



REVIEW

Treatment-Related Cognitive Impairment in Patients with Prostate Cancer: Patients' Real-World Insights for Optimizing Outcomes

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ABSTRACT

Cognitive impairment (CI) is an issue that needs to be at the forefront of unmet healthcare needs in patients with prostate cancer (PCa) as it can negatively impact quality of life during long-term care. CI in patients with prostate cancer is thought to be influenced by treatment, androgen deprivation therapy (ADT), and novel androgen receptor (AR) pathway inhibitors in particular; however, current understanding is limited on how treatment affects cognition. Additionally, the experience of patients with CI who are receiving PCa treatment is not well understood or represented in clinical literature,

which is a barrier to optimal patient outcomes in managing prostate cancer treatment-related cognitive impairment (PCa-TRCI). To help understand the patient journey and elucidate management gaps in PCa-TRCI, an international roundtable of healthcare provider and patient panelists was convened. The panelists focused on four key topic areas: (1) the patient experience when afflicted with, or at risk of, PCa-TRCI, (2) the physical, emotional, and social impact of CI on patients' quality of life (QoL), (3) the challenges that patients with PCa-TRCI face, and their impact on clinical decision-making, and (4) ways in which managing PCa-TRCI should evolve to improve patient outcomes. The purpose of the roundtable was to include patients in a direct discussion with healthcare providers (HCPs) regarding the patient journey and highlight real-world evidence of areas where patient outcomes could be improved in the absence of clinical evidence. The resulting discussion highlighted important healthcare gaps for patients with, and at risk of, PCa-TRCI and offered potential solutions as a roadmap to effective medicine.

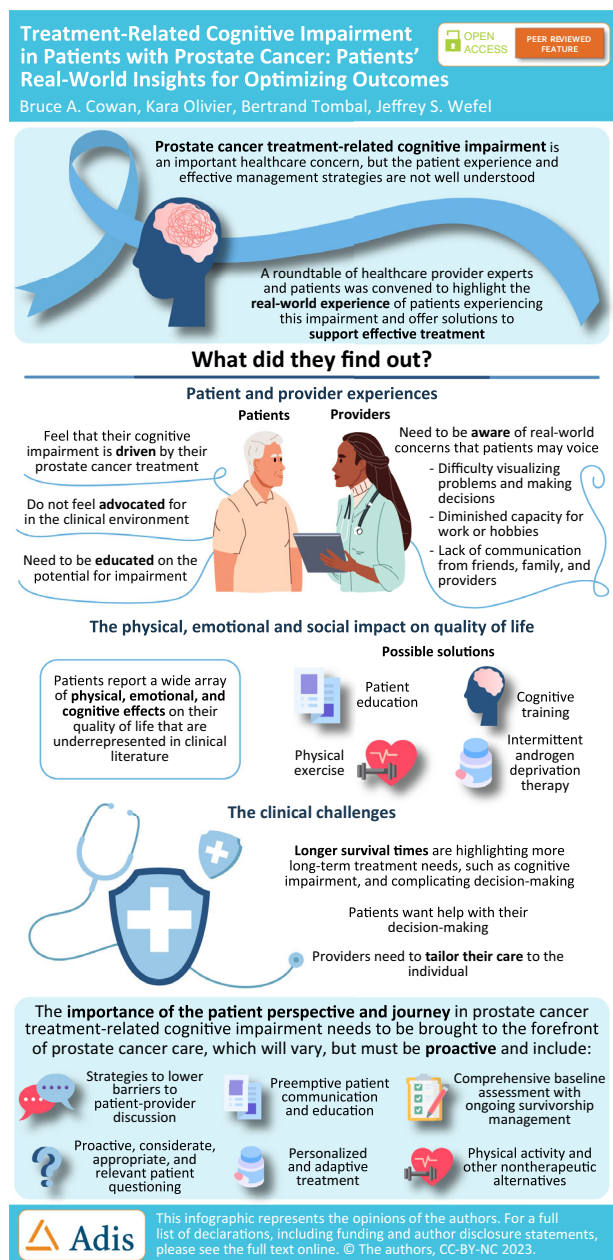
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Graphical Abstract:



Key Summary Points

An international roundtable was convened with a panel of healthcare providers (HCPs) and patients to help gain insights into the patient journey with prostate cancer (PCa) and cognitive impairment (CI).

There is little PCa-specific research on cognitive care in patients with PCa.

Both patients and clinicians provided insights and strategies to optimize outcomes and improve CI management in patients with PCa.

Insights from the roundtable indicated that pre-emptive education is vital, as CI can be challenging to diagnose, difficult to manage once manifested, and negatively impact patients' quality of life (QoL).

Management of CI is an important aspect of PCa care that requires ongoing research to improve diagnosis, management, and patient QoL.

