytoclastic vasculitis, Purpura, Angioedema*. *Musculoskeletal and connective tissue disorders:* Uncommon: Joint swelling. *Renal and urinary disorders:* Rare: Urinary retention*. *Reproductive system and breast disorders:* Uncommon: Vulvovaginal pruritus. *Investigations:* Uncommon: Blood pressure increased, GGT increased, AST increased, ALT increased. * signifies adverse reactions observed during post-marketing experience. Prescribers should consult the SPC in relation to other adverse reactions.

Overdose: Treatment for overdose should be symptomatic and supportive. In the event of overdose, pulse rate, blood pressure, and ECG monitoring is recommended.

Basic NHS Cost: BETMIGA 50 mg x 30 = £29, BETMIGA 25 mg x 30 tablets = £29

Legal classification: POM

Marketing Authorisation number(s): EU/1/12/809/001 – 018

Marketing Authorisation Holder: Astellas Pharma Europe B.V. Sylviusweg 62. 2333 BE Leiden. The Netherlands.

Date of Preparation of Prescribing information: June 2019

Job bag number: BET_2019_0023_UK

Further information available from: Astellas Pharma Ltd, Medical Information: 0800 783 5018. For full prescribing information, please see the Summary of Product Characteristics, which may be found at www.medicines.org.uk

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Astellas Pharma Ltd. on 0800 783 5018

October 2020

References: 1. Chancellor MB et al. Int Urol Nephrol 2016;48:1029–36. **2.** BETMIGA Summary of Product Characteristics. **3.** Maman K et al. Eur Urol 2014; 65: 755–65.

BET_2020_0076_UK

Article Category: Urological Oncology

Management of patients who opt for radical prostatectomy during the COVID-19 pandemic: An International Accelerated Consensus Statement.

Authors:

Zafer Tandogdu[1,2], Justin Collins[1], Greg Shaw[1], Jenifer Rohn[2], Bela Koves[3], Ashwin Sachdeva[4], Ahmed Ghazi[5*], Alexander Haese[6*], Alex Mottrie[7*], Anup Kumar[8*], Ananthakrishnan Sivaraman[9*], Ashutosh Tewari[10*], Benjamin Challacombe[11*], Bernardo Rocco[12*], Camilo Giedelman[13*], Christian Wagner[14*], Craig G. Rogers[15*], Declan G Murphy[16*], Dmitry Pushkar[17*], Gabriel Ogaya-Pinies[18*], Jim Porter[33*], Kulthe Ramesh Seetharam[19*], Markus Graefen[20*], Marcelo A. Orvieto[21*], Marcio Covas Moschovas[19*], Oscar Schatloff[22*], Peter Wiklund[10*], Rafael Coelho[23*], Rair Valero[24*], Theo M. de Reijke[25*], Thomas Ahlering[26*], Travis Rogers[19*], Henk G van der Poel[27*], Vipul Patel[19*], Walter Artibani[28*], Florian Wagenlehner[29], Senthil Nathan[1], Truls Erik Bjerklund Johansens[30], Peter Hawkey[31, 32], John Kelly[1,2]

1. University College London Hospital, Department of Urology, London, UK
2. University College London, Medical School, London, UK
3. Department of Urology, Budapest Hospital, Hungary
4. Freeman Hospital, Department of Urology, NHS Foundation Trust, Newcastle Upon-Tyne, UK
5. University of Rochester, Department of Urology, Rochester, USA
6. Leitender Arzt für roboterassistierte Urologie, Martini-Klinik am UKE GmbH, Universitätsklinikum Hamburg-Eppendorf
7. OLV Hospital, Department of Urology, Belgium
8. Department Urology ,Robotics and Renal Transplant ,Superspeciality Block,Safdarjang Hospital and VMMC, New Delhi, India
9. Apollo Hospitals, Department of Urology, Chennai, India
10. Icahn School of Medicine at Mount Sinai, Department of Urology, New York, USA
11. Guy's and St Thomas' Hospitals , Department of Urology, London, UK
12. University of Modena and reggio emilia, department of Urology AOU di Mldena, Italy

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/BJU.15299

13. Marly Clinic and the San José Hospital, Bogota, Colombia
14. St. Antonius - Hospital Gronau , Head of Robotic Urology, Gronau, Germany
15. Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan, USA
16. Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Australia
17. MSMSU,Urology, Moscow, Russia
18. Hospital Universitario Rey Juan Carlos, Madrid, Spain
19. Adventhealth Global Robotics Institute, Celebration Place, Florida, USA
20. Martini-Klinik, University-Hospital Hamburg-Eppendorf, Hamburg, Germany
21. Clinica Alemana, Department of Urology, Santiago, Chile
22. Sudmedica Health, Department of Urology, Valparaiso, Chile
23. University of São Paulo School of Medicine, São Paulo, Brazil
24. Scott Department of Urology, Baylor College of Medicine, Houston, Texas, USA
25. Amsterdam UMC, University of Amsterdam, Department of Urology, The Netherlands
26. University of California, Irvine, Orange, California, USA
27. Department of Urology, Netherlands Cancer Institute, Amsterdam, The Netherlands
28. University of Verona, Department of Urology, Verona, Italy
29. Department of Urology, Pediatric Urology and Andrology, Justus-Liebig-University, Giessen, Germany
30. Institute of Clinical Medicine, Department of Urology, University of Oslo, Oslo, Norway
31. Institute of Microbiology and Infection, University of Birmingham, Birmingham,UK
32. Queen Elizabeth Hospital Birmingham, UK
33. Swedish Medical Center, Seattle, USA

*Delphi working group.

Keywords: Covid-19,pandemic, cold site, prostate cancer, Delphi, nosocomial, Coronavirus, surgery

Word count: 3,437

References: 28

Corresponding author:

Zafer Tandogdu

Email: drzafer@gmail.com

Phone: +44 747 747 33 47

Address: University College London Hospital, Westmoreland Street, Department of Urology, London, UK

DR. ZAFER TANDOGDU (Orcid ID : 0000-0002-5309-3656)

Article type : Original Article

Abstract

Background: Coronavirus disease-19 (COVID-19) pandemic caused delays in definitive treatment of patients with prostate cancer. Beyond the immediate delay a backlog for future patients is expected. Such delays can lead to disease progression.

Objective: We aimed to develop guidance on criteria for prioritization for surgery and reconfiguring management pathways for non-metastatic stage of prostate cancer who opt for surgical treatment. A second aim was to identify the infection prevention and control (IPC) measures to achieve low likelihood of COVID-19 hazard if radical prostatectomy was to be carried out during the outbreak and whilst the disease is endemic.

Design, Setting and Participants: An accelerated consensus process and systematic review. We conducted a systematic review of the evidence on COVID-19 and reviewed international guidance on prostate cancer. These were presented to an international prostate cancer expert panel (n=34) through an online meeting. The consensus process underwent three rounds of survey in total. Additions to the second- and third-round surveys were formulated based on the answers and comments from the previous rounds.

Outcome Measures: Consensus opinion was defined as ≥80% agreement, which were used to reconfigure the prostate cancer pathways.

