nature reviews urology

https://doi.org/10.1038/s41585-023-00778-3

Review article

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Sexual health and treatment-related sexual dysfunction in sexual and gender minorities with prostate cancer

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Abstract

Prostate cancer treatment has substantial effects on sexual health and function. Sexual function is a vital aspect of human health and a critical component of cancer survivorship, and understanding the potential effects of different treatment modalities on sexual health is crucial. Existing research has extensively described the effects of treatment on male erectile tissues necessary for heterosexual intercourse; however, evidence regarding their effects on sexual health and function in sexual and gender minority populations is minimal. These groups include sexual minority — gay and bisexual — men, and transgender women or trans feminine people in general. Such unique effects in these groups might include altered sexual function in relation to receptive anal and neovaginal intercourse and changes to patients' role-in-sex. Sexual dysfunctions following prostate cancer treatment affecting quality of life in sexual minority men include climacturia, anejaculation, decreased penile length, erectile dysfunction, and problematic receptive anal intercourse, including anodyspareunia and altered pleasurable sensation. Notably, clinical trials investigating sexual outcomes after prostate cancer treatment do not collect sexual orientation and gender identity demographic data or outcomes specific to members of these populations, which perpetuates the uncertainty regarding optimal management. Providing clinicians with a solid evidence base is essential to communicate recommendations and tailor interventions for sexual and gender minority patients with prostate cancer.

Sections

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Key points

- Pleasurable receptive anal and neovaginal intercourse occur through the stimulation of the prostate, surrounding pelvic anatomy, and supplying neurovasculature, including branches of the pudendal, pelvic splanchnic and hypogastric nerves.
- Sexual dysfunctions following prostate cancer treatment experienced by sexual minority men (SMM) include problematic receptive anal intercourse, erectile dysfunction, climacturia, anejaculation, decreased penile length, and changes in orgasm.
- SMM with prostate cancer should be counselled regarding different treatment-related toxicities depending on their role-in-sex (top, bottom, versatile, side).
- Anal dilators (to assist with receptive anal intercourse), vacuum pumps (to induce stronger erections for insertive intercourse) and penile constriction rings (to manage climacturia) should be discussed with SMM.
- Gender minorities with prostate cancer are a heterogeneous cohort with a range of anatomy and hormonal milieu, requiring a nuanced and detailed conversation when discussing treatment options and relevant toxicities.
- Consultations about prostate cancer with sexual and gender minorities should include counselling on the resumption of receptive anal intercourse, condom use, HIV pre-exposure prophylaxis and anal douching.

Introduction

Prostate cancer is the most common malignancy in males, or individuals born with prostates, with a 5-year overall survival of 98%[1–3]. This relatively high overall survival means that treatment paradigms focus on both survival and maintenance of quality of life (QoL). Prostate cancer can be treated with radical prostatectomy (RP), external beam radiation (EBRT), brachytherapy, androgen deprivation therapy (ADT) or combination therapies depending on the risk group[4], each of which is associated with toxicity profiles that can affect patient QoL.

Sexual function is a vital aspect of human health and maintaining the capacity for pleasurable sexual activity after cancer therapy is a crucial component of both QoL and survivorship[5]. Sexual dysfunction is one of the most common and distressing effects of prostate cancer treatment[6], with more than 95% of prostate cancer survivors reporting some sexual dysfunction[3,7] and approximately 50% of prostate cancer survivors describing treatment-related sexual dysfunction as having a moderate-to-big impact on their quality of life[8].

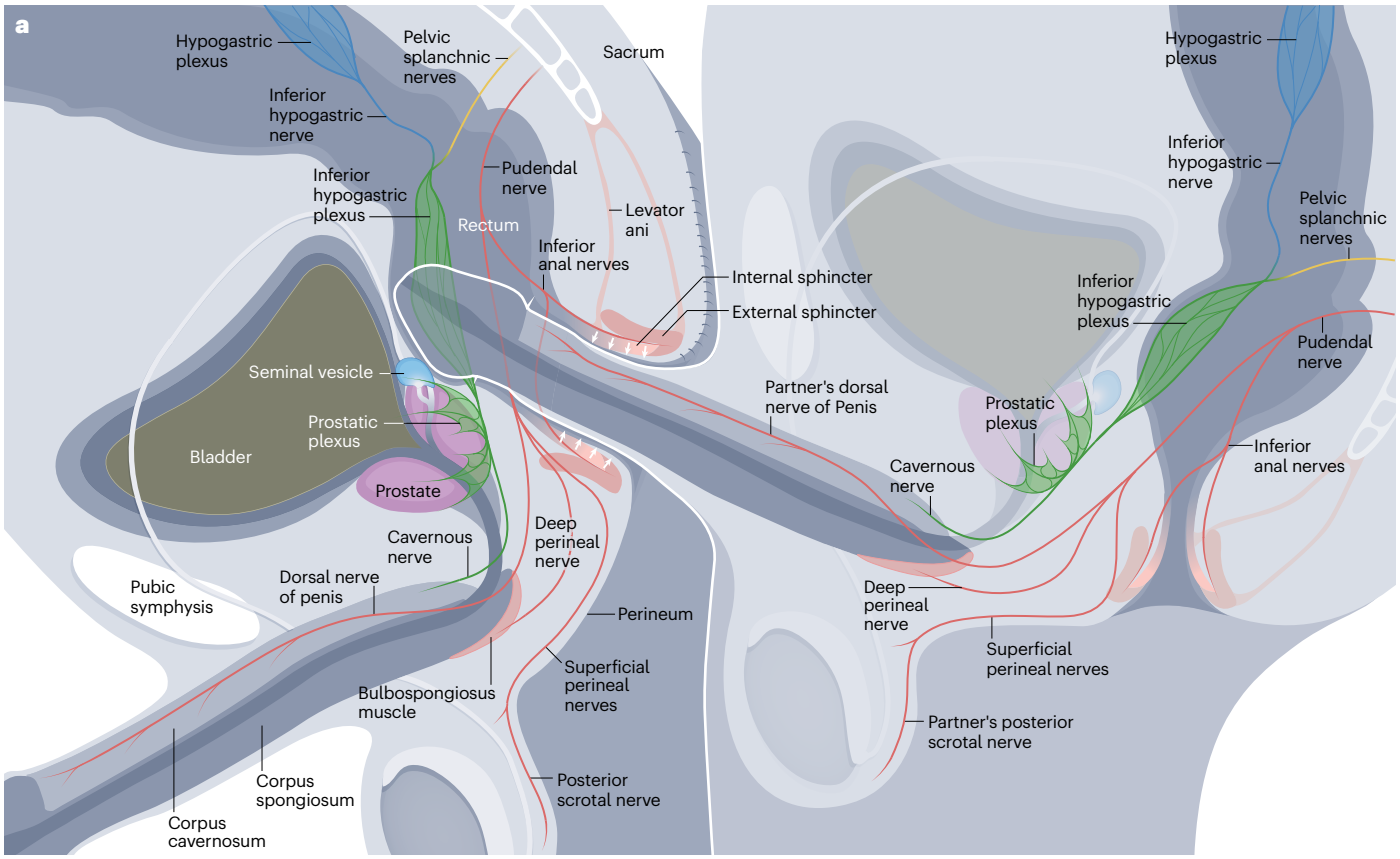
However, although the effect of prostate cancer treatment on male penile erectile tissues and the supplying neurovasculature necessary for heterosexual intercourse is well documented[7,8], data on the effects of treatment on sexual function in sexual and gender minorities are scarce. Sexual and gender minorities include individuals who identify as lesbian, gay, bisexual, transgender, gender diverse, asexual, queer, and intersex as well as those who do not but whose sexual orientation, gender identity, or reproductive development vary from traditional, societal, cultural or physiological norms[9].

Sexual and gender minorities represent approximately 7% of the global population[10], and this value is likely an underestimate owing to the criminalization of identifying as a sexual and gender minority. Thus, this population accounted for an estimated 98,998 new annual prostate cancer cases globally in 2020 (ref. 2), or an estimated 20,181 new annual prostate cancer cases in the USA in 2023 (ref. 1) (slightly less than the estimated 24,810 new annual cases of all central nervous system tumours in 2023 (ref. 1)). Furthermore, in the USA in 2022, there were approximately 246,626 sexual and gender minority prostate cancer survivors[3], and using data from the UK, this number is projected to treble by 2040 (ref. 11), suggesting that there will be approximately 740,000 people from sexual and gender minorities in the USA with prostate cancer in 2040, underscoring that the number of people from sexual and gender minorities with prostate cancer is substantial.

Approximately 1 in 8 (ref. 1) gay and bisexual men or sexual minority men (SMM) will develop prostate cancer — no evidence is available to suggest that SMM are at a greater risk of developing prostate cancer[12]. However, compared with the cisgender male population, transgender women (TGW), people recorded male sex at birth or who have feminine gender identity, are likely to have a substantially lower risk of developing prostate cancer[13], with a recent population-based study showing that 0.26% (6 of 2,281) of TGW on hormone replacement therapy developed prostate cancer[13], probably owing to the protective nature of oestrogen-supplementing gender-affirming hormone therapy (GAHT) as well as underdiagnosis owing to prostate-specific antigen (PSA) suppression[14].