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article, go to <https://doi.org/10.6084/m9.figshare.24442792>.

INTRODUCTION

Globally, prostate cancer (PCa) is the second most common malignancy diagnosed in men,

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with an estimated 288,300 new cases and 34,700 deaths in the USA alone in 2023. PCa is a disease most commonly seen in older men, with a median age at diagnosis of 67 years [1, 2]. Advances in screening and treatment efficacy have increased PCa diagnosis and reduced mortality rates, increasing 5-year relative survival from 89.71% in 1990 to 97.07% in 2015 [1–3]. This increase in survival, while a positive change overall, has created a host of new healthcare concerns and highlighted knowledge gaps regarding the long-term effects of treatment [3–5]. One major concern is the growing awareness and increasing prevalence of cognitive impairment (CI) that is frequently reported in patients with PCa [4, 6–9].

Cognitive function is the ability of the brain to acquire, process, store, and retrieve information, which can become impaired as a result of variety of factors that are often comorbid, including age, genetics, disease, and treatment [6, 10, 11]. Impaired cognitive function associated with cancer is often referred to as cancer-related cognitive impairment (CRCI); however, this is a broad diagnosis across many diseases. This manuscript focuses on CI as it relates to PCa and PCa treatment as there is little actionable clinical data in this healthcare space [5, 12]. For simplicity, and to help bring awareness to the gap in this clinical niche, CI associated with PCa treatment is referred to as prostate cancer treatment-related cognitive impairment (PCa-TRCI) in this manuscript. However, it is important to note that “PCa-TRCI” is not a clinically recognized term.

PCa-TRCI is likely caused by a multitude of factors, and while it is thought to be exacerbated by long-term exposure to treatments such as androgen deprivation therapy (ADT), chemotherapy, and novel androgen receptor (AR) pathway inhibitors, it is a clinically complex entity warranting further research [3, 7, 8, 13–15]. PCa-TRCI is an important clinical concern, as CI can negatively impact quality of life (QoL), including work and social relationships, autonomy, and self-confidence, particularly during long-term care [8, 16–18].

Management of PCa-TRCI is difficult for a number of reasons. First, adequate care of PCa-TRCI requires a consideration of overall QoL,

which includes cognitive function. Unfortunately, healthcare providers (HCPs) and patients alike may not prioritize cognitive management as an important aspect of PCa care. Second, HCPs knowledge, skill, and training may be limited regarding the patient-centered communication necessary for effective management of cognitive concerns [19–21]. Third, a gap in clinical data for treatment-related CI, including PCa-TRCI, compounds the difficulty in management and highlights the need for real-world insight that can guide future research and be used as a roadmap for future research and clinical care.

Indeed, patients with PCa-TRCI face a difficult road to effective treatment. Such treatment requires personalized care and informed decision-making that can overcome barriers which reduce patients’ ability to navigate their treatment choices. This highlights a need for a shift in healthcare where both patient and HCP work together to implement individualized PCa-TRCI management programs, including education of potential barriers to individualized care [20, 22–25].

To help facilitate this shift in healthcare, a roundtable panel of HCPs and patients convened to raise awareness of the healthcare problem that is presented by PCa-TRCI and gain insight from participants with real-world experience where clinical data are few. A key purpose of the roundtable was to include patients challenged by PCa-TRCI in a direct discussion with HCPs and allow patients to share their healthcare journey. One important caveat acknowledged at the outset of the roundtable is that CI itself can distort the ability of individuals to recall, recount, and expound upon their clinical experiences with CI. Therefore, attention was given to commonalities of concerns expressed by the individual patients and HCP participants.

This manuscript highlights healthcare gaps in the PCa-TRCI healthcare space which were discussed by patient and HCP participants during the roundtable and offers potential solutions as a roadmap to effective PCa-TRCI care. To the best of our knowledge, this is the first roundtable conversation of its kind detailing

the journey of the patient with PCa experiencing PCa-TRCI.

METHODS

The multidisciplinary roundtable on PCa-TRCI was held on February 28, 2023, in an international virtual forum with six representatives, including three patients (one of whom was also a patient advocate) and three HCPs (a neuropsychologist, a urologist, and a nurse practitioner). Each participant was invited on the basis of their personal experience with CI as a patient with PCa, patient advocacy expertise, or clinical expertise diagnosing, treating, and/or managing CI. All participants were aware that their responses would be used to form a publication.