Results: Evidence on the delayed management of patients with prostate cancer is scarce. There was 100% agreement that prostate cancer pathways should be reconfigured and develop measures to prevent nosocomial COVID-19 for patients treated surgically. Consensus was reached on prioritization criteria of patients for surgery and management pathways for those who have delayed treatment. IPC measures to achieve a low likelihood of nosocomial COVID-19 were coined as "COVID-19 cold sites".

Conclusion: Re-configuring management pathways for prostate cancer patients is recommended if significant delay (>3-6 months) in surgical management is unavoidable. The mapped pathways provide guidance for such patients. The IPC processes proposed provide a framework for providing radical prostatectomy within an environment with low COVID-19 risk during the outbreak or when the disease remains endemic. The broader concepts could be adapted to other indications beyond prostate cancer surgery.

Funding: No funding was received for this project

1 Introduction

The coronavirus disease-19 (COVID-19) pandemic has affected healthcare at multiple levels with inevitable delays in provision of care for patients with other conditions, such as cancer . This includes men with non-metastatic prostate cancer who are awaiting surgical treatment (1, 2). Prostate cancer is a heterogenous disease, with a global annual incidence of 1.3 million and 419,000 deaths per annum (3). Non-metastatic prostate cancer is categorized into three main groups (low, intermediate and high) based on risk of disease progression (4, 5). Radical treatment, including surgery or radiotherapy, mostly benefits men with intermediate or high-risk disease with a life-expectancy of over 10 years (5). Prolonged delay in treatment will probably result in disease progression with consequent loss of ability to preserve peri-prostatic structures impacting on functional outcomes. Furthermore, the expected duration of delays to curative treatment remains unclear but any delay will result in a backlog of the number of men awaiting radical treatment. Delays to the diagnostic pathway from prostate specific antigen (PSA) testing to biopsy will also add to the backlog and result in later presentation of more advanced disease, which poses a risk to patient wellbeing. Mitigation of these risks during the COVID-19 pandemic necessitate reconfiguration of management pathways and development of strategies to prioritize patients. An additional challenge is the need to protect both patients and healthcare workers from contracting COVID-19 until the disease is either eradicated or vaccines are developed whilst ensuring the safe delivery of radical treatment for those in need.

The first aim of this study was to develop guidance on reconfiguring the management pathways for prostate cancer patients with non-metastatic disease whose radical surgical treatment is delayed due to the COVID-19 outbreak. A second aim was to identify the basic requirements of achieving low likelihood of COVID-19 hazard within a health care unit intending to offer prostate cancer surgery whilst the corona virus remains in population (a so-called COVID-19 “cold” site). We used an accelerated consensus by adapting the Delphi methodology to provide guidance in the absence of substantial evidence during the COVID-19 outbreak. In addition, we hope that the infection prevention and control principles (IPC) will be of relevance for other specialties planning to deliver surgery as long as COVID-19 remains in community without definitive treatments or vaccines.

2 Material and methods

The study consisted of three objectives where each phase informed the subsequent phase. First, a systematic review of the literature and current published guidelines was completed in accordance with the PRISMA statement (6). Second, the systematic review informed a series of questions from which answers by consensus was sought. Third, the obtained consensus, in turn, helped map a pathway for the reconfiguration of prostate cancer management for patients who opt for surgery if a backlog develops during the COVID-19 outbreak and establish the components for how to deliver surgery whilst COVID-19 can spread in community.

2.1 Evidence synthesis: COVID-19 & Prostate Cancer

The first teleconference was conducted on Saturday April 4th 2020 and the second on Tuesday April 7th 2020. At the inception of this project there was limited evidence published for COVID-19 and its impact on surgery. The available evidence was used to develop questionnaires for the Delphi consensus process. This process was carried out by authors with expertise in infectious diseases (ZT, PH, JR, TEBJ, FW, BK). A systematic review of the literature was carried out using MEDLINE (accessed from PubMed to identify published articles from January 01, 2020 to March 30, 2020 (further details in Supplement I). Guidelines and recommendations regarding COVID-19 published by World Health Organization (WHO), Center for Disease Control (CDC), European Center for Disease Control (ECDC) and National Institute for Clinical Excellence (NICE) were reviewed. Publications identified from reference lists of these documents were also reviewed.

The aim of this evidence synthesis work was to identify questions relevant to:

a) Frequency of asymptomatic COVID-19 patients
b) Incubation period of COVID-19
c) Sensitivity and specificity of available diagnostic tests for COVID-19 in asymptomatic patients
d) Stages of contagiousness
e) Duration of contagiousness
f) Risk factors for severe outcomes in patients who develop COVID-19
g) In hospital IPC measures that can be implemented to establish an environment protective for both the patient and health care workforce before, during and after radical prostatectomy
h) Prostate cancer management guidelines, to review existing pathways and suggest modification in order to minimize risk during the pandemic (supplement II)

The prostate cancer guidelines and recommendations published by the European Association of Urology (EAU) and National Comprehensive Caner Network (NCCN) were reviewed (ZT, JC, GS). Information summarized by these documents was used to establish the baseline of current expected practice for prostate cancer patients who are eligible for radical treatment.

2.2 Expert panel teleconference meeting

An advisory panel was formed that was comprised of key opinion leaders with a specialist expertise in infectious diseases, prostate cancer management and/or robotic surgery programs (supplement III). J.K., P.H., J.C. and Z.T. chaired panels. In total thirty-eight experts from four continents including seven countries from Europe (Belgium, Germany, Hungary, Italy, Netherlands, Norway, UK) were brought together to discuss and develop an international standard for the development of a cold site for managing prostate cancer during the pandemic. At the time of the consensus, Europe was at the centre of the pandemic and experts were selected from countries with different healthcare contexts to allow generalizability of findings. Experts with recent experience in managing PC patients during the COVID-19 crisis were included (Italy/Spain/New York/ California). Thirty-six panel members were qualified as surgeons (including four members of the EAU section of Infections in Urology, for which three have expertise in nosocomial infections) and two were experts on infection prevention and control as well as virology (supplement III for composition of panel and roles). The teleconference meetings comprised presentations (supplement IV) on the subject matter, clarifications of current evidence and reviews of the literature findings. Overviews of the various strategies development of "COVID-19 cold" sites were discussed.

2.3 Internet survey and consensus process

Following the teleconference, the consensus process was conducted amongst the experts. An internet survey (Google forms) was generated and sent to the 34 members of the panel (Supplement V). An accelerated e-consensus-reaching exercise, over three consecutive days, by using the Delphi methodology, was then applied (7). The Delphi method structures group communications so that the process is effective in allowing a group of individuals to deal with a complex problem. We consented participants prior to the process and its time points. This was particularly important in accelerating the process.

Questions in which there was ≥80% consensus were removed from the next round of the survey. Repeated iterations of anonymous voting continued over three rounds, where an individual's vote in the next round was informed by knowledge of the entire group's results in the previous round. To be included in the final recommendations each survey item had to have reached group consensus (≥80% agreement) by the end of the three survey rounds. In the Delphi process the finding of 'consensus' is more relevant than the level of consensus. Levels of consensus are reported in Supplement V.