The most common sexual activities among SMM include masturbation, oral intercourse and anal intercourse[15]. The most common sexual practices of TGW continue to be investigated, but also include masturbation, oral intercourse, anal intercourse, as well as neovaginal intercourse[16,17]. In receptive anal intercourse and receptive neovaginal intercourse, the prostate is one of the primary organs responsible for sexual pleasure[18–21]. Unfortunately, the damage and toxicity caused to this vital organ, the surrounding tissues and the supplying neurovasculature by cancer-directed therapies is poorly understood[22,23]. Improving the understanding of the effects of prostate cancer treatment in patients who participate in anal and neovaginal intercourse is essential. The American Society of Clinical Oncology (ASCO) has reported that knowledge of the health-care needs and outcomes for effective interventions among SMM and TGW populations is insufficient[24]. Furthermore, practitioners lack the necessary tools to guide treatment discussions, promote patient-centred conversations, and enable shared decision-making, when appropriate, in this population[25,26]. This problem continues to be perpetuated, as data regarding both SMM and TGW are often omitted from cancer-related clinical trials[27].

In this Review, we provide a detailed overview of how sexual dysfunction in SMM and TGW patients differs from that of heterosexual cisgender male patients following prostate cancer treatment, including understanding how the prostate functions in receptive anal and neovaginal intercourse, which is essential to provide context to interpret the existing literature on sexual outcomes in SMM and TGW. Additionally, we identify techniques and therapies used to manage iatrogenic damage responsible for sexual dysfunction in SMM following prostate cancer treatment and, given the limited literature available on TGW with prostate cancer, we address sexual dysfunction in this patient population. Overall, this Review establishes a framework for clinicians to counsel SMM and TGW with prostate cancer, as well as support provision of equitable and personalized care to these historically oppressed patient populations.


a
Hypogastric plexus
Pelvic splanchnic nerves
Sacrum
Inferior hypogastric nerve
Inferior hypogastric plexus
Pudendal nerve
Rectum
Levator ani
Inferior anal nerves
Internal sphincter
External sphincter
Seminal vesicle
Prostatic plexus
Bladder
Prostate
Cavernous nerve
Deep perineal nerve
Pubic symphysis
Dorsal nerve of penis
Perineum
Superficial perineal nerves
Bulbospongiosus muscle
Posterior scrotal nerve
Corpus spongiosum
Corpus cavernosum
Partner's dorsal nerve of Penis
Hypogastric plexus
Inferior hypogastric nerve
Pelvic splanchnic nerves
Inferior hypogastric plexus
Pudendal nerve
Prostatic plexus
Inferior anal nerves
Cavernous nerve
Deep perineal nerve
Superficial perineal nerves
Partner's posterior scrotal nerve

b

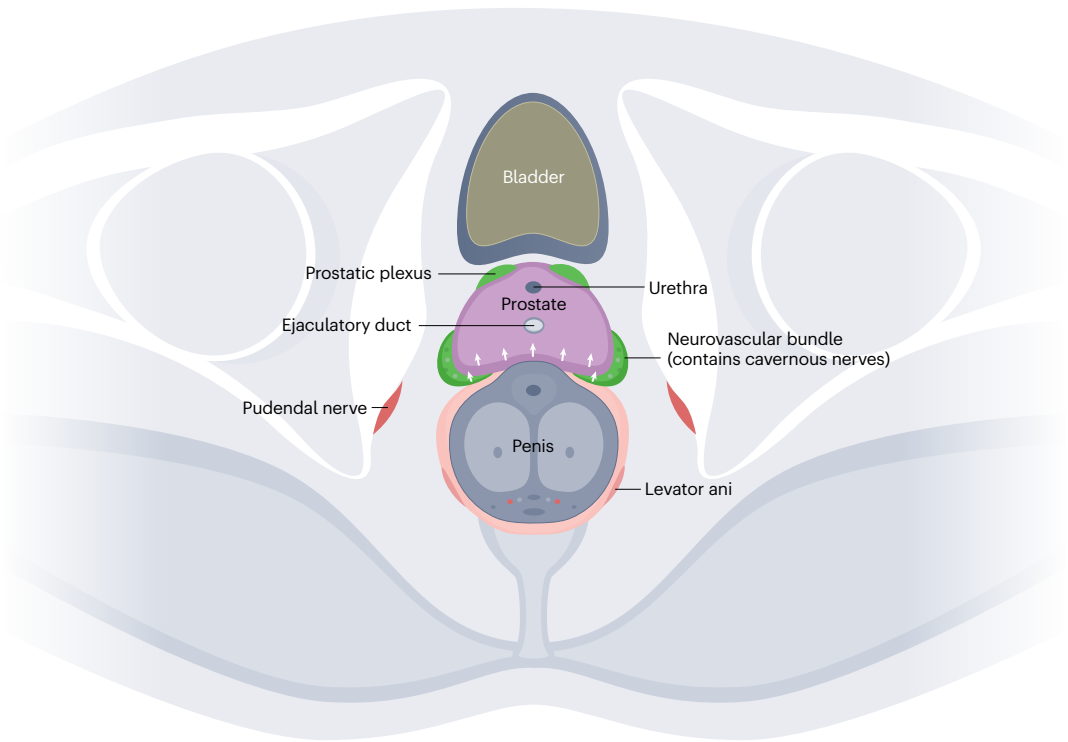

Bladder
Prostatic plexus
Urethra
Prostate
Ejaculatory duct
Neurovascular bundle (contains cavernous nerves)
Pudendal nerve
Penis
Levator ani

Fig. 1 | Anatomy of pleasurable anal intercourse. a, Representative sagittal image illustrating the pelvic anatomy involved in pleasurable anal intercourse. The average prostate is 3 cm (cephalocaudal)[233] and located 5 cm superior of the anal verge[234]. The average length of an erect penis is 13.61 cm (ref. 235), and thus the penis can likely traverse the prostate. The thrusting motion of the penis can stimulate the surrounding nerves and facilitate pleasurable receptive anal intercourse. **b**, Representative axial image of pleasurable receptive anal intercourse. The prostate is located anterior to the rectum. The partner's penis is tightly situated in the anorectum. The thrusting motion of the body and penis can stimulate the nerves wrapping around the prostate, including the cavernous nerves in the neurovascular bundle, the pudendal nerves, and the nerves of the prostatic plexus, eliciting pleasure and orgasm for both partners.

The prostate and anal intercourse

Recognizing the role of the prostate in pleasurable receptive anal intercourse (RAI) is important to understand the effects of prostate cancer treatments on sexual health for sexual and gender minorities.

The role of the prostate is twofold: first, it provides seminal fluid for male ejaculate (procreative function) and, second, it facilitates orgasm (recreative function)[28]. Orgasm prompts the release of neurotransmitters resulting in muscular, sensory and vascular changes, which are experienced locally and globally throughout the body. Although a large component of the orgasm is neuropsychiatric, the neural circuitry of an orgasm is poorly understood. Orgasms are multifactorial and can be experienced by physical stimulation (including areas outside the genitalia) and psychological stimulation[29]. In many people with a prostate gland, an orgasm is accompanied by ejaculation; however, the two events occur through separate neuropsychological pathways and can, therefore, occur independently[30]. Additionally, orgasm and/or ejaculation can occur without a penile erection or penile structures[31–33]. Reports have suggested increased orgasm intensity through prostatic stimulation, with 12 pelvic muscle contractions compared with 4–8 contractions associated with penile orgasm[32].

In addition to the prostate, pleasure from RAI is experienced through pressure and stimulation of the surrounding nerves in the perianal skin, anus and rectum[18] inducing orgasm, penile excitation and ejaculation (Fig. 1a,b). The nerves implicated in orgasm, ejaculation, erection and pleasurable RAI in people with prostates include the pudendal, hypogastric and pelvic splanchnic nerves and their associated branches[18,34] (Fig. 2a). Touching the penis elicits an erection through afferent sensory impulses through the dorsal nerve of the penis, a branch of the pudendal nerve, causing reflex activation through efferent signal to the cavernous nerves (located adjacent to the prostate gland)[35]. The cavernous nerves are branches from the inferior hypogastric nerve and receive input from the pelvic nerves[35], and facilitate penile erection[35]. Thus, putting direct pressure on the cavernous nerves can elicit a penile erection. Moreover, stimulation of the glans penis will elicit external anal sphincter contraction through the bulbocavernosus reflex[36,37]. The main sensory afferent input for ejaculation arises from the pudendal nerve, which then sends efferent impulses through the hypogastric nerve to ejaculatory structures and efferent motor impulses through branches of the pudendal nerve to control pelvic floor muscle contraction, including the bulbospongiosus and ischiocavernosus muscles (deep perineal nerve), and external anal sphincter contraction (inferior anal nerve)[35] (Fig. 2).

Similarly, manipulation of the anus and the surrounding skin induces erotic stimulation through afferent sensory impulses from the inferior anal and perineal nerves (branches of the pudendal nerve)[19,38]. Manipulating the sensitive anus and adjacent skin can stimulate anal sphincter contraction and lead to changes in breathing and physiological behaviour[19,39,40]. In fact, the anal-wink reflex is a well-established reflex to assess spinal cord injury and by stroking the sensitive perianal skin, physicians test the tone and strength of resultant external anal sphincter contraction[41,42].

These interconnected neural networks between the penis and the anorectal area illustrate that stimulation of one area can cause reaction in the other[43]. Studies have suggested that involuntary erections can occur during enemas or digital rectal examinations, supporting this connection[19]. Furthermore, inserting an object such as a finger or penis into the anus and/or rectum can stimulate the nerves surrounding the prostate and seminal vesicles, including the cavernous nerves, potentially through direct stimulation and movement of the prostate and other structures eliciting these nerves[19,44]. Conversely, studies have illustrated that cyclists who have pelvic pain or numbness could suffer from erectile dysfunction (ED) related to pudendal nerve entrapment[45].