A literature search of the PubMed database was conducted to develop the key discussion topics (listed below) before the roundtable. The search included research articles, systematic reviews, and meta-analyses in the English language published between January 1, 2000 and September 10, 2022. Search terms included “cancer-related cognitive impairment,” “CRCI,” “cognitive changes,” “cognitive dysfunction,” “cognitive impairment,” “decision-making,” “healthcare gaps,” “patient challenges,” “patient preference,” “patient need,” “practice gaps,” “prostate cancer,” and “treatment-related.” This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

The panelists focused their discussion on four key topics:

- The patient experience with PCa-TRCI
- The physical, emotional, and social impact of PCa-TRCI on patient QoL
- The challenges that a patient with PCa-TRCI faces and their impact on clinical decision-making
- Ways in which PCa-TRCI management should evolve to improve patient outcomes

Content from the roundtable discussion is described herein, supported with evidence from scientific literature, where possible. This

manuscript provides insights into the journey of patients with self-diagnosed PCa-TRCI regarding the patient experience with PCa-TRCI, decision-making challenges, QoL impact, gaps in care, and potential future PCa-TRCI management directions. These insights are intended to serve as a call to action for HCPs caring for patients with PCa who are experiencing or at risk of experiencing PCa-TRCI, guide future research, and to inform both HCPs and patients with PCa about the nuances of PCa-TRCI management in the absence of clinical data.

DISCUSSION

Patient Experience with PCa-TRCI

Literature Review on the Patient Experience

At the time of publication, there is inconsistent data for ADT-induced CI, particularly regarding extent to which ADT can affect cognition in specific cognitive domains [16, 17, 26]. Additionally, potential single-agent therapeutic causes of CI and specific cognitive domains remain unclear [17, 27]. While ADT may dominate the PCa treatment landscape, it is important to note that treatment-related CI has been documented in PCa and other cancers with multiple therapies, including chemotherapy, hormonal therapy, AR pathway inhibitors, and statins [8, 13, 15, 28–31].

Real-World Insights into the Patient Experience

The three patient participants with PCa-TRCI reported self-diagnosed CI problems that were apparent in their careers and hobbies which heavily involved visuospatial processing. For example, tasks such as video gaming or software development were nearly impossible, a finding also shown in previous studies of CI [7, 12, 24]. When asked if they thought that their symptoms were related to their PCa, age, or PCa treatment, each patient expressed that their CI symptoms started only after treatment with ADT, were “overwhelmingly driven by treatment,” and were greatly reduced or halted after completing ADT treatment. One patient

clarified that he believed treatment with ADT to be the dominant cause of CI in PCa and that CI for patients with PCa is largely an ADT-specific problem.

It is important to note that this discussion does not represent a scientific work, as no quantitative data has been collected. Therefore, any attributions to PCa-TRCI made by the patients are strictly opinion and cannot be conclusively attributed to their ADT treatment.

Real-World Insights into Clinical Recognition

Regardless of the cause, CI is inherently difficult to diagnose, easily confused or conflated with other symptoms (anxiety, depression, etc.), and difficult to treat once manifested. Additionally, a lack of clinical data exacerbates this difficulty and highlights the need for education which informs patients and HCPs of the potential for CI *before* it manifests so patients and HCPs can act to pre-emptively mitigate PCa-TRCI. Both HCPs and patients need to increase their awareness of potential cognitive symptoms and complaints, and for education on the potential for PCa-TRCI.

Given the difficulty in CI diagnosis and assessment, it is important to recognize barriers to clinical recognition of CI. HCPs and patients identified five key barriers: unrecognition of CI by HCPs as a clinical possibility, undervalued self-reporting of CI, poor patient–provider communication, lack of access to multidisciplinary clinics, and “infinitesimally small” participation in clinical trial research. Of these barriers, only clinical unrecognition of CI could not be substantiated by previous literature [21, 25, 32–34]. As a result of these barriers, a disconnect exists between the issues and symptoms that HCPs are clinically identifying, and those which patients are identifying. This disconnect was attributed by roundtable participants to poor patient–provider communication, variation in patient contact time with HCPs, and insufficient pre-emptive patient and HCP education about the potential for CI.

As a real-world example of a barrier to clinical recognition, one roundtable patient participant reported never being communicated with by his physician regarding his memory or attention or being screened/assessed for CI.

Additionally, he had little communication from friends, coworkers, family, or caregivers, and his symptoms and struggles went undetected by those closest to him. As such, he did not feel advocated for during his PCa management while experiencing PCa-TRCI.

Literature Review on Communication

Previous studies of PCa have shown that this lack of communication can limit patients’ ability to advocate for themselves and highlighted the need for HCPs to be more proactive in educating patients about the potential for PCa-TRCI. Addressing this need can lead to more effective management and better patient outcomes, though doing so requires HCPs to have a better understanding of the patient experience with PCa-TRCI than can be found in clinical literature [18, 24, 35, 36].