The process applied adhered to the principles of Delphi methodology of, (i) selection of panel members -experts, (ii) development and application of questions in rounds (iii) evolution of responses and (iv) divergence towards a consensus (7). Although, the implementation of a Delphi process can be variable, the strict time frames we applied is novel. Therefore, we have coined the process as a consensus statement.

2.4 Pathway development

The purpose of the pathway development and mapping is to systematically assemble evidence to provide guidance for clinicians. The existing pathways were reviewed and reconfigured using available evidence, published similar pathways and input from the consensus process (4, 5, 8). Subsequent to the consensus process, plausible scenarios to plan for delays in radical surgical treatment from the point of risk stratification of prostate cancer onwards were illustrated in a one-page comprehensive flow-chart. This was an iterative process whereby the consensus panel was consulted to review the prepared pathway until agreement was reached.

3 Findings

3.1 Evidence and guidance for COVID-19

The evidence acquisition process included 2,430 records reviewed and 30 full texts were used (Figure 1). Further studies and recommendations were obtained from WHO, CDC, ECDC and NICE. Findings are provided in Supplement-I.

3.2 Consensus process

Consensus was reached on multiple items (84.3%, n=75/89). Results of the three rounds are summarized in Figure 2 and details are provided in supplement V. The main statements of the consensus process are summarized in Table 1**Error! Reference source not found.**. A detailed summary of the statements is provided in supplement VI.

3.2.1 Delivery of surgery

The panel reached consensus on multiple items that collectively contribute to re-arranging a hospital site to deliver radical prostate surgery within a COVID-19 protected environment. These are summarized in Table 1 and the panel agreed to define such sites that adhere to the principles as "COVID-19 cold". The panel reached consensus that resource allocation to "COVID-19 cold" sites should be guided by the resource requirement of COVID-19 patients in individual regions and countries.

Principles of patient flow prior, during and after surgery are dependent on the sensitivity and specificity of COVID-19 diagnostic tests as well as the time taken to obtain results. At the time of manuscript preparation there remained a paucity of rapid tests with a high sensitivity and specificity. Therefore, the panel agreed on a set of basic principles and assumptions to be used to keep the risk of COVID-19 as low as possible within the "COVID -19 cold" sites. The principles that were agreed on include accounting for the incubation period of COVID-19, the need to operate on patients with minimal risk of contagiousness, and isolation of patients after surgery until catheter is removed (on average 10 days). The panel could not reach consensus on how to implement the preoperative process

to ensure that surgery is performed on patients with the least likelihood of contagiousness. Based on the discussions and the reviewed literature the scenarios discussed are illustrated in Figure 2.

3.2.2 Rationing prostate cancer surgery

Panel reached consensus on rationing prostate cancer patients using the EAU risk classification tool, age and risk factors for COVID-19 worse outcomes. Statements agreed are provided in Table 1. A conceptual summary of the agreed principles is summarized in Figure 3.

3.2.3 Re-configuration of management pathways

Consensus was achieved to re-arrange pathways for patients whose definitive treatment will be postponed using the EAU risk stratification. A conceptual pathway that was mapped based on the panel consensus, and is provided in Figure 4 and details of statements, in Table 1. Discussion

4 Discussion

In this study an international expert panel developed consensus statements to reconfigure surgical pathways if there was a delay due to the impact of the COVID-19 outbreak. This challenging task was achieved through an accelerated consensus process. The statements were developed with the intention to be utilized as part of a comprehensive response to maintain essential healthcare services while simultaneously ensuring care for acutely ill COVID-19 patients. The ability of a country to maintain essential health care services will be influenced by its underlying resources, incidence of COVID-19 and other cases. Therefore, the consensus was developed to address re-organization of the pathways of prostate cancer patients who opt for surgery until health-care systems resume routine services. In addition, throughout the outbreak there will be variability in the strategic allocation of resources dependent on the incidence of COVID-19. The panel has agreed to ration cases for surgery and the underlying concepts to achieve this in a protected environment that minimise risk to the patient and healthcare staff to additional adverse outcomes of COVID-19. These will be helpful for countries that can allocate resources for cancer surgery during the different stages of the pandemic. Beyond this the rationing strategy for prostate surgery cancer will remain relevant once the pandemic is over in prioritizing patients within the backlog.

We reached consensus on multiple items related to delivery of surgery and postoperative care, if possible, during the outbreak. Two key concepts that were agreed largely shape the remaining statements of the consensus for delivery of surgery. The first concept is to simultaneously ensure safety of the patient and healthcare staff regarding COVID-19 (i.e. prevention and control of nosocomial COVID-19). The second concept is to assume that at any given time point a patient or healthcare professional can be contagious. Lack of rapid and accurate diagnostics shaped these concepts. This means that at the point of entry to a “COVID-19 cold” site it is not possible to

distinguish if individuals are contagious or not. Viral RNA detection methods can identify individuals shedding the virus but this does not necessarily indicate contagiousness(9). Lack of reliable serology tests and unknown duration of contagiousness after COVID-19 are additional complexities that the panel considered. Nosocomial infections of the virus within a "COVID-19 cold" site delivering elective prostate cancer surgery could result in serious consequences and defeat the purpose of such a site. Initial series indicate that in COVID-19 treatment sites nosocomial infection rate could be up to 41%(10). Concepts adopted by the panel can be considered as a safe option that maintains the "COVID-19 cold" site functional throughout the outbreak until the corona virus is either eradicated from community or vaccine is developed. However, these concepts generate significant operational challenges including reconfiguration of the work and patient flow and utilization of large amounts of personal protective equipment (PPE).

Concerns of inadequate global PPE stockpiles mean that effective and appropriate use of PPE is imperative to maintain safe healthcare provision as long as COVID-19 remains in community (11). Adjustment of PPE composition based on likelihood of contagiousness was successful during the 2015 Middle Eastern Respiratory Syndrome outbreak and similar approaches can be adopted for "COVID-19-cold" sites to ensure efficient use of PPE(12). Due to absence of definitive diagnostics a combination of measures can be utilized to decrease the likelihood of COVID-19 contagiousness of an individual and guide PPE use. A key strategy can be isolation of the patient prior to surgery in combination with diagnostics (summarized in Figure 2 and supplement-VII). We failed to reach consensus on isolating patients for 48 hours in a designated room (external to but near the hospital) and screening the surgical candidate at entry and end of isolation. At the final consensus meeting it became apparent that panel members who rejected this statement were concerned that infrastructure to deliver this was not available at their own site. Current knowledge indicates that the incubation period on average is 5 days but this can extend up to 14 days(13). Therefore, the safest duration of pre-operative isolation would be 14 days. This could be combined with an RNA-viral test at the beginning and end of isolation if resources allowed. Isolation of patients can be carried out in single isolation rooms or cohort rooms based on IPC guidance(14). Our panel also suggested that countries that can't provide the required resources for patients to isolate in hospital prior to surgery should instead, advise patients to self-isolate at home. Countries will need to adapt these recommendations to what is achievable within their means. The success of self-isolation at home prior to surgery relies on the compliance of patients. To improve compliance to quarantine of suspected cases Taiwan utilized mobile tracking technology to monitor patient movements(15). Interventions to improve compliance to self-isolation at home prior to surgery will be a challenge that needs to be addressed uniquely for each country and culture. Overall, the success of a "COVID-19 cold" site will be dependent on the applied process, hospital resources, efficient use of PPE and compliance with the recommendations that are regularly updated as new evidence emerges. Finally, the panel provided a set of

recommendations to decrease PPE consumption during surgery such as placing the robotic surgical console in a separate room and utilizing telemedicine as suggest by WHO(11, 16). This would be subject to local regulations.