During RAI, as the partner's penis is thrusting against the prostate, the movement of both the penis and the prostate can elicit pleasure, erection, ejaculation and orgasm likely through stimulation of the pudendal nerve[40] and/or stimulation of the cavernous nerves, located between the prostate and the rectum[46] (Fig. 1a,b) causing pleasure as well as reflex external anal sphincter contraction[41,42,47] (Fig. 2a). Contraction of the anal sphincter around the insertive partner's penis will activate the partner's dorsal nerve, causing a stronger reflexive erection, in turn increasing pressure on the prostate, surrounding neurovasculature and skin[35]. Potentiating these neurocircuits through sustained repetitive activation will allow for pleasurable intercourse and will ultimately build to an orgasm for both partners[30].

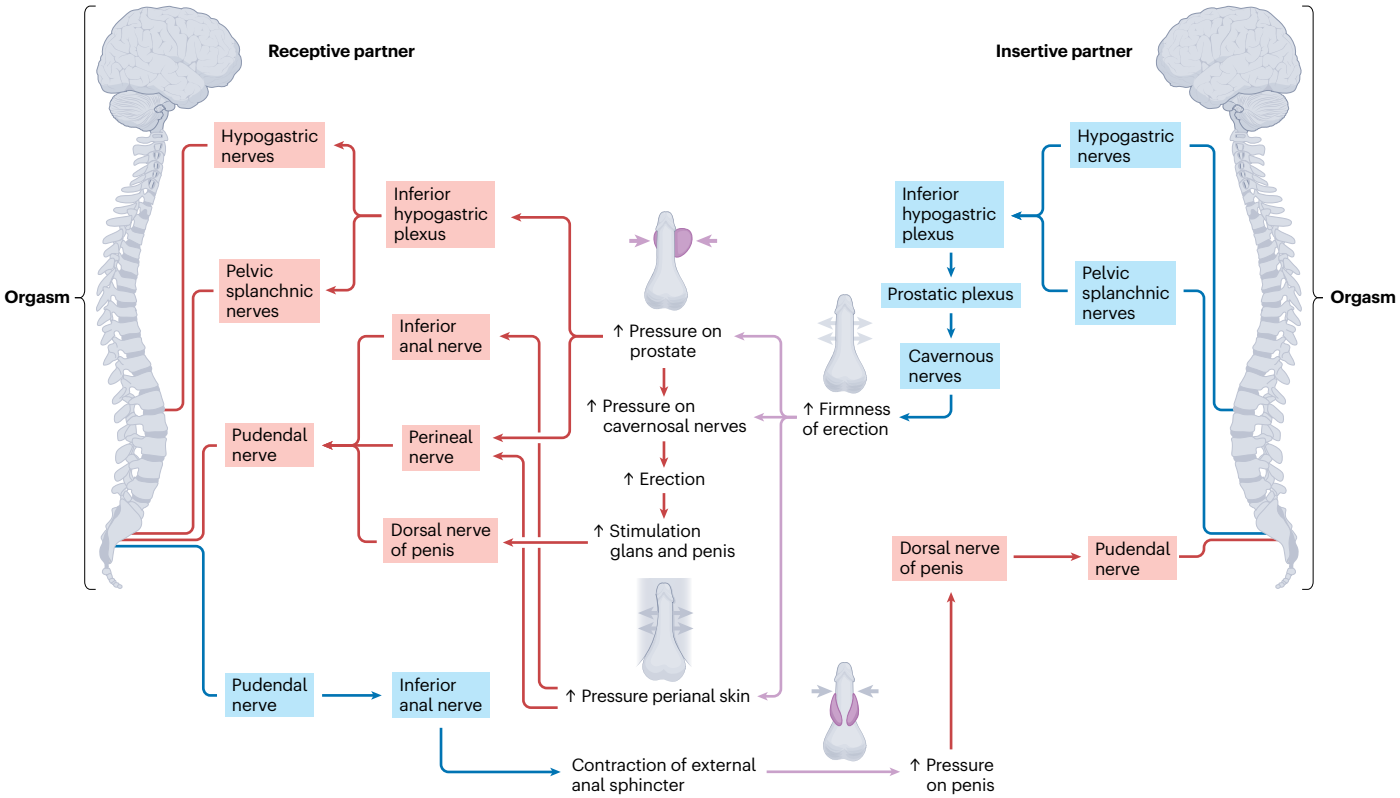
Prostate pleasure toys can help to support the role of the prostate in orgasm and pleasure during RAI; these place pressure on the prostate and rectal wall in order to induce an erection and intensify orgasm[48]. A 2018 study (n = 806) analysing differences in sexual behaviour found that SMM in same-sex relationships experienced extreme pleasure and frequent orgasms from RAI. SMM had a similar level of satisfaction from orgasm via anal entry (mean 4.60, 5 is most satisfactory) as cisgender heterosexual men who have vaginal intercourse with women (mean 4.69). Although the importance of this conclusion is unknown, anal–penile orgasms were rated higher than oral–penile orgasms in male–male relationships (mean 4.18) and male–female relationships (mean 4.36)[49].

Together these studies have helped uncover the complex roles of the anus, rectal wall, perianal skin and nerves in creating powerful orgasms and facilitating pleasurable anal intercourse. A comprehensive understanding of the anatomy and physiology of pleasurable RAI is essential for clinicians to effectively counsel SMM patients undergoing prostate cancer treatment.

Sexual dysfunction and prostate cancer

Sexual dysfunction after prostate cancer treatment is multifactorial and has widespread effects on QoL and survivorship outcomes. Issues influencing sexual dysfunction and distress include patient age, comorbidities, baseline sexual function and practices, and treatment modality (Fig. 3).