Owens et al. (2021) describes that HCPs who have extended contact with patients throughout their journey, such as nurse navigators, are more likely than surgeons to have the trust in the patient–provider relationship necessary for effective communication [37]. Additionally, Wefel et al. (2020) details that specialist and nonspecialist HCPs outside of neuropsychology clinics often lack knowledge of potential concerns for CI and thus no relevant information is given to patients regarding these concerns [8]. While failings in communication have been recognized in previous literature, a gap in patient education could not be substantiated and likely highlights another gap in clinical data that would benefit from increased clinical awareness [19, 20, 37, 38].

A lack of standardized definition and measure/assessment instruments for CI in PCa management means that its negative impact on patients with PCa may be underestimated and at-risk patients are not being identified. This need for more effective definitions and tools to assess treatment-specific cognition effects has been recognized in previous literature [27, 39]. Solutions to this lack of healthcare-wide, standardized clinical definition and assessment for PCa-TRCI will likely take years to implement. However, previous literature shows that a patient–provider relationship that stresses open, bidirectional communication at all levels of

healthcare can be implemented on an individual basis, which may also apply to PCa and CI management [20, 40, 41].

Real-World Insights, Recommendations, and Potential Solutions

Roundtable patients confirmed that a dialogue with HCPs would be both helpful and welcome to facilitate information exchange regarding the potential for CI. However, two patients clarified that they had not experienced dialogue being opened or initiated by HCPs, nor were they aware of how dialogue should begin, adding that “feedback through the whole journey has been very poor.” Subsequently, the patients were asked what they would like their treating HCPs to ask them about CI; one responded, “Anything at all,” and indicated frustration that these discussions were not happening. HCP participants in turn suggested that this lack of dialogue may be due to HCPs being unfamiliar with what symptoms and complaints to expect from patients with PCa-TRCI as a result of the lack of clinical data and research on the subject. One HCP suggested that involving a specialist, such as a neuropsychologist who is trained in CI care, in the management of patients at risk for PCa-TRCI may enhance CI management without further burdening primary healthcare providers.

Impact of CI on QoL for Patients with PCa-TRCI

Literature Review on QoL

It has been shown that CI in other cancers can have a profound impact on QoL through impaired autonomy and function, including patients’ ability to navigate the complexities of clinical decision-making [8, 18]. Unfortunately, there is little PCa-specific clinical data on the physical, emotional, and social impact of treatment-related CI on QoL in patients with PCa-TRCI, which is a gap that should be brought to the forefront of unmet healthcare needs in patients with PCa. Compounding this gap is the indication that HCPs may view QoL in patients with PCa as an extraneous or “soft” patient need and prioritize survival over QoL, which is a

barrier to understanding the patient’s QoL experience [4, 22, 42]. While survival is of paramount importance, concerns for survival must also be balanced with QoL concerns. Previous literature shows that HCPs need to understand the patient-experienced impact of CI, as this impact can reduce patient–provider communication and complicate decision-making, which may negatively impact QoL [19, 40, 43].

Real-World Insights into QoL

To better understand how treatment-related CI might affect QoL, roundtable patients were asked to describe their ongoing journey with PCa-TRCI, starting with the initial stages after their PCa diagnosis. One patient detailed that the stages after diagnosis involved a lengthy process that began with anxiety, fear, and depression, which then progressed to coping and acceptance, adding that their overall mood was greatly influenced by positive or negative outcomes. Patients were then asked how their PCa-TRCI symptoms impacted their daily life—from their work to their family and social lives—and their overall QoL. Patients reported that their CI problems were apparent to themselves both at work and at home with anything involving decision-making, visuospatial processing, or executive function.

This emotional progression and negative QoL impact is substantiated by previous studies where patients experienced marked distress after diagnosis that contributed to diminished disease coping and QoL [7, 23, 42]. Unfortunately, an important distinction made by the patients is that their symptoms of CI were not outwardly apparent and, as such, concerns that were brought up to their family, coworkers, and HCPs were sometimes not taken as seriously as they would have liked. This led to the patients feeling unheard and not advocated for in their PCa management, particularly when their QoL is diminished as a result of CI from their PCa treatment.

Recommendations and Potential Solutions

Both parties in the patient–provider relationship need to be candid about everything related

to treatment in a way that does not worsen negative side effects. This information should include both positive and negative treatment effects and realistic expectations for treatment outcomes, a conclusion that is also made in previous studies [7, 37, 44, 45]. Patients need to know to blame their treatment and inform their healthcare providers of any cognitive concerns they may have. If patients start treatment and experience cognitive concerns without being informed of the potential for cognitive side effects, the unexpected negative effects will cause patients to doubt the treatment. This doubt will in turn enhance their negative outlook, even if they experience oncologic benefit, which will reduce their QoL. Patient participants confirmed this experience, stating that their own QoL decreased after PCa treatment because their expectations were that the treatment would help them, not cause adverse effects.