Reconfiguration of patient and healthcare staff flow is a vital IPC measure to achieve and protect a "COVID-19 cold" site. A hospital in Sichuan, China, applied rigorous IPC measures including reconfiguration of flow within an emergency radiology department, succeeding in protecting all healthcare staff from COVID-19 despite carrying out 3,340 CT scans on COVID-19 suspected cases within 47 days (17). Our panel agreed to take further measures to control staff flow, such as changing working shifts to a week or beyond and reside at the hospital site. It is expected that this can help in effective resource allocation by negating the need for frequent screening of healthcare staff and reduce risk of transmission of COVID-19.

Decrease in available resources to maintain essential health care services, limited PPE supply and risk of COVID-19 adverse outcomes in the general population have created the urgent need to ration prostate cancer surgery(11, 18). We agreed that the decision to offer prostate cancer surgery during the pandemic should be made by weighing up the risk of prostate cancer disease progression and the risk of COVID-19 adverse effects (Figure 4). Of note, it is currently unclear whether surgery during the pandemic increases the risk of mortality from COVID-19. Although a recent paper based upon a small heterogenous cohort of COVID-19 confirmed cases undergoing elective surgery at an early time point during the current pandemic has indicated that this could be the case(19), however selection bias within this cohort limits our ability to refute or support this hypothesis. Nevertheless, patients who developed severe COVID-19 features within this surgical cohort tended to be older patients with one or more co-morbidities. Our proposed approach to select patients for prostate cancer surgery during the pandemic prioritizes younger patients with higher risk disease with only one or zero co-morbidities.

Prostate cancer risk stratification was considered to play a crucial role in selecting patients most likely to benefit from surgery during the pandemic. The panel agreed that patients with low risk disease should be placed on active surveillance protocols, irrespective of their preference for immediate surgery. This is supported by findings from e.g. the PIVOT study reporting only minor survival benefit amongst patients with low-risk disease treated with surgery(20). We agreed that NCCN criteria can be used to further subgroup the intermediate-risk patients and active surveillance can be offered to the favorable group per results from the PROTECT trial(21) and observational data(4, 22). Furthermore, inaccurate initial disease staging is known to result in subsequent upstaging in approximately 30% patients with intermediate-risk disease(23). Beyond that there is concern that non-targeted biopsies and absence of MRI scans for staging can miss extra prostatic extension(24). Thus, the panel agreed upon closer surveillance of conservatively managed intermediate-risk patients, with

repeat staging with MRI at 6 months if available. The proposed pathway advises that patients upstaged at this point should be offered immediate definitive treatment or ADT, after weighing up the risk of COVID19 adverse effects.

Patients with non-metastatic high-risk prostate cancer may be managed by either immediate surgery in the absence of COVID-19 risk features, or alternatively offered ADT until safe to proceed to surgery, although this will have a considerable impact on the patients' Quality of Life. Previous observational studies have shown that it may be safe to defer surgery in high risk disease by up to 90 days, with the use of ADT(25). However, recent modeling estimates have predicted that the COVID-19 pandemic may continue for more than 3 months and possibly until a vaccine is developed (26), which is likely to delay treatment for a subset of older patients with high-risk prostate cancer and multiple co-morbidities. Based upon data from the control arm of the STAMPEDE trial, it is anticipated that 32% of patients with N0 and 47% of patients with N1 disease within this ADT treated cohort are likely to progress over a 2-year period(27). In addition, long-term ADT should be avoided in patients with multiple pre-existing co-morbidities due to risk of developing additional co-morbidities(28).

External beam radiotherapy (EBRT) can also be considered for men with prostate cancer(5). During the pandemic this option would possibly have limited use as it requires multiple and frequent hospital visits (total 20 to 25 hospital visits within four to five weeks) increasing the risk of COVID-19 for the patient(5). The rapid response group of the EAU guidelines suggested to postpone RP until the end of the pandemic whilst suggesting that EBRT can still be offered(29). They also suggested keeping outpatient visits as low as possible, which contradicts with offering RT during the pandemic. With the introduction of "COVID-19 cold" sites the heterogeneous epidemiology of the pandemic is taken into account and the multiple risks accompanying can be mitigated and provide surgery as an option for patients if necessary.

Our approach to employ a consensus process was particularly helpful in accomplishing our objectives. The Delphi process is useful for complex issues that cannot be subject to clinical studies. For such circumstances they are impactful and help in standardizing management. The COVID-19 outbreak has created circumstances with great uncertainty that reflected on to urological practice (30). For instance, an online survey identified that in 13% of urology practices urologists were encouraged by their managers not to ware face masks (30). The time sensitive issues meant that we had to apply an accelerated process to achieve our objectives. In our study we adhered to the fundamental principles of a Delphi consensus process(7.)The methodology does not dictate the duration of the process but due to the nature of urgency and scale of the events we applied an accelerated process. To our knowledge this is a novel approach that has not been published before. This was time intensive and to achieve success all participants were consented prior to entering the study to adhere to the strict time schedule. The process also required similar consent for the questionnaire development by experts in

infectious diseases (PH, JR), nosocomial infections in urology (ZT, TEBJ, FW) and prostate cancer surgical management (GS, JC, JK). The accelerated consensus we carried out by adhering to the principles of Delphi methodology is novel and we refer to it as a consensus statement. Despite the strengths of the work there are some caveats. Firstly, the panel members were from 16 different countries around the world, but most were from Europe and the U.S. We therefore concentrated on establishing the basic principles for reconfiguring pathways and the IPC measures that can be adjusted for local needs. Second, certain items such as double swap test prior to surgery that could be beneficial from an IPC point of view did not reach consensus. This was due to concerns of local resources of the participants and we have proposed several different alternative pathways as illustrated in figure 3. Thirdly, we did not present with a local audit tool for the proposed reconfigured pathways yet measuring the impact can be useful. However, this was found to be challenging due to the complexity of the pathway. Finally, we only reviewed the pathway for patients with localized prostate cancer that opt for radical surgical treatment. Despite this cohort can benefit from the current work there is more to be done for reconfiguring the pathways for localized prostate cancer.

Future research related to this work should encompass the measurement of the impact of pathway reconfiguration. Such research should prioritize patient related outcomes including cancer progression, side effects related to ADT and functional outcomes following delayed surgery. Furthermore, studies of "COVID-19-cold" sites should measure the frequency, characteristics and implications of COVID-19 cases following surgery. The impact on healthcare workforce should also be measured, including their well-being and frequency of hospitals acquired COVID-19. Health-economic assessment of the "COVID-19-cold" sites could be challenging. Nevertheless, the cost and utility of a "COVID-19-cold" site can be estimated against the absence of such a site during the pandemic.