a **Genitopelvic neuroanatomy of pleasurable anal intercourse**



b **Genitopelvic neuroanatomy of pleasurable neovaginal intercourse**

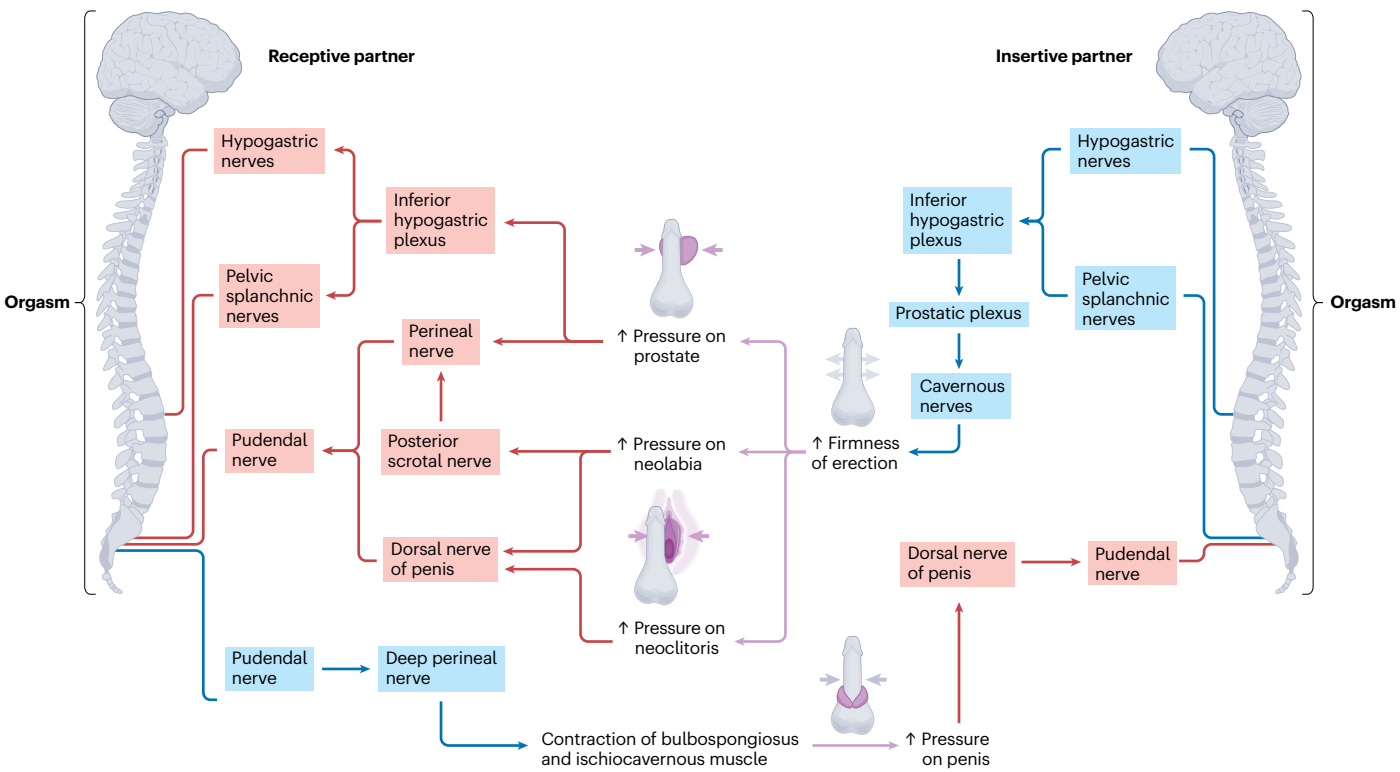


Fig. 2 | Genitopelvic neuroanatomy of pleasurable anal and neovaginal intercourse. a, Schematic diagram illustrating the genitopelvic neuroanatomy involved in pleasurable anal intercourse. Pressure from a penis on the prostate, cavernous nerves and surrounding sensitive perianal skin will elicit pleasure, orgasm and external anal sphincter contraction through various neural pathways. These afferent pathways include (1) pressure on prostate causing afferent signals through stimulation of branches of the pudendal, pelvic splanchnic and hypogastric nerves; (2) direct and indirect stimulation of the cavernous nerves causing an erection and stimulating the glans penis leading to afferent impulses through the dorsal nerve of the penis (branch of the pudendal nerve); and (3) stimulation and the anocutaneous skin causing afferent sensation through the perianal nerves (hair-bearing skin) and inferior anal nerves (non-hair-bearing skin). These afferent pathways cause reflex activation of the efferent motor inferior anal nerve (branch of the pudendal nerve) causing external anal sphincter contraction (bulbocavernosus reflex, anal wink reflex). Tightening of the external anal sphincters around the insertive partner's penis will in turn cause a reflex erection and lead to more pressure and more stimulation of the receptive partner's prostate, local nerves and sensory skin. Ultimately, the sustained repetitive activation of these sensory circuits will continue to intensify, build and ultimately lead to an orgasm for both partners. **b**, Schematic diagram illustrating the genitopelvic neuroanatomy involved in pleasurable neovaginal intercourse. Pressure from a penis on the prostate, sensitive neoclitoris and sensitive neolabia will elicit pleasure, orgasm and pelvic floor muscle contraction through various neural pathways. These afferent pathways include (1) pressure on prostate causing afferent signals through stimulation of branches of the pudendal, pelvic splanchnic and hypogastric nerves; (2) stimulation of the neolabia leading to afferent impulses through the branches of the perianal nerve (dorsal nerve of the penis and posterior scrotal nerve); and (3) stimulation of the neoclitoris causing afferent sensation through the preserved dorsal nerve of the penis. These afferent pathways cause reflex activation of the efferent motor perianal (branch of the pudendal nerve) causing pelvic floor muscle contraction (bulbocavernosus reflex, anal wink reflex). Tightening of the bulbospongiosus and ischiocavernosus muscles around the insertive partner's penis will in turn cause a reflex erection and lead to more pressure and more stimulation of the receptive partner's prostate, local nerves and sensate organs including the neoclitoris and neolabia. Ultimately, the sustained repetitive activation of these sensory circuits will continue to intensify, build and lead to an orgasm for both partners.

The importance of patient characteristics

Patient demographics, including age and comorbidities, can influence sexual dysfunction and are an important consideration. Studies suggest that SMM with prostate cancer might be diagnosed at a younger age than heterosexual men, but might also have a higher comorbidity burden. For example. the median age at which a patient with prostate cancer is diagnosed is 67 years old[50]. However, a cross-sectional survey study of 401 SMM with prostate cancer revealed a mean age of 63.5 years (standard deviation (s.d.) 6.6)[51] whereas a cross-sectional survey study of 92 SMM from the USA and Canada reported that the average age at diagnosis was 57.8 years[52]. Another cross-sectional study from Australia of 119 SMM and 224 cisgender heterosexual men reported a significant difference in age, with SMM diagnosed at an average age of 64.25 (s.d. 8.18) years compared with 71.54 (s.d. 8.98) years in cisgender heterosexual men ($P < 0.001$)[53]. Hypotheses to explain this difference include the possibility that older SMM might be more reluctant to disclose their sexual orientation[12,54], as well as increased serum PSA caused by prostate stimulation during RAI[55]. The earlier detection of prostate cancer in SMM might also be explained by the unique health-seeking behaviour of this cohort. A potential lack of complete health-care services from a primary care provider means that many SMM might have multiple caregivers to address their specific health-care needs. For example, many SMM separate their sexual health provider from their primary care provider[56]. Additionally, sexual health, along with mental health, is a primary health concern for SMM[57]. Thus, health-care fragmentation and increased concern regarding sexual health might mean that SMM are more inclined to seek medical care for sexual dysfunction, underlying causes of which include prostate cancer, leading to earlier detection of the disease.

Comorbidities might also differ for SMM. A study of 383 SMM compared comorbidity prevalence in SMM with published samples of cisgender heterosexual prostate cancer survivors. The exploratory study showed a similar prevalence of diabetes for SMM (12%) and cisgender heterosexual men (13%), and a lower prevalence of obesity for SMM (20%) compared with cisgender heterosexual men (32%)[58]. However, both blood vessel disease and mental health disorders were more common among SMM (53% versus 45% and 46.6% versus 15–27%, respectively[58]). The same study also found that comorbidities in SMM were associated with worse QoL and sexual function[58]. Supporting this conclusion is another study that found that patients with higher comorbidity scores experience decreased recovery to baseline erectile function following radical prostatectomy, independent of age[59]. Additionally, baseline erectile score is an important prognosticator for erectile function following treatment[26].

Maintaining the capacity for pleasurable sexual activity after cancer therapy[3] is especially important for SMM with prostate cancer who might engage in more frequent and variable sexual activities than cisgender heterosexual men. In fact, studies show that SMM are more sexually active than cisgender heterosexual men and have more casual and multiple sexual partnerships[60,61]. In two studies, ~46–50% of SMM were married and/or living with a partner[51,52], consistent with Ussher et al., in which 50% of SMM were partnered compared with 86% of cisgender heterosexual men ($P < 0.001$) who were married or in a relationship[53]. Ussher and colleagues also reported that the length of the relationship for partnered SMM patients is significantly shorter: only 81% of SMM relationships were reported to last >2 years compared with 93% of heterosexual relationships. Thus, sexual dysfunction following treatment can be especially distressing to patients without a partner, who might be sexually active and seeking relationships.

The effects of different treatment modalities

In addition to age, comorbidities, relationship status and baseline sexual function and practices, sexual dysfunction is affected by the treatment modality used[4], as well as by anatomical preservation during treatment[62,63]. In both surgery and radiotherapy, the extent of anatomical preservation, including nerve and vessel preservation, can be predictive of the extent of ED[62,63].

In the general population, radical prostatectomy is associated with short-term worsening of sexual function compared with EBRT alone for the treatment of localized prostate cancer. The prospective CEASAR study compared radical prostatectomy, EBRT, and active surveillance at a 3-year follow-up point and reported that the adjusted mean Expanded Prostate Index Composite (EPIC) sexual domain score for men undergoing surgery had declined significantly more than for men undergoing EBRT (mean difference −11.9 points, 95% CI −15.1 to −8.7)[26]. Furthermore, data from the ProtecT trial illustrated that radical prostatectomy was associated with an increased incidence of ED than EBRT at 6 years after treatment (surgery: 16%, EBRT: 27%)[64], but at 12 years

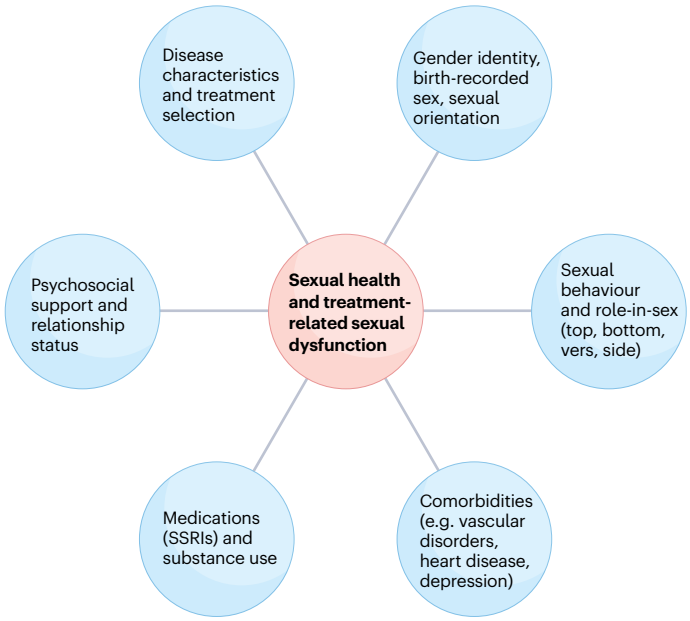


Fig. 3 | Biopsychosocial assessment of sexual health and treatment-related sexual dysfunction. Assessing sexual health and treatment-related sexual dysfunction in a patient is multifactorial. Understanding the patient's background is imperative. This understanding includes aspects of a patient's gender identity, birth-recorded sex, sexual orientation, sexual behaviour and role-in-sex (top, bottom, versatile, side), comorbidities that could influence sexual function (such as vascular disorders, heart disease or depression), medications and substances that could impair sexual function (for example, selective serotonin reuptake inhibitors (SSRIs)), a patient's relationship status and psychosocial support, as well as their disease characteristics and treatment selection.

the number of patients with erections firm enough for, presumably vaginal, intercourse approached similar percentages between the two groups (RP: 13%, EBRT: 15%), although ED impacted the QoL of a higher proportion of patients treated with RP (45%) compared with EBRT (34%) at 12 years[65]. Additionally, in the Prostate Cancer Outcomes Study (PCOS), patients undergoing surgery were more likely to have ED than those who received EBRT at 2 years and 5 years after treatment, although no difference was observed by 16 years[66].