Real-World Insights into a Lack of Treatment Options

Patients expressed disappointment that most of the literature they were familiar with merely mentioned the impact of cognition on QoL without offering viable solutions to improve their QoL. Additionally, one patient believed sharing his concerns about PCa-TRCI to be irrelevant, as he felt there were few viable solutions available. When his concerns were eventually shared, he felt dismissed by his provider after only being offered treatment cessation as a solution and no other options at the time. Another patient added that he believes there are no realistic options for CI treatment once symptoms occur. Indeed, there are no US Food and Drug Administration (FDA)-approved therapeutic options for CI or PCa-TRCI, currently, and none of the patient participants were offered non-therapeutic alternatives [6].

Recommendations and Potential Solutions

HCP participants suggested cognitive training and physical exercise as options, both strategies recognized in clinical and patient guidelines [46, 47]. These recommendations are important, as cognitive training has been shown to

decrease a patient's perceived CI, and exercise has been shown to have a marked effect on mental health and cancer management, including a reduction in depression, anxiety, and distress [29, 35, 48–50]. However, there are barriers to initiation and adherence to these solutions, particularly for exercise, if it has not been a part of a patient's lifestyle previously [51]. Patient participants were willing to make the necessary lifestyle or behavioral changes required for exercise and cognitive training to help them cope with their PCa-TRCI. However, even with this willingness, the necessity and benefits of these changes may be unknown to most patients as HCPs are not recommending these changes pre-emptively. When asked why, if these solutions are guideline-recommended, they are not recommended at the patient level, participants indicated that they may not be known to HCPs treating PCa, though this could not be supported by previous literature.

For example, one patient indicated that after an unrelated severe adverse event, he received strong diet and exercise recommendations that were presented as a necessity. In comparison, this level of strong recommendation was absent in his PCa treatment. This anecdote highlights the importance of HCPs recommending these solutions pre-emptively and the detriment to effective medicine when providers do not offer them as patients may not make the necessary changes on their own. To this point, previous literature indicates a strong influence of HCP-provided recommendation and information on patient treatment choice, though these studies are limited and do not involve cognition [43, 52, 53].

Another approach to mitigating CI in the absence of therapeutic options is treatment with intermittent ADT (IADT), which was suggested by HCP participants as it has been shown to balance oncologic benefit with a reduction in CI and marked improvement in QoL. HCP participants indicated that their patients appreciate this approach, though they clarified that most HCPs are not embracing intermittent treatment or de-escalation strategies, despite being recommended in clinical guidelines. They explained that this lack of IADT implementation may be due to the relative novelty of

clinical data and the increased burden on HCPs having to learn yet another treatment protocol, both of which are reasons supported by previous literature [31, 54].

The anecdotal evidence presented during this topic indicates that HCP recommendations of the suggested treatment options and preemptive patient education are necessary to decrease the impact of PCa-TRCI on patient QoL. That the patient participants were not aware of some viable treatment options and no PCa-TRCI specific treatment option could be found in the literature may highlight the clinical gap in patient education and clinical research, though this generalization is a difficult conclusion to make given the small sample size of this discussion.

Patient Challenges and Their Impact on Clinical Decision-Making

Literature Review on Patient Challenges

Little is known about the challenges that patients with PCa face with cognitive complaints, or how these challenges impact clinical decision-making. Patients with PCa-TRCI want more help in managing their symptoms, regardless of their disease stage, and while this highlights the importance of incorporating PCa-TRCI management into clinical practice, there is limited high-quality evidence detailing the most effective way to help patients with PCa with their cognitive concerns [6, 7, 23]. The crux of the challenges in PCa-TRCI management is that a substantial increase in survival is altering issues being brought to the forefront of PCa care, and participants want PCa-TRCI to be included on the list. This shift in survival means that the challenge is now to increase survival time *while* maintaining or improving QoL [2, 3, 35, 43, 47].

Real-World Insights into Patient Challenges

With this extended survival in patients with PCa, patients' needs now include treating longer-term concerns, such as CI and other adverse effects. These effects are not novel or suddenly appearing; patients are simply living longer and having more opportunity to

experience adverse effects which is corroborated by previous literature [3]. This increase in survival also allows for more clinical visits and opportunities to bring concerns up with their providers. One patient summarized this by saying that it is now likely that a patient's remaining lifetime will *not* be negatively impacted by PCa, which means that QoL must assume greater importance and that cognition is not something to be ignored.

Patient participants explained that their physical and cognitive consequences greatly affect their preferences in care and decision-making. Unfortunately, two patients also suggested that their preferences are often overlooked by HCPs, and previous studies corroborate that patients are only asked for their preferences in medical decisions half of the time [20, 21, 40]. The lack of clinical evidence for PCa-TRCI management combined with the increased survival of patients with PCa has created a set of challenges in clinical decision-making that falls squarely on the patients' shoulders, much to the disappointment of the roundtable patient participants.