In summary, the panel reached consensus on two main domains. Firstly, if COVID-19 remains in community surgical procedures for the treatment of prostate cancer should be carried out in a setting where the likelihood of COVID-19 related hazards and consequences are kept low. To achieve this, the panel agreed on the concepts to which the healthcare environment, patients and healthcare workforce must adhere. Secondly, agreement was reached on re-configuring the management pathways for prostate cancer patients if significant delay (>3-6 months) in curative management was unavoidable. The EAU risk classification system was adopted, and follow-up pathway of each risk group was refined. Finally, some of the broader concepts could be adapted to other indications beyond prostate cancer surgery.

Conflicts of Interest

Zafer Tandogdu declares no conflicts of interest.

Legends

Table 1. Consensus view on re-organization of management pathways for prostate cancer patients eligible for surgical treatment during the COVID-19 pandemic.

Figure 1. Flow chart of the published literature review to develop the consensus questionnaire. In addition, recommendations from WHO, CDC, ECDC and NICE were also reviewed in developing the questionnaire.

Figure 2. Summary of the Consensus process.

Figure 3. Protocols for prevention of COVID-19 before, during and after surgery**.** (1) No intervention: The patient flow followed prior to the COVID-19 outbreak. This flow does not reduce the risk of operating on COVID-19 (+) patients. It exposes the patient, health care professionals and other patients on wards to increased risk of COVID-19. The panel advised against operating on patients with high likelihood of COVID-19. This scenario would be the most personal protective equipment - exhaustive approach. (2) Isolation only: In this protocol the patient is kept under isolation for a set period of time that would ideally cover the incubation period of COVID-19. If patient remains asymptomatic throughout isolation, they can be assumed to be at low risk for COVID-19. Implementation of this strategy should account for logistics such as self-isolation vs. isolation at a designated site selected by the COVID-cold hospitals. The success of this strategy relies on strict isolation and ideally should cover 14 days (97.5% of patients incubation period) (3) Isolation and screening protocol. In this protocol the patient is screened for viral RNA at the beginning and the end of the isolation period. It could be helpful in different ways. First, it can reduce the duration of the isolation period (i.e. Double swap negative within 48 hours low likelihood of COVID-19 carrier). Second, if a long isolation is suggested (i.e. 2 weeks) the first screen can be considered as a safety check at entrance of self-isolation. Thus, if a patient is positive on first screen that means their surgery should be postponed. Therefore, useful in scheduling for theatres. The two-week isolation with double swabs at entrance and exit of isolation is the safest option until the self-isolation compliance can be secured that negates the exit swab. See supplement VI for different strategies on implementing this approach. (4) Screening only. This protocol assumes utilisation of a rapid diagnostic test that informs the clinicians regarding COVID-19 contagiousness and immunity status of individuals. Protocols 2-4 assume that the COVID-19 outbreak is ongoing and therefore suggests that patient self-isolates after discharge until removal of indwelling urinary catheter (consensus by panel).

Figure 4. A conceptual illustration of surgical prioritization process of prostate cancer patients during the COVID-19 pandemic.

Figure 5. Conceptual pathway for prostate cancer patients whose definitive treatment will be delayed.

5 References

1. Naspro R, Da Pozzo LF. Urology in the time of corona. Nature Reviews Urology. 2020.

2. Campi R, Amparore D, Capitanio U, Checcucci E, Salonia A, Fiori C, et al. Assessing the Burden of Nondeferrable Major Uro-oncologic Surgery to Guide Prioritisation Strategies During the COVID-19 Pandemic: Insights from Three Italian High-volume Referral Centres. European Urology.

3. Collaboration GBoDC. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncology. 2019;5(12):1749-68.

4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Prostate Cancer. Version 4.2018. 2018.

5. N. Mottet (Chair) PCV-c, R.C.N. van den Bergh, E. Briers (Patient Representative), M. De Santis, S. Fanti, S. Gillessen, J. Grummet, A.M. Henry, T.B. Lam, M.D. Mason, T.H. van der Kwast, H.G. van der Poel, O. Rouvière, I.G. Schoots, D. Tilki, T. Wiegel, Guidelines Associates: T. Van den Broeck MC, N. Fossati, G. Gandaglia, N. Grivas, M. Lardas, M. Liew, L. Moris, D.E. Oprea-Lager, P-P.M. Willemse. EAU Guidelines: Prostate cancer. European Association of Urology; 2020 2020.

6. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Medicine. 2009;6(7):e1000097.

7. Iqbal S, Pipon-Young L. The Delphi method. Psychologist. 2009;22:598-601.

8. Maclennan SJ, Maclennan SJ, Imamura M, Omar MI, Vale L, Lam T, et al. Urological cancer care pathways: development and use in the context of systematic reviews and clinical practice guidelines. World journal of urology. 2011;29(3):291-301.
9. Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020.
10. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. Jama. 2020.
11. Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19) World Health Organization; 2020 19/03/2020.
12. Park J, Yoo SY, Ko JH, Lee SM, Chung YJ, Lee JH, et al. Infection Prevention Measures for Surgical Procedures during a Middle East Respiratory Syndrome Outbreak in a Tertiary Care Hospital in South Korea. Sci Rep. 2020;10(1):325.
13. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. Annals of internal medicine. 2020.
14. Reducing the risk of transmission of COVID-19 in the hospital setting. National Institute of Clinical Excellence; 2020 12/04/2020.
15. Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: Big Data Analytics, New Technology, and Proactive Testing. Jama. 2020;323(14):1341-2.
16. eHealth WHOGOf. Telemedicine: opportunities and developments in Member States: report on the second global survey on eHealth. Geneva: World Health Organization; 2010.

17. Huang Z, Zhao S, Li Z, Chen W, Zhao L, Deng L, et al. The Battle Against Coronavirus Disease 2019 (COVID-19): Emergency Management and Infection Control in a Radiology Department. Journal of the American College of Radiology : JACR. 2020.

18. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 28.: World Health Organization; 2020 17 February 2020.

19. Lei S, Jiang F, Su W, Chen C, Chen J, Mei W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020:100331.

20. Wilt TJ, Jones KM, Barry MJ, Andriole GL, Culkin D, Wheeler T, et al. Follow-up of Prostatectomy versus Observation for Early Prostate Cancer. The New England journal of medicine. 2017;377(2):132-42.

21. Bryant RJ, Oxley J, Young GJ, Lane JA, Metcalfe C, Davis M, et al. The ProtecT trial: analysis of the patient cohort, baseline risk stratification and disease progression. BJU international. 2020;125(4):506-14.

22. Klotz L, Vesprini D, Sethukavalan P, Jethava V, Zhang L, Jain S, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2015;33(3):272-7.

23. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. The Lancet. 2017;389(10071):815-22.

24. Shaw GL, Thomas BC, Dawson SN, Srivastava G, Vowler SL, Gnanapragasam VJ, et al. Identification of pathologically insignificant prostate cancer is not accurate in unscreened men. British Journal of Cancer. 2014;110(10):2405-11.

25. Fang D, Zhou L. Androgen deprivation therapy in nonmetastatic prostate cancer patients: Indications, treatment effects, and new predictive biomarkers. Asia-Pacific journal of clinical oncology. 2019;15(3):108-20.