Moreover, EBRT can be given in combination with ADT; which — when compared with EBRT alone — is associated with worse sexual outcomes, including an increased incidence of ED, ejaculatory issues, decreased libido and worse sexual recovery[67,68].

Although various different fractionation regimens are commonly used for EBRT, data have demonstrated that the use of hypofractionated radiotherapy does not increase post-therapy ED prevalence compared with conventionally fractionated radiotherapy[67,68]. Thus, shorter courses of EBRT can be used without an increased risk of ED. Additionally, brachytherapy might be associated with better post-treatment erectile function than EBRT as one study showed that ED caused partner-related distress in 44% of surgical patients, 22% of those who received EBRT and 13% of those who had brachytherapy at 1 year, suggesting that it should be considered in all patient groups[69]. However, another study showed similar sexual function quality of life scores at 2 years in patients treated for localized prostate cancer, measured with the Prostate Cancer Symptom Index (PCSI, in which higher score correlates with more dysfunction) were not different between the brachytherapy and EBRT cohort, although better than the radical prostatectomy cohort (ERBT: mean 59.2, 95% CI 53.6–64.7; brachytherapy, mean 61.6, 95% CI 53.5–69.7; RP: mean 73.7, 95% CI 69.2–78.1; active surveillance: mean 56.6, 95% CI 52.1–61.0)[25].

Finally, although the data regarding proton irradiation are limited, one study found that erections firm enough for vaginal penetration decreased from 90% to 72% and 67% at 1-year and 5-year follow-up, respectively. This is especially relevant to SMM, as a harder erection is required for anal penetration than for vaginal penetration[70,71]. Thus, comparative studies investigating photon and proton therapy are required to understand the effects of these treatment modalities on sexual dysfunction[72]. However, when considering these data, one must be aware of a possible bias, as younger patients with fewer comorbidities (and better baseline erectile function) tend to select surgery rather than EBRT and brachytherapy[73]. Notably, not all treatment options are available to all patients, as treatment recommendations are a function of cancer characteristics, disease extent, patient comorbidities and patient age, among other factors.

Considering QOL

The effects of prostate cancer treatments on QoL within the SMM community are multifactorial. *Restore*-2, one of the largest studies investigating the toxic effects of prostate cancer treatment on SMM (n = 401), observed that SMM had significantly worse urinary, sexual, bowel and hormonal functional outcomes after prostate cancer treatment than the 'general population' (assumed to be cisgender heterosexual men)[51]. Within the SMM cohort of 401 patients, the type of treatment significantly affected sexual and hormonal outcomes, but age and race and/or ethnicity did not seem to have an effect. More specifically, use of the EPIC Domain Scores showed no differences in sexual outcomes between radical prostatectomy/cryotherapy (EPIC sexual overall mean 38.2, s.d. 21.7) and radiation (EBRT and/or brachytherapy) (EPIC sexual overall mean 45.0, s.d. 22.5). However, combination of surgery and/or radiation (brachytherapy/EBRT) with hormonal treatment resulted in significantly worse sexual outcomes (EPIC sexual overall mean 25.9; s.d. 18.8)[51]. In a separate study by the same group, no significant difference was observed between surgery and radiation alone on sexual function QoL by multivariate analysis; however, combination therapies were associated with significantly worse outcomes when controlled for race, age, relationship status and sexual orientation[74].

The toxic effects of treatment

Toxic effects of prostate cancer treatment can, of course, be experienced by both cisgender heterosexual men and SMM. However, in SMM, they have been reported to be very common, and include anejaculation (reported by up to 94% of SMM), ED (90%), change in orgasm (87%), decreased sexual confidence (78%), penile changes (66%), anodyspareunia (65%) and climacturia (49%)[75].

Anejaculation

Anejaculation is to be expected following radical prostatectomy[76], as it is caused by the removal of the prostate and seminal vesicles (Table 1 and Fig. 3). Reported rates of anejaculation after radical prostatectomy vary widely, ranging from 11 to 91%[77]. Ejaculation is considered important in some SMM relationships and intercourse, as the visual representation of ejaculate can be symbolic to show that sexual pleasure was achieved[78,79]. In fact, SMM associate the inability to visualize ejaculate with worse sexual outcomes after radical prostatectomy[80,81].

In a prospective study of men from the general prostate cancer population, 225 receiving EBRT and 112 receiving brachytherapy, 72% of them lost the ability to ejaculate normally. Furthermore, the proportion of these patients experiencing anejaculation at 1, 3 and 5 years was 16%, 69% and 89%, respectively[82]. The aetiology of ejaculatory dysfunction following radiation therapy might be related to atrophy, fibrosis, scarring of the ejaculatory ducts and/or urethral strictures leading to obstruction (Fig. 4b). The addition of ADT to a radiation regimen will likely worsen ejaculatory dysfunction[82]. The pathogenesis of ejaculatory dysfunction with ADT is likely caused by a reduction in circulating testosterone. Studies have shown that lower levels of testosterone correlate with ejaculatory dysfunction[83] hypothesized to be due to testosterone having a central and peripheral role in regulating ejaculation, especially as the androgen receptor (AR) has been found in areas of the central nervous system that facilitate ejaculation[84].

In a study of 1,273 healthy men in the general population without prostate cancer, 46% reported reduced ejaculatory volume and 66% were bothered by this condition[85]. However, a study conducted by Wassersug and colleagues reported that ejaculatory dysfunction following prostate cancer treatment caused more distress ($P = 0.04$) for SMM (mean 3.32, s.d. 1.46) than for cisgender heterosexual men (mean 2.67, s.d. 1.54) measured on a Likert scale (1 = not bothered, 5 = extremely bothered)[86]. Similarly, a different study by Amarasekera and colleagues, using a database review of 308 SMM and 306 cisgender heterosexual men from the general population (47 had prostate cancer), revealed that, although treatment effectiveness was the most important outcome for both SMM and heterosexual men (69.1% SMM versus 70.4% heterosexual cisgender men, $P = 0.54$) when considering a treatment choice for prostate cancer, ejaculatory function was significantly more important for SMM (53.7%) than for heterosexual men (26.4%, $P < 0.0001$) when making this decision. In this study, no difference was reported in the importance of preservation of penile length or erectile function between SMM and heterosexual men, further emphasizing the importance of ejaculation to SMM[87]. The importance of ejaculatory function was also illustrated by Ussher and co-workers[53], who reported that ejaculatory concern was significantly greater for SMM than for heterosexual men (2.62 versus 1.85, $P < 0.0001$).

Climacturia

Climacturia — orgasm-associated urinary incontinence — occurs when expulsion of urine occurs during orgasm (Table 1). A retrospective study of 412 patients who underwent EBRT or RP showed that climacturia was present in 5.2% and 28.3% of patients after EBRT and surgery, respectively[88] and bothersome climacturia is reported by ~47% of all prostate cancer survivors[89].

The mechanisms of the development of climacturia are unknown, but might be due to decreased urethral length as well as damage to the internal sphincter caused by prostate cancer treatment combined with relaxation of the external sphincter during orgasm, leading to urination[90]. No association has been shown between daytime

Table 1 | Treatment-related sexual dysfunction in sexual minority men

Sexual dysfunction	Importance	Treatment consideration	Rehabilitation and restoration
Anodyspareunia	In the general SMM population, lifetime prevalence of AD is 61%[97] and point prevalence is 14%[101]. In SMM prostate cancer survivors, the point prevalence of AD ranges from 23 to 34%[101,102]	RP: removes prostate (24%)[102] EBRT: damages prostate, surrounding structures; causes bowel toxicity (25%)[102] BT: damages prostate, surrounding structures; causes bowel toxicity (25%)[102] ADT: might be protective against AD and bowel toxicity when combined with radiation[102,103]	Anal dilator[178] Dildos, butt plugs[178] Prostate massage vibrator[188,189] Lubricant[48,209] Alkyl nitrites (poppers)[193]
Climacturia	Oral intercourse is more common in SMM than in heterosexual men[93]. This toxicity can be embarrassing when engaging in insertive oral intercourse	More studies are needed to understand treatment differences	Pelvic floor exercises[172] Penile constriction ring (cock ring)[173] Surgical management (mini-jupette)[175,176]
Anejaculation	Ejaculate can be important to some SMM and be symbolic of sexual pleasure[78–81]	RP: 100%[76] EBRT: 11–91%[77] BT: 11–91%[77] ADT: might worsen ejaculatory dysfunction[82]	Research is needed to circumvent anejaculation following prostate cancer treatment
Erectile dysfunction	An erection must be 33% more rigid for anal intercourse than for vaginal intercourse[70,71]	RP: worse at 6 years[64], no difference at 16 years compared with EBRT[65,66] EBRT: worse with ADT[67,69]	PDE5 inhibitors[165,166] VEDs[168,169] Penile constriction ring (cock ring)
Penile changes	The size and shape of the penis is important to participants of insertive anal and oral intercourse. Penis size is emphasized in gay culture[127]	RP: penile shortening ranges from 0.5 to 5 cm (refs. 121,122) EBRT: when combined with ADT, there might be penile shortening[125]	PDE5 inhibitors[171] VEDs[169,170]
Orgasm changes	Orgasm function and type at baseline might differ between SMM and heterosexual men[115]	RP: anorgasmia (37%)[105] and dysorgasmia (12–18%)[106,107] EBRT: anorgasmia (29%)[109] and dysorgasmia (15%)[111] BT: anorgasmia (49%)[109] and dysorgasmia (26–40%)[112,113] ADT: might weaken orgasm sensation[114]	Tamsulosin[105] Cabergoline[177]

AD, anodyspareunia; ADT, androgen deprivation therapy; BT, brachytherapy; EBRT, external beam radiation therapy; PDE5, phosphodiesterase 5; RP, radical prostatectomy; SMM, sexual minority men; VED, vacuum erectile device.