For example, patients expect little support from HCPs, despite their desire for support—one patient even indicated that his patient journey had reduced his expectations for clinical support to zero. While it is always important for patients to do their own research and remain abreast of potential CI solutions, the lack of clinical support made it a necessity for roundtable patients. Once armed with information from their research, the patients then had to advocate for themselves, which complicated an already complex process. Furthermore, it created a barrier to effective solutions and decision-making by shifting the onus of CI management toward the patient.

To this end, one patient wanted the onus of PCa-TRCI management to be more evenly balanced to reflect the patient–provider education necessary for effective healthcare. To which an HCP agreed and reported that often patients, not other doctors, inform them about impactful programs and resources, which frustrates patients because they have to get the information for themselves. Research on patients' clinical expectations and personal beliefs on

treatment selection is scarce across many cancers, including PCa. This scarcity of research highlights the importance of understanding the patient journey and the utility of real-world findings from patients experiencing PCa-TRCI detailed in this manuscript [7, 23].

Recommendations and Potential Solutions

For effective PCa-TRCI management and decision-making, it is important for the HCP to understand *which* patient is at risk, meaning that treatment considerations should be variable and made in an individualized manner. As examples, financial hardship greatly affects a patient's ability to afford therapies or to interrupt work/home life for healthcare appointments. These can be barriers to treatment and ongoing care that HCPs need to be aware of and alter their care accordingly. The effect of financial hardship on general patient care is also substantiated in previous literature, though PCa-specific data could not be found and is likely an important area for future PCa research [47, 55, 56]. This example highlights the need for HCPs to understand their patients' individual limitations and tailor their care, when feasible, to help patients overcome challenges and achieve optimal outcomes. Participants emphasized that this tailored care should include pre-emptive education on the increased potential for PCa-TRCI *before* symptoms manifest.

Evolving PCa-TRCI Management and Potential Solutions

Real-World Insights into Evolving PCa-TRCI Management

PCa-TRCI care should evolve to facilitate closing the healthcare gaps highlighted in the previous topics. In particular, the importance of the patient perspective and journey in PCa-TRCI management needs to be brought to the forefront of PCa care. Altering HCPs' perceptions of PCa-TRCI and facilitating patient advocacy can help to achieve this and are necessary for improving CI management in patients with PCa.

Consistent and ongoing assessment of cognitive function is vitally important for effective

management of CI, and PCa-TRCI should be placed on the same level as sarcopenia and other serious health concerns for clinical consideration. Patient participants listed visuospatial awareness, decision-making skills, attention, processing speed, language, and memory as cognitive domains which should be assessed and incorporated into PCa-TRCI management, which are reinforced by previous literature and guidelines [47, 57]. HCP participants clarified that a multitude of stressors, which are recognized in previous literature, may contribute to CI in patients with PCa and make assessment, diagnosis, and treatment difficult and complex [6, 35, 58]. These stressors should be assessed together for a more accurate clinical picture; however, there is no standardized definition or measure selection for CI, which may mean that its negative impact on patients is underestimated with at-risk patients unidentified [39].

Recommendations and Potential Solutions

To help correct the underestimation of PCa-TRCI, clinically recognized and sensitive cognitive measures need to become standardized and more commonly used in both the research and clinical settings, as recognized in previous literature [24, 39]. Additionally, as confident diagnoses typically result from comprehensive neuropsychological assessments, one HCP suggested following evidence-based guidance for assessment of cognitive function outlined in the three papers Wefel et al. (2020) [8], Schagen et al. (2014) [30], and Noll et al. (2018) [29] as a roadmap for HCPs selecting cognitive measures.

Establishing a complete baseline *before* treatment is essential to ensuring accuracy and efficacy in ongoing assessment and management, as HCPs need a measurable data point that is both quantifiable and actionable. Establishing a complete baseline is also supported by previous studies and guidelines, as it encourages recognition of any changes in cognitive function along the patient journey [8, 19, 31, 59]. Baselines should include a complete personal assessment on all fronts (physical, emotional, etc.), as it is important to exclude anything that may be contributing to CI outside of PCa, or PCa treatment. Initial baseline workup and any

follow-up assessments should include changes in life, such as exercise regimens or family loss; cardiovascular events; and medical history, to avoid interactions and understand metabolic changes.

One recommended tool which has been shown to help establish a baseline, enhance patient–provider communication, improve decision-making capability, and aid in delivering high-quality care is patient-reported outcome measures (PROMs) [12, 19, 59, 60]. HCPs suggested that the patient assessment questions listed in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Survivorship (version 1.2022) and the outcomes recommended in Morgans et al. (2015) are effective PROMs to help assess important cognitive concerns [47, 61].