26. Prem K, Liu Y, Russell TW, Kucharski AJ, Eggo RM, Davies N, et al. The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. The Lancet Public Health.

27. James ND, Spears MR, Clarke NW, Dearnaley DP, Mason MD, Parker CC, et al. Failure-Free Survival and Radiotherapy in Patients With Newly Diagnosed Nonmetastatic Prostate Cancer: Data From Patients in the Control Arm of the STAMPEDE Trial. JAMA Oncol. 2016;2(3):348-57.

28. Ng HS, Koczwara B, Roder D, Vitry A. Development of comorbidities in men with prostate cancer treated with androgen deprivation therapy: an Australian population-based cohort study. Prostate cancer and prostatic diseases. 2018;21(3):403-10.

29. EAU Guidelines Office Rapid Reaction Group: An organisation-wide collaborative effort to adapt the EAU guidelines recommendations to the COVID-19 era European Association of Urology; 2020.

30. Teoh JY-C, Ong WLK, Gonzalez-Padilla D, Castellani D, Dubin JM, Esperto F, et al. A Global Survey on the Impact of COVID-19 on Urological Services. European Urology.

COVID-19 pandemic impact on prostate cancer patients

1. Disruption in health care services for prostate cancer patients
2. Immediate delay in curative management
3. Increase in backlog resulting in subsequent delays
4. Overall increase in likelihood of disease progression

Basic requirements for a unit to deliver prostate cancer surgery whilst sustaining low risk for COVID-19 transmission and consequences

1. Capacity to screen for COVID-19
2. Infection prevention and control protocols (IPC) adapted for COVID-19 to be applied for patients
3. IPCs adapted for COVID-19 to be applied by the health care workforce
4. Rearrangements of the hospital space and workflow that aims to create and maintain areas with low likelihood of COVID-19 transmission hazard
5. Protocols for rapid isolation of COVID-19-suspected cases detected in the unit into areas separate from COVID-19 free wards
6. Areas with COVID-19-suspected or proven patients that are separate from the prostate cancer screening, treatment and follow-up areas
7. Utilization of telemedicine whenever possible to ensure good communication and planning whilst minimising hospital admissions

The seven items above collectively contribute to decreasing the risk of COVID-19 transmission (likelihood of hazard) and its consequences (severity of hazard) within a site that delivers prostate cancer surgery. We define such a site as a "*COVID-cold site*".

Resource allocation for COVID-19-free prostate cancer surgical units

1. In accordance with local resource allocation required for COVID-19 patients
2. Guided by COVID-19 local epidemiology, overall hospital capacity and its estimated future capacity

COVID-19 considerations for patients planned for surgery

Soon before surgery	***Surgery***	***After surgery***
1. Patient should be screened for contagiousness of COVID-19 2. Application of optimal general hygienic measures (i.e. hand disinfection) 3. Account for the lag period between becoming contagious and testing positive for COVID-19 and the potential for false negative tests*. 4. If possible, consider self-isolation of asymptomatic patient prior to surgery, ideally at a location	1. Patient should be non-contagious of COVID-19 2. Consent the patient for COVID-19 related risks and hazards	1. Self-isolate at home after discharge *at least* until indwelling urinary catheter is removed safely (including travel to and from hospital) 2. Do not routinely screen for COVID-19 prior to discharge if asymptomatic

designated by the hospital whereby the patient flow is reviewed and monitored[ψ] 5. Avoid public transportation		
COVID-19 considerations for the healthcare workforce that will deliver prostate cancer surgery treatment in COVID-cold sites		
1. Symptomatic healthcare workers should self-isolate and should not attend COVID-19 cold sites 2. Asymptomatic healthcare workers should be screened and reviewed for COVID-19 prior to a shift[Δ] 3. Evidence for the optimal screening method is unclear (symptoms vs. viral load vs serology vs imaging)* 4. Liaise with local IPC teams to identify the optimal screening protocol applicable to your region. 5. Follow future evidence for antibody screening as a tool to establish risk for healthcare worker (an ideal workforce may be one that has acquired immunity to COVID-19).		
Personal protective equipment (PPE)	***Workflow***	***Theatre space***
1. Assume that all patients and healthcare workers may be contagious until definitive screening tests are available 2. Use PPE during clinical tasks involving face-to-face contact with patients 3. Level and composition of PPE to be agreed by local IPC teams for each task (i.e. ward rounds, change of catheter, surgery) 4. Evidence is evolving and an adaptive approach should be implemented 5. Consider rational use of PPE due to perceived shortages in supply(8)	1. Change the working schedule to ensure safe delivery of service to patients 2. Adapt the working schedule to minimize risk of staff contracting COVID-19 outside the workspace 3. Consider developing weekly shifts where staff is isolated and accommodated on site for the full duration of their shift (the longer the shifts the better for working/screening time ratio) 4. Consider commuting to work in private vehicle where possible or accommodate locally	1. Decrease number of people in theatre 2. Do not allow observers 3. Keep training activity to a minimum 4. If robotic surgery is utilized and local regulations permit, consider placing the console outside the theatre to decrease PPE consumption and traffic in theatre 5. Consider additional measures to minimise risk according to type of surgery and exposure to types of bodily fluids, aerosols, droplets and surgical plume 6. Consider separate anaesthetic room for intubating and extubating patients, to decrease likelihood of infective aerosol (respiratory) dispersal 7. Consider a safety protocol in adherence with local IPC guidance for handling of PPE and other utensils after use