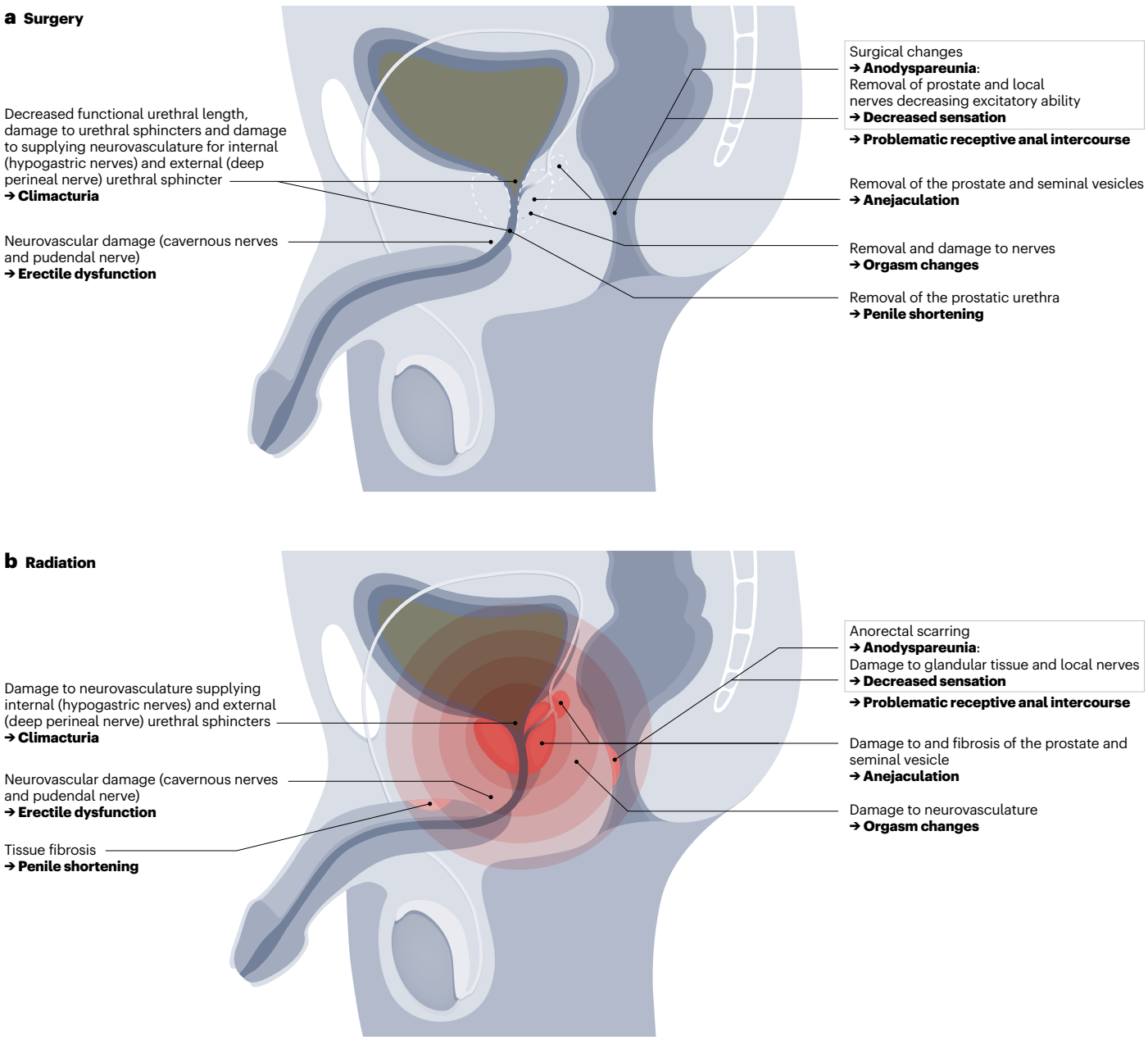


Fig. 4 | Pathophysiology of treatment-related sexual dysfunction in sexual minority men with prostate cancer. a, Representative sagittal image of the effect of radical prostatectomy on sexual health outcomes. Removal of the prostatic urethra and the prostate/seminal vesicles leads to penile shortening and anejaculation, respectively. Removal of the prostate and local nerves as well as scarring can affect pleasurable receptive anal intercourse owing to the lack of nerves and physical prostate to incite surrounding nerves during intercourse. Damage to the urethral sphincters and nerves as well as decreased functional urethral length can lead to climacturia, and when nerve sparing is not an option, erectile dysfunction can be affected by damage to the cavernous nerves and pudendal nerve. General damage to the pelvic nerves responsible for pleasure can lead to changes in orgasm. **b**, Representative sagittal image of the effect of radiation (external beam or brachytherapy) on sexual health outcomes. Radiation can cause fibrosis and scarring and damage to the neurovasculature, leading to problematic receptive anal intercourse from potential anodyspareunia and potential decreased sensation. Tissue fibrosis also leads to change in penile size and shape as well as climacturia. Prostatic and seminal vesicle damage and atrophy can lead to anejaculation, and nerve damage and tissue fibrosis can cause erectile dysfunction. General damage to the pelvic nerves responsible for pleasure can lead to changes in orgasm.

urinary incontinence or orgasm-related urinary leakage and climacturia, emphasizing its unique pathophysiology[76], but loss of functional urethral length might be a cause of climacturia, as decrease in penile length was found to be an independent predictor of its occurrence[91] (Fig. 4a). Supporting this hypothesis, a video urodynamic study comparing the functional and morphological aspects of bladders in (presumably)

cisgender heterosexual men reporting ($n = 7$) and not reporting ($n = 5$) climacturia at least 1 year after bladder neck-sparing radical prostatectomy found that functional urethral length was significantly reduced in patients experiencing climacturia (mean 20.3, s.d. 4.0) than in those not experiencing this dysfunction (mean 35.2, s.d. 4.8, $P = 0.02$)[92].

Climacturia causes considerable distress to the SMM community, possibly because both insertive and receptive oral intercourse are more common in this population than in heterosexual men[93]. After prostate cancer treatment, ~52% of SMM reported involuntary urination during intercourse or at orgasm[74], and in a separate study of 124 SMM, 65% noted a change in urinary patterns and 40% reported that activities were limited by urinary issues[94]. In a qualitative study of 16 SMM, urinary incontinence and climacturia were particularly anxiety provoking, as the majority of the patients participated in oral sex and mutual masturbation[95]. Thus, further studies are needed to understand how treatment modality affects climacturia in this patient population and how climacturia might differ between SMM and heterosexual men.

Problematic receptive anal intercourse

Problematic RAI encompasses anodyspareunia (pain during or after RAI), decreased prostate sensation and issues with RAI orgasm[18]. Understanding problematic RAI and the contribution of prostate cancer treatments is especially important for SMM with prostate cancer as one study showed that 56% (225 of 401) of SMM prostate cancer survivors engaged in RAI in the preceding 4 weeks of survey administration[96]. In *Restore*-1, 37% (25 of 68) of SMM patients with prostate cancer responded that pleasurable RAI was painful or lacked feeling after treatment. Additionally, 65% (46 of 71) of SMM reported that they sometimes, often, or always have issues with experiencing an orgasm with RAI after treatment for prostate cancer, and 27% (25 of 93) reported dissatisfaction with the quality of RAI after their treatment[74]. However, although this study illustrates that prostate cancer treatment likely contributes to problematic RAI by affecting orgasm and prostate sensation, more research is needed to elucidate the pathophysiology as it relates to orgasm and prostate sensation.

Anodyspareunia. Anodyspareunia is another contributor to problematic RAI, and it was first acknowledged as a sexual dysfunction in 1997, when parallels were drawn between painful vaginal intercourse (dyspareunia) and anodyspareunia[97]. Anatomical and physiological factors that can make RAI painful include lack of natural lubrication, the anorectal angle and the tightness of the anal sphincter[98,99]. Inadequate lubrication, lack of foreplay and psychological factors, such as anxiety and internalized homophobia, were identified as increasing the risk of anodyspareunia[100,101].

The lifetime prevalence of anodyspareunia in the general SMM community is 61%, which is notably higher than the lifetime prevalence of difficulty getting an erection (40%) and difficulty ejaculating (39%) in SMM[97]. One study reported that 14% of 404 SMM in the general population could not have intercourse at all owing to anodyspareunia[101]. A larger study of 1,752 SMM reported that 59% of 1,190 SMM engaging in RAI had experienced some degree of pain in the previous 4 weeks[100]. Even so, although painful receptive intercourse and anodyspareunia are exceedingly prevalent in the SMM population, only 6% of SMM with prostate cancer reported that their providers even discussed anal intercourse with them, let alone mentioned anodyspareunia as a toxic effect of prostate cancer treatment[102].