Importantly, an HCP clarified that while a PROM may help to identify an area in need of clinical follow-up, subsequent objective cognitive testing is needed to accurately diagnose CI, differentiate it from other symptoms, and direct care to the relevant patient concern, as is recognized in Ryan et al. (2020) [59]. Both HCP and patient participants further clarified that this information must also be collected in an appropriate clinical setting, or the efficacy of the assessment is lowered.

Real-World Insights into Educational Support

While PROMs were suggested, it is important for HCPs to ask appropriate and relevant questions during clinical assessment. This should be done with the understanding that some issues, such as sexual function, are more difficult for patients to discuss/define and will require greater HCP attention and understanding to elicit effective information. For example, HCPs need to be mindful of how many questionnaires patients may have received and how this potential “mountain” of questions might affect the patients’ ability or desire to respond accurately.

Unfortunately, this level of healthcare personability is something with which HCPs can be uncomfortable or which can be difficult to achieve given the time constraints of a typical healthcare consultation. Importantly, spending time and resources on sending patients home

with questionnaires or educational resources was not felt to be effective by some of the panelists as there were concerns that this would not result in actionable interventions without professional monitoring. Two patients were unsure of specific educational support which would help recognize and address cognitive issues but stipulated that nearly anything would be beneficial relative to their current experience, as long as it was actionable and received in the correct setting.

Providers often take a back-end treatment approach, only offering management strategies once symptoms emerge. However, once a cognitive problem arises, it is often too severe and established to be managed efficiently, which highlights the importance of proactive and early communication and education with patients regarding the potential for PCa-TRCI. To this point, one patient mentioned that pre-emptive patient education on the potential for PCa-TRCI was vital as a preventative measure in light of the lack of therapeutic options and difficulty of treating CI, once symptomatic. Repetitive education is the key to actionable change for both patient and HCP, as neither will likely take any action unless they are reinforced with the knowledge on multiple occasions across a long period of time.

Recommendations and Potential Solutions

As participants in this discussion highlighted multiple times that effective therapeutic options for PCa-TRCI are lacking, alternative nontherapeutic options and resources are an appealing choice as an important part of the evolution of PCa-TRCI management. HCPs indicated that they are comfortable recommending sleep hygiene, sleep aids, memory aids, physical activity, social and cognitive engagement, and support facilities. Physical activity, in particular, has demonstrated an ability to balance oncologic benefit with a reduction in long-term adverse effects in previous studies [49–51, 57]. In addition to the recommendations by HCPs, one patient participant indicated a resource that he co-developed called Life on ADT, which includes the ADT Book, and is a patient-centered educational program for patients with PCa who are on or

about to start ADT [62, 63]. Another patient recommended the True North Sexual Health and Rehabilitation e-Clinic (SHAREClinic), which is a free online clinic to help patients with PCa cope with sexual side effects that can occur as a result of PCa or PCa treatment [64]. Additionally, strategies which attempt to lower the barriers to patient–provider discussion, such as telehealth or mobile communication apps, may be helpful to some patients. The caveat is that the accessibility and efficacy of these aids will depend upon age (mobile apps may fall short in older patients), and these strategies are not often discussed in the clinical setting.

CONCLUSION

At the conclusion of the discussion, both patients and HCPs were asked to come up with key takeaway pearls and call-to-action strategies that were highlighted during the discussion (Table 1). Each of these items is intended to help stress the importance of the patient journey to HCPs and improve patient outcomes by providing a roadmap for HCPs and patients to follow for effective PCa-TRCI management.

The complexity of CI—including different clinical definitions of CI, unclear prevalence estimates, and the weak association between cognitive concerns and objectively assessed CI—contributes to difficulties in the identification and management of CI [18, 39]. As a result of this complexity, each patient with CI will have different needs, making an individualized regimen—with different tools, information, and treatments for every patient—necessary. Unfortunately, this individualized treatment is still lacking, which highlights the need for a cultural, systemic, and personal shift in care to alleviate these clinical challenges.

One important clarification made during this discussion is the difficulty of implementing this necessary individualized care while HCPs are facing challenges of their own, such as being overworked, on top of the difficulty in keeping their patients' PCa-free with a sustainable QoL. Additionally, the lack of specific data on managing treatment-related CI in patients with PCa is a detriment to effective care, particularly

to HCPs' ability to deliver effective care, given their own challenges. Future PCa-specific research that asks relevant questions of PCa-TRCI management, while being mindful of HCPs' own limitations, is vital to understanding how to reduce the healthcare burden of PCa-TRCI.

Although no novel clinical data were presented, collected, or analyzed, this roundtable discussion served as an important opportunity for patients to connect with expert HCPs and share their individual experiences and concerns while highlighting areas where PCa-TRCI management may be improved.