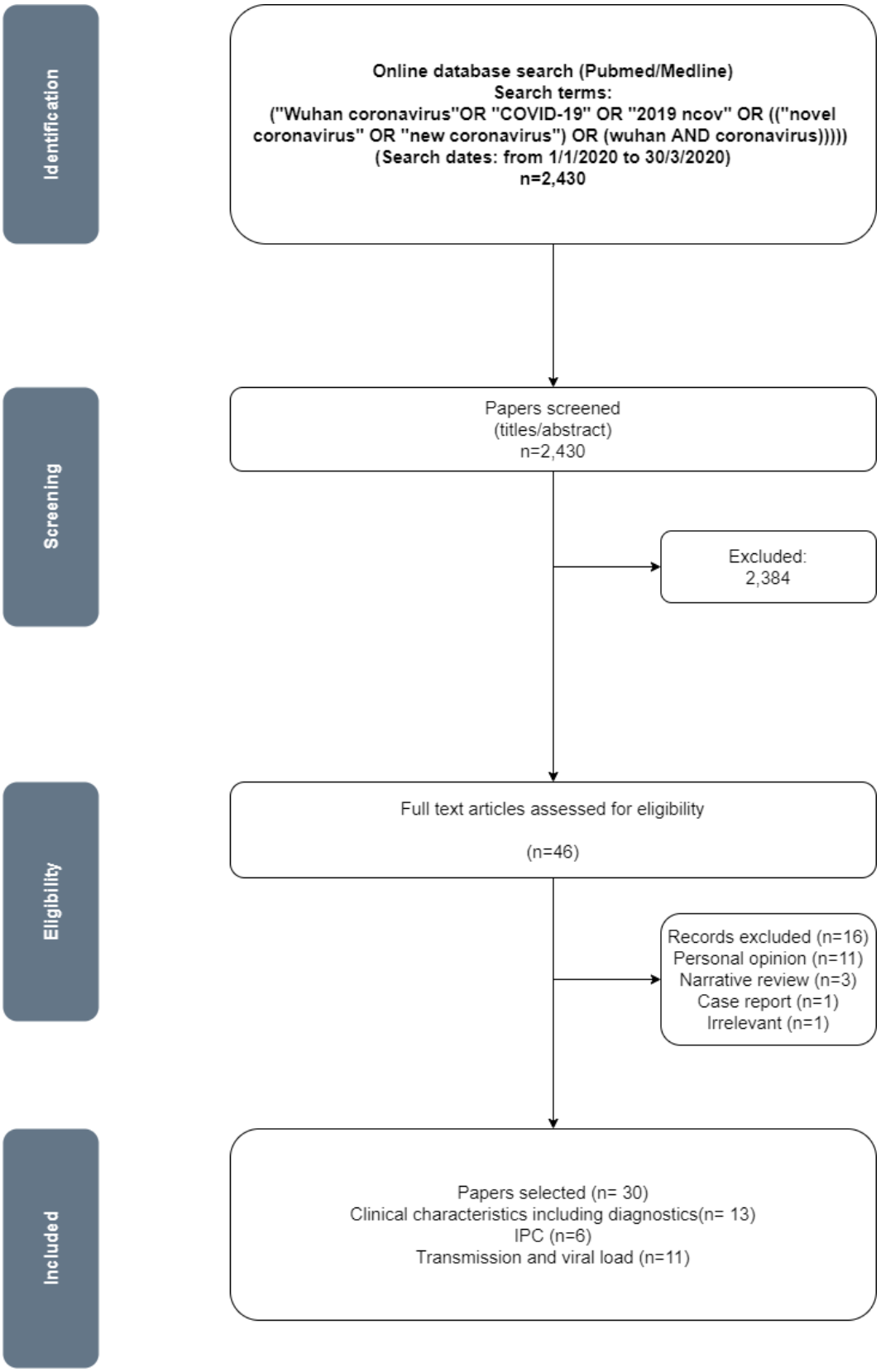
<table>
<tr><th colspan="2">Criteria to use for rationing & prioritization of management of non-metastatic prostate cancer patients</th></tr>
<tr><td>Prostate cancer risk stratification</td><td>Patient risk factors for worse outcomes of COVID-19</td></tr>
<tr><td>1. Use the European Association of Urology (EAU) risk stratification tool
2. For intermediate-risk, if needed apply the NCCN criteria for further rationing of patients with unfavourable risk features
3. For high-risk if needed apply the NCCN criteria for further rationing of patients with very high-risk features
4. The same criteria are applicable for rationing management of patients planned for salvage surgical treatment</td><td>1. If a patient is prioritized to receive surgery based on cancer features, further prioritize with COVID risk factors (medical conditions related with COVID-19 adverse outcomes, supplement-I)
2. If patient is prioritized based on cancer features, further prioritize younger men to receive surgery
3. Prioritize, predicted straight forward cases (i.e. no previous abdominal surgery, obesity, TURP)</td></tr>
<tr><th colspan="2">Prostate cancer risk groups & relevant management in case of significant delay (>3-6 months) of curative treatment</th></tr>
<tr><td>Low-risk</td><td>Active surveillance and do not offer surgery during the pandemic even if patient is keen for surgery</td></tr>
<tr><td>Intermediate-risk</td><td>1. Do not offer androgen receptor blockers for patients whose treatment has been deferred unless there is doubt surrounding diagnostic accuracy/ upgrading or upstaging
2. Arrange first follow-up appointment in three months
3. Use PSA for follow-up
4. DRE and TRUS not advised for follow-up during pandemic
5. MRI may be used (if capacity allows) in select cases where PSA kinetics and cancer characteristics cause concern</td></tr>
<tr><td>High-risk</td><td>1. If possible, offer surgery on the basis of risk of disease progression
2. Consider duration of anticipated delay in surgical treatment prior to commencing LHRH analogues
3. If ADT planned offer LHRH analogues and if not preferred, consider Bicalutamide 150mg
4. Arrange first follow-up appointment in three months
5. Use PSA and MRI for follow-up: PSA after 3 months and unless concerning PSA kinetics MRI after 6 months (if capacity allows)
6. DRE, TRUS and bone scan are not advised for routine follow-up</td></tr>
<tr><th colspan="2">Consideration of pelvic lymph node dissection for patients offered surgery</th></tr>
<tr><td colspan="2">1. The balance of survival benefit and harms of ePLND for intermediate and high risk are unclear
2. ePLND provides improved clinical staging for intermediate and high-risk disease</td></tr>
</table>

3. For high risk patients adhere to the decision-making process to which you normally adhered prior to the COVID-19 pandemic whilst taking care to avoid inherent risk of complications
Post-surgical follow up protocols
1. Aim at keeping hospital visits to a safe minimum 2. Arrange first postoperative PSA check at 3 months 3. Where possible (i.e. no peri-operative complications and uneventful catheter removal), use tele-medicine for clinical consultations