In a secondary analysis of *Restore*-1, the authors sought to understand anodyspareunia further[102], defined by a single self-reported question that asked patients if they experienced pain severe enough to stop RAI in the last 4 weeks, and patients reporting rarely, sometimes, often, or always (as opposed to not at all), were classified as having anodyspareunia. Using these parameters, the prevalence of anodyspareunia was reported as 23%. In addition, patient demographics – including age, race/ethnicity, educational attainment, geographic location and relationship status – did not correlate with the presence of anodyspareunia. Poorer mental health function (measured using the Mental component of the short-form-12 health survey (SF-12 Mental questionnaire)) correlated with an increased likelihood of experiencing anodyspareunia (OR 0.95; 95% CI 0.91–0.99). Furthermore, although not statistically significant, worse bowel symptomatology measured with EPIC-Bowel Function and EPIC-Bowel Bother, which captures bowel habits and abdominal pain (for example, uncontrollable leakage of stools) trended towards an increased likelihood of experiencing anodyspareunia (function: OR 0.96; 95% CI 0.92–1.00; bother: OR 0.97; 95% CI 0.94–1.00).

The incidence of post-treatment anodyspareunia also varies somewhat with the treatment received. For example, 24% of SMM experienced anodyspareunia after surgery, which was similar to that following radiation (either EBRT or brachytherapy), after which 25% of SMM experienced anodyspareunia. Surprisingly, after combination therapies including EBRT + ADT and RP + ADT, 0 of 7 (0%) SMM experienced anodyspareunia[102]. Thus, ADT might have a protective effect. In a retrospective study of 2,752 patients with prostate cancer, ADT was shown to have a protective effect against proctitis and rectal bleeding when combined with brachytherapy[103]. The authors hypothesize that this effect is likely due to ADT causing a reduction in prostate size and a resultant reduction in radiation target volume. However, ADT is known to decrease libido and negatively affect erectile function, so the relevance of a protective effect of ADT against anodyspareunia needs further research and discussion. Further studies are required to elucidate how various treatment modalities and combinations influence the incidence of problematic RAI, including anodyspareunia, in prostate cancer survivors (Table 1).

Orgasm changes

Changes in orgasm function include anorgasmia, altered or decreased orgasm sensation, and dysorgasmia (orgasm-associated pain) (Table 1). Treatment for prostate cancer has been associated with all of these changes[104]. After radical prostatectomy, patients might experience anorgasmia (37%)[105], decreased orgasm (37%)[105], or dysorgasmia (12–18%)[106,107], although nerve-sparing techniques and younger patient age might be associated with improved orgasm-related outcomes[108]. Patients might also experience anorgasmia after radiotherapy (EBRT: 29.1%, brachytherapy: 49.3% (decreased orgasm/anorgasmia))[109] decreased orgasm (29.6% EBRT, 23.7% EBRT + brachytherapy)[110], or dysorgasmia (EBRT: 15%[111], brachytherapy: 26–40%[112,113]). Additionally, the combination of radiation with hormonal therapy can further diminish orgasmic function[114].

Orgasm changes following prostate cancer treatment might not differ significantly between SMM and heterosexual men. A study of 460 cisgender heterosexual men and 96 SMM showed no difference in orgasm satisfaction after prostate cancer treatment between the two groups[86], although in another study, SMM had better self-reported orgasms (4.24; s.d. 3.31) than cisgender heterosexual men (2.33; s.d. 2.53; $P < 0.001$) following prostate cancer treatment using the changes in sexual functioning questionnaire (CSFQ-14- M)[53].

By contrast, in the general male population (that is, men who do not have prostate cancer), SMM might have more difficulty experiencing orgasm pleasure measured with Patient-Reported Outcomes

Measurement Information System Sexual Function and Satisfaction v2.0 questionnaire (PROMIS SexFS), where raw scores are converted to a calibrated T-score (range: 1–100, mean 50, s.d. 10) with a higher score reflecting more of the concept, (for example, more orgasm ability, more orgasm pleasure). In this study, orgasm ability was the same among gay (52.2; 95% CI 50.8–53.7, n = 293), bisexual (50.6; 95% CI 48.2–53.1, n = 121) and heterosexual (52.0; 95% CI 51.4–52.6, n = 1,382) men, but orgasm pleasure was lower for gay (48.9; 95% CI 47.6–50.2) and bisexual (46.7; 95% CI 44.0–49.5) men than heterosexual men (51.1; 95% CI 50.5–51.7)[115]. Thus, although changes in orgasm after prostate cancer treatment might not differ between SMM and cisgender heterosexual men, recognizing that orgasm function at baseline might differ between the cohorts is important. Moreover, it is important to note that in these studies orgasm and orgasm function were not differentiated by insertive or receptive intercourse. Future studies are needed to identify any potential differences in treatment-related orgasm issues by insertive or receptive intercourse, which would provide greater insight into treatment-related orgasm dysfunction with RAI.

Erectile dysfunction

ED is a common, well established toxic effect of prostate cancer treatment (Table 1). In a study of SMM following prostate cancer treatment, 85% of men reported that their erections were not firm enough for intercourse[74].

However, reports of ED after prostate cancer in SMM are variable. A study by Ussher and colleagues showed that erectile function was significantly better in SMM (EPIC EF: 21.2) than in cisgender heterosexual men (16.5) following prostate cancer treatment[53]. In subsequent analyses, Ussher's group identified that 72% of SMM reported ED at ~5.9 years after diagnosis (12 active surveillance, 56 surgery, 15 radiation, 2 ADT, 34 combination therapies)[94]. These data are supported by outcomes from a separate study, in which SMM (n = 89) reported better erectile function (38.7, s.d. 2.6) than cisgender heterosexual patients (n = 225) (29.5, s.d. 1.5) as assessed using the EPIC score[52]. Additionally, also using EPIC to assess sexual function, SMM from *Restore*-1 (40.5, s.d. 23.6) showed significantly better erectile scores than SMM in *Restore*-2 (35.5, s.d. 21.2) and the cisgender heterosexual men validation sample (29.5, s.d. 23.8). Although *Restore*-1 (ref. 116) and *Restore*-2 both recruited sexual and gender minorities (SMM and TGW), and although no TGW with prostate cancer enrolled in *Restore*-2, *Restore*-2 inclusion criteria also required patients to report a sexual and/or urinary problem[51].

By contrast, a 2013 study reported similar rates of ED (P = 0.83) and ability to orgasm with penetration (P = 0.91) between SMM and cisgender heterosexual men[86], but, conversely, a pilot study analysing bicalutamide (ADT monotherapy) for prostate cancer treatment in SMM (12 patients) and heterosexual men (17 patients) reported that SMM scored lower (28.7) than heterosexual men (56.1) on the International Index of Erectile Function (IIEF) score[117].

Although erectile function is important to all patients, it might be of particular clinical significance among the SMM community, as studies have estimated that an erection must be 33% more rigid for anal intercourse than for vaginal intercourse[62,63]. Furthermore, ED might be associated with increased distress in the SMM community as a survey study in the general community found that patients who engage in more sexual activity reported more distress from ED[118]. Additionally, the size and hardness of erection is considered important in the SMM community and the size and function of the penis is integral in SMM relationships[119]. In a survey study of 648 SMM, SMM desired an above average erect penis (mean 4.87, s.d. 0.97), with 4 being average (1 = smallest erect phallus, 7 = largest erect phallus)[120].

Change in penis size and shape

Prostate cancer treatment can affect the length and girth of the penis (Table 1). In the general population, studies show penile shortening ranges from 0.5 cm to 5 cm after radical prostatectomy[121,122]. This change might be caused by removal of the prostatic urethra[123] as well as hypoxia in the penile tissue and resultant muscle loss and fibrosis[124]. Although substantially less evidence exists describing the effect of radiation on the size and shape of the penis, one study (n = 46) showed that EBRT combined with ADT can shorten the penis, with the stretched penile length decreasing by an average of 5.6 cm at 18 months from the initiation of neoadjuvant hormone therapy[125].

Although there is an increasing emphasis on penis size in the general population with evolving sociocultural views of the male body reflected by the increase in the size of the penis over time in artwork[126]; among SMM, penis size is likely even more emphasized owing to the focus on body image in gay culture and the 'double presence' of the penis in sexual minority relationships and encounters[127]. Additionally, the size and shape of the penis might be particularly important to those who participate in the insertive role in anal intercourse[128].

However, a study has also suggested that, even if prostate cancer treatment does affect penile shape, SMM (n = 16) might not experience any difference in self-esteem and self-image compared with heterosexual men (n = 131) after surgery[129] or other treatments. However, these data should be interpreted with caution as a major limitation of this study was a small sample size. Even so, penile size and shape are likely to not be the only important factor relating to self-esteem and image for SMM, emphasizing that overall sexual satisfaction in SMM is multifactorial.

Decreased libido

Loss of libido, or decreased sexual desire, following prostate cancer and its treatment is very common, with 41.3% (n = 414) of cisgender heterosexual men stating that their sexual desire was completely gone 2 years after diagnosis in one particular study[130]. Decreased libido can be worsened by the use of hormone therapy[131] (Table 1). In a study by Ussher et al., SMM reported significantly better sexual interest (7.82; s.d. 3.12) and sexual frequency (4.40; s.d. 1.97) than heterosexual men (interest 5.43; s.d. 3.22; frequency 2.63; s.d. 2.22) after prostate cancer treatment[53]. Another study by the same group analysing 124 SMM who had survived prostate cancer showed that 58% of men report "absent", "poor" or "okay" libido and 65% of these patients stated that low libido was problematic[94]. In an exploratory qualitative study of three gay couples managing sexual dysfunction after radical prostatectomy, all patients noted a decrease in libido after surgery and one patient stated that he felt "castrated". However, within this exploratory study, two of the three patients also attributed these symptoms to confounding variables, such as medical comorbidities and advancing age[132].