CONCLUDING REMARKS

The overall aim of this roundtable was to hear real-world experiences from patients with PCa who experienced CI as a result of their PCa treatment, first-hand. The real-world experiences, concerns, and insights highlighted in this discussion are intended to serve as a roadmap for current practice, further PCa-TRCI assessment and research, and wider HCP and patient community discussion of PCa-TRCI. However, as this was not a scientific study, these insights can only be considered generalizations. The patient perspective is often lacking in clinical representation and is important to take into consideration when optimizing patient care and conducting future research. Care of patients with PCa has evolved rapidly in the last decade, and the increasing numbers of PCa survivors reflect this; however, healthcare must continue to evolve and rise to meet the emerging challenges highlighted in this discussion.

LIMITATIONS

As a result of the subjectivity of a roundtable conversation and the resulting anecdotal evidence presented, there were a number of limitations to this study. First, the discussion attempted to direct HCPs and researchers in the field of PCa care toward areas where clinical data are lacking using first-hand, real-world experience from patients and

Table 1 Key takeaways for a roadmap to effective PCa-TRCI care

Shared by patients	Shared by HCPs
<i>Communication</i>	
Communicate: Effective PCa-TRCI management requires bidirectional communication between patient and provider	Repetition: A new treatment paradigm will not improve patient outcomes unless repetitive communication and education are implemented
<i>Practice change</i>	
Discuss: Patients need more time to discuss important issues with HCPs during consults, and HCPs need to be prepared to discuss the totality of information required, including personal details	Advocate: Patients need continuous HCP advocacy to affect specific behavioral changes, such as physical activity. Advocacy for these changes must include the reason these behavioral changes are necessary
Inform: HCPs and members of the healthcare team must be informed of the potential for PCa-TRCI and communicate this risk to patients	Monitor: Cognition needs to be a vital sign in all aspects of oncology healthcare. Continuous and constant CI monitoring is essential, and every HCP, regardless of specialty, should know to monitor cognition
Empower: Patients need to feel confident that they are heard and empowered on their healthcare journey, particularly when advocating for themselves	Individualize: The paucity of clinical data in the PCa-TRCI management space highlights the necessity for guideline-mediated care on an individualized basis
<i>Education/research</i>	
Mitigate: Pre-emptive patient education on the potential for treatment-induced CI <i>before</i> symptoms manifest is vital to mitigate PCa-TRCI	Prioritize: Both HCPs and patients are flooded with educational literature. HCPs need to prioritize the important aspects of PCa-TRCI care highlighted in this discussion and select educational resources that reinforce these areas
Understand: HCPs need evidence-based education which enhances their understanding of PCa-TRCI as a viable concern so they can initiate treatment	Standardize: HCPs need a standardized PCa-specific assessment protocol which includes important questions to ask patients who may be experiencing PCa-TRCI
Recognize: More research on the patient perspective is needed to bring PCa-TRCI recognition to the forefront of unmet healthcare needs	Guide: Future clinical guidelines need to recognize PCa-TRCI as an important concern and guide HCPs toward detailed, evidence-based management strategies

Table 1 was created with the help of LoveLive Graphics, Ltd (Macclesfield Cheshire, UK) HCP healthcare provider, PCa prostate cancer, PCa-TRCI prostate cancer treatment-related cognitive impairment, CI cognitive impairment

experts. However, the subjective, anecdotal nature of the discussion, coupled with the small sample size, means that the ideas presented here reflect the lived experience of the roundtable participants and may not generalize to a larger population or reflect the experiences of all patients with PCa. Second, each of the three patients in the roundtable received ADT as

a PCa therapy, which is a limitation when extrapolating their experiences to other PCa treatments. Third, the paradox of relying on patients with CI to recall and comment on healthcare information they received or did not receive while they had CI may mean that patients may have misrepresented, or misremembered, their clinical experiences and the

information exchanged between patient and provider. Fourth, this manuscript suggests that more discussion with patients with PCa about CI risks associated with specific treatments could be helpful and, while this may be the case, this has yet to be documented in the scientific literature. Finally, HCP participants expressed their disappointment in hearing the poor patient experiences during this roundtable, agreeing that they are not unique to this discussion and should serve as an important reminder to HCPs that these experiences must be considered. Importantly, HCPs clarified that they are also not the experiences of all patients and the expressions of only three patients cannot fully represent the community of patients with PCa.

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Declarations

Conflict of Interest. Jeffrey S. Wefel has received financial compensation for consulting from Bayer and for research support from GT Medical Technology, Juno, Novocure. Bruce A. Cowan received financial compensation for consultancy work with Bayer. Bertrand Tombal has received financial compensation as an advisor and speaker for Amgen, Astellas, AstraZeneca, Bayer, Ferring, Janssen, MSD, Myovant, Novartis, and Pfizer. Kara Olivier declares that she has no competing interests.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. The authors have specified in the Methods section that all participants were aware that their responses would be used to form a publication.

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