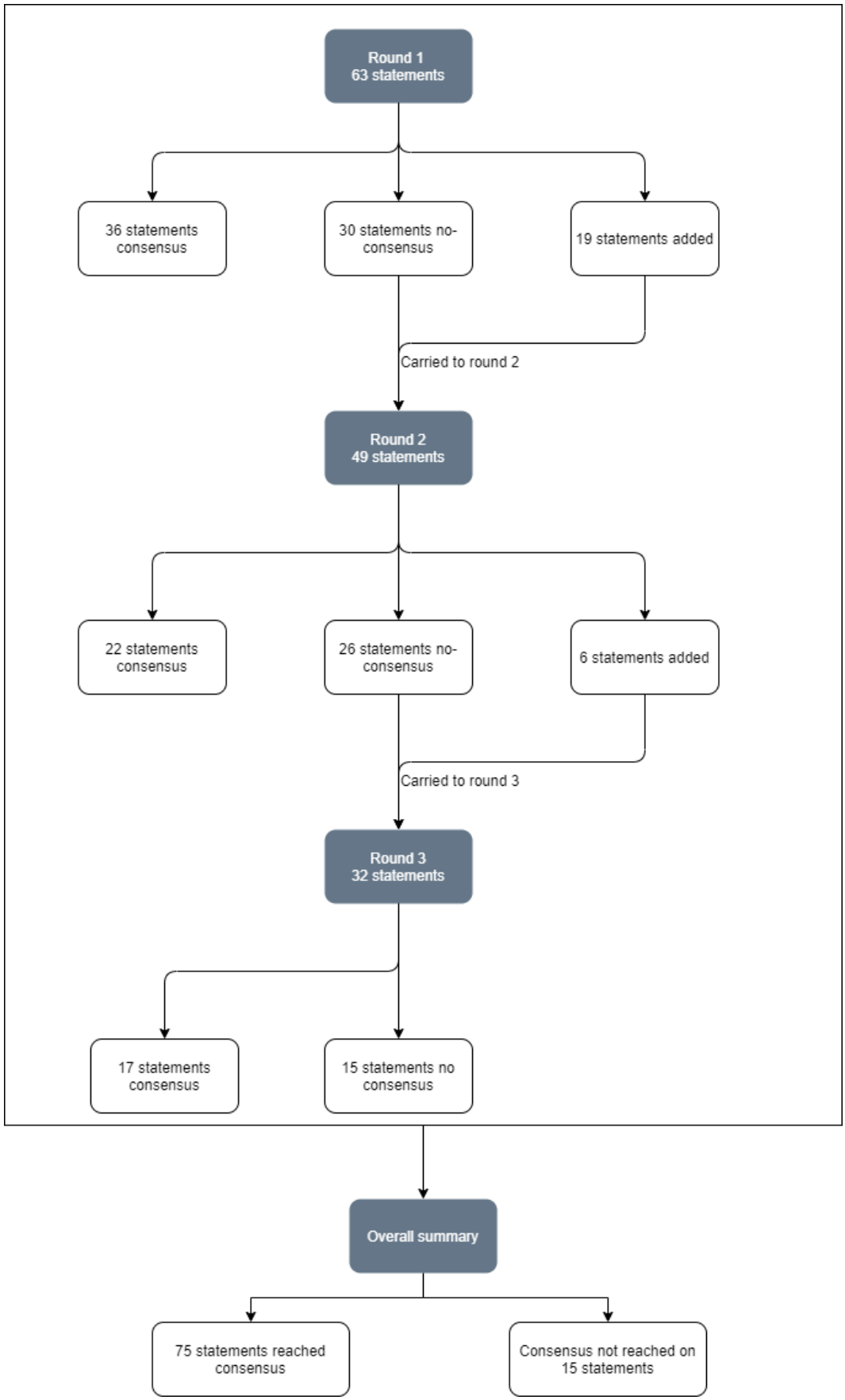
* At the time of the consensus and writing the manuscript no screening approach based on either single or combination of tests, has been found to offer <5% false negative rate. Testing location (out of hospital vs in hospital) process is also unclear.

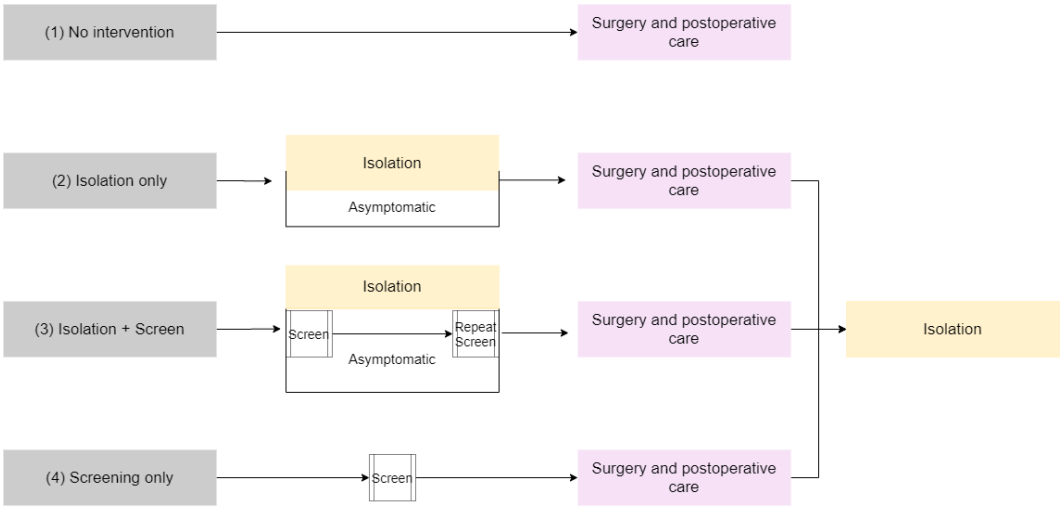
Δ Re-arrangement of the working hours of the healthcare workforce is intended to reduce the likelihood of getting infected with COVID-19 outside the COVID-19 free hospitals.

Ψ Isolation strategy is unclear. Possible options are to isolate for 2 weeks prior to surgery at home and ensure isolated travel to hospital. Lack of evidence at multiple levels prevented the panel from giving specific advice but the concept for isolation was agreed.

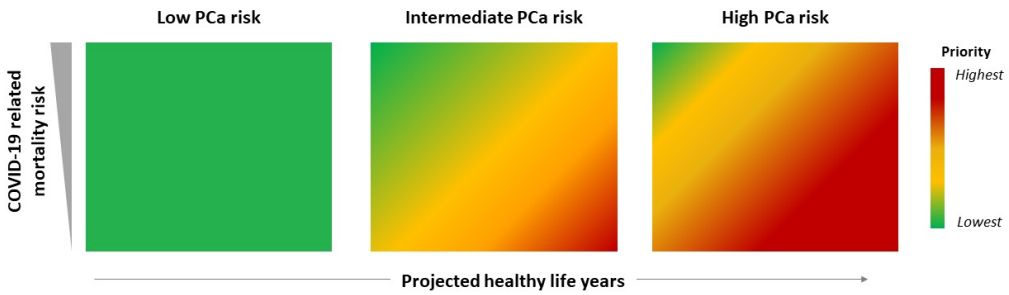


bju_15299_f1.png

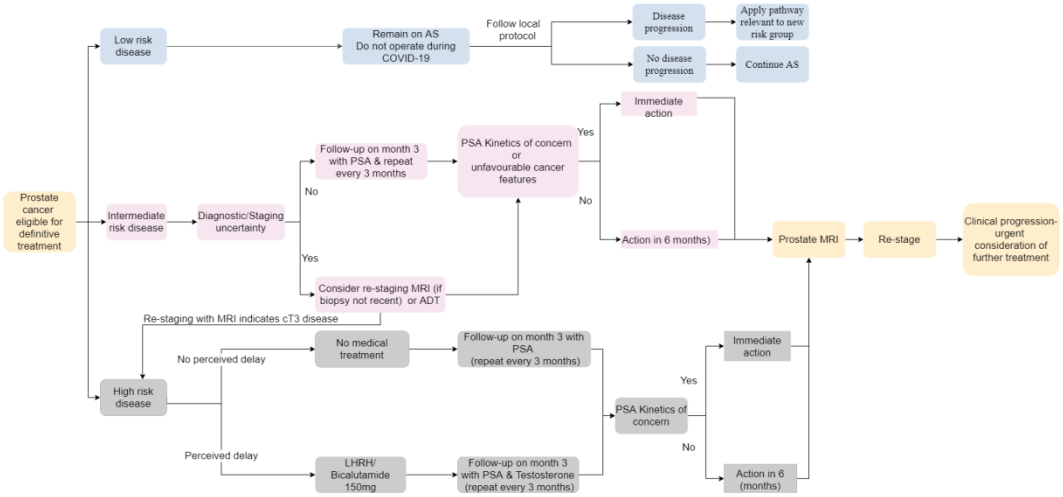




bju_15299_f3.png



bju_15299_f4.jpg



bju_15299_f5.png