Change in role-in-sex

In patients with prostate cancer and survivors who participate in anal intercourse, the damage and toxic effects to the prostate, rectal wall, perianal skin and the surrounding neurovasculature necessary for sexual pleasure can lead to a change in a patient's role-in-sex[22]. Within the general SMM community, 8–29% of SMM are the insertive partner ('top'), 13–50% are the receptive partner ('bottom'), and 29–58% are both ('versatile' or 'vers')[133,134]. Change in role-in-sex can have many negative implications for intercourse and mental health as one's role-in-sex can be a substantial part of one's identity in the SMM community[135] (Fig. 5).

Ussher and colleagues' study examining change or loss in role-in-sex before and after surgery or radiation reported that patients

identifying as the insertive partner (top) decreased from 31% to 12%, those identifying as the receptive partner (bottom) increased from 19% to 24%, those who considered themselves a versatile partner (vers) decreased from 20% to 8%, and the proportion of men who reported in engaging in no anal intercourse increased from 31% to 56%[94]. Additionally, patient interviews demonstrated that a change in role-in-sex challenged relationship dynamics owing to partner incompatibility[94]. This sentiment was echoed in a study by Hart and colleagues, who noted from qualitative interviews that changes in sexual function and position were distressing to partners of SMM prostate cancer survivors. In particular, the authors noted that only 40% of the insertive patients who were 'tops' before treatment continued to be strict 'tops' afterwards[52]. Furthermore, in *Restore*-1, although ~92% of SMM had a strong sense of a role-in-sex before treatment, only 45% had any sense of a role-in-sex after treatment[74]. More specifically, patient role-in-sex identification included 42% tops/vers-tops, 37% bottoms/vers-bottoms and 18% vers before prostate cancer treatment, compared with 8% tops/vers-tops, 65% bottoms/vers-bottoms and 5% vers after treatment. Moreover, an overall decrease in total percentage (~92 to ~45%) suggests that treatment affects both role-in-sex and sexual activity, and it suggests that many SMM might no longer be sexually active as they no longer identify with any role-in-sex (Fig. 5).

Changes to role-in-sex might also be dependent on treatment modality. In a study of 15 SMM who underwent different prostate cancer therapies, patients were asked about their role-in-sex before and after treatment. Within the surgery group, 3 of 4 tops and 3 of 3 bottoms had to change their role-in-sex identity. Within the radiation group (EBRT ± ADT and brachytherapy), all patients maintained their role-in-sex identity before and after treatment (5 tops continued to be tops and 2 bottoms continued to be bottoms). However, although results suggest that different prostate cancer treatments might affect role-in-sex differently, the small sample sizes mean that this topic warrants further study and evaluation[136].

Outercourse and the emergence of the 'side'. The societal concept of sexual pleasure and intimacy is expanding, and it is becoming more widely accepted that pleasure and intimacy can be experienced through intercourse as well as outercourse[137,138]. As per the Sexual Medicine Society of North America, outercourse is a subjective term and might include kissing or mutual masturbation[139]. Thus, when discussing role-in-sex, it is important to acknowledge that SMM might not participate in anal intercourse and might participate in oral intercourse or outercourse. An internet-based survey of 24,787 SMM aged 18–87 years old in the USA showed that the most common behaviour among SMM was kissing a partner on the mouth (74.5%), oral sex (72.7%) and partnered masturbation (68.4%). In this cohort, anal intercourse occurred among less than half of participants (37.2%) and was most common among younger SMM aged 18–24 (42.7%)[15], which is considerably younger than the median age of SMM diagnosed with prostate cancer. This suggests that some SMM might not engage in anal intercourse (either insertive or receptive) and instead engage in other sexual activities such as oral intercourse or mutual masturbation. This role-in-sex has been colloquially termed 'side'[140,141].

Psychological distress

A cancer diagnosis — including that of prostate cancer — can lead to substantial psychological distress, including anxiety, depression and, potentially, decreased sexual desire, and patients with prostate cancer are known to experience mental health conditions including depression and anxiety[142]. Associated treatments for these psychological concerns might also contribute to sexual dysfunction. For example, antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (for example, clomipramine), antipsychotics[143] and benzodiazepines[144] are associated with a risk of sexual dysfunction and might cause decreased libido, ejaculatory issues and ED[145,146] (Fig. 3).

SMM are known to have more mental health conditions than the general population, including increased prevalence of anxiety, depression and substance use disorder[147]. SMM prostate cancer survivors consistently report worse mental health outcomes than heterosexual men. In one study, SMM scored significantly worse than heterosexual men (mean 46, s.d. 0.8 and mean 58, s.d. −0.7, respectively; $P < 0.0001$) on the Short Form-12 QoL survey[74]. This effect is further emphasized by both Rosser[51] and Ussher[53], who both reported that SMM scored significantly worse on Functional Assessment of Cancer Therapy Prostate (FACT-P) subscales and overall FACT-P than a cisgender heterosexual comparative sample (Rosser ($n = 401$)[51], mean 112.9, s.d. 19.3; Ussher ($n = 119$)[53], 114, s.d. 22.7; heterosexual validation sample ($n = 96$)[148], mean 130.5; s.d. 16.3). Additionally, these studies found that SMM

Sexual dysfunctions to consider depending on role-in-sex

Top	Vers	Bottom	Side
• Erectile dysfunction • Penile shortening • Anejaculation • Orgasm changes • Decreased libido	• Problematic receptive anal intercourse (anodyspareunia, decreased prostate sensation) • Erectile dysfunction • Penile shortening • Anejaculation • Decreased libido	• Problematic receptive anal intercourse (anodyspareunia, decreased prostate sensation) • Anejaculation • Decreased libido	• Climacturia • Erectile dysfunction • Penile shortening • Anejaculation • Decreased libido

Mitigation strategies and considerations for particular roles in sex

Top	Vers	Bottom	Side
Changing position: discuss condoms, STIs, and PrEP	Poppers and PDE5 inhibitors (e.g. sildenafil) are contraindicated	Abstain from receptive anal intercourse after treatment and discuss best anal cleaning practices	Discuss cock rings as a treatment for climacturia and erectile dysfunction

Fig. 5 | Patient-centred conversations based on role-in-sex. At consultation, the health-care provider must enquire about the role-in-sex of a patient. A patient's role-in-sex can influence treatment recommendations, guide conversations and, when applicable, affect shared decision-making. Although discussing all treatment-related sexual dysfunctions is important, particular toxic effects of interest depend on the role-in-sex. For someone who identifies as a top: erectile dysfunction, penile changes, anejaculation, dysorgasmia as it relates to the penis, and libido. For someone who identifies as versatile: problematic receptive anal intercourse, erectile dysfunction, penile changes, anejaculation, dysorgasmia as it relates to the penis and prostate, and libido. For someone who identifies as a bottom: problematic receptive anal intercourse, anejaculation, dysorgasmia as it relates to prostate sensation, libido. For someone who identifies as a side: climacturia, erectile dysfunction, penile changes, anejaculation and libido. Additionally, physicians should explain at consultation and again at follow-up appointments the implications of changing role-in-sex, the contraindication of combining alkyl nitrites (poppers) with phosphodiesterase 5 (PDE5) inhibitors, and the time course of abstinence from engaging in receptive anal intercourse with sexual and gender minorities. PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

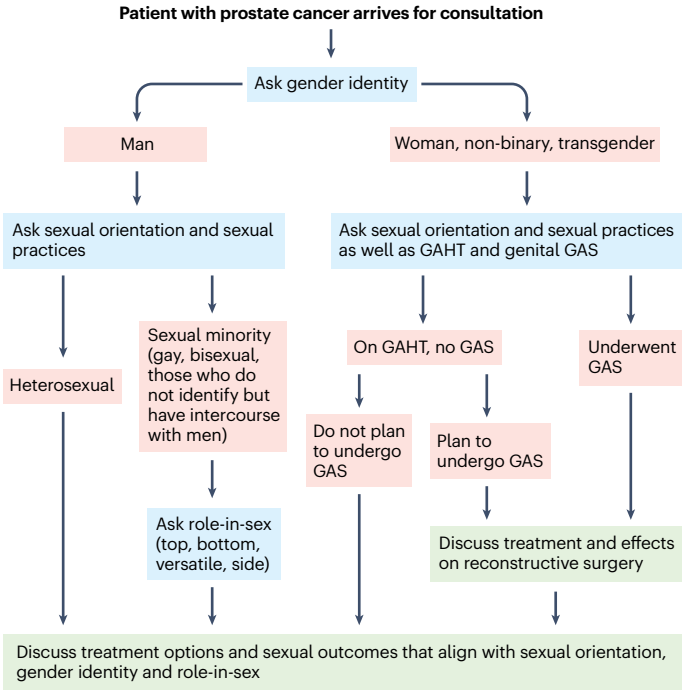


Fig. 6 | Patient-centred consultation guidance for patients with prostate cancer. To guide patient-centred conversations about prostate cancer treatment selection, physicians should enquire about gender identity, sexual orientation, sexual practices, role-in-sex, gender-affirming hormone therapy (GAHT) and genital gender-affirming surgery (GAS). Answers to these questions will guide patient-centred treatment conversations that align with a patient's role-in-sex, sexual orientation and gender identity, and enable informed treatment selection.

scored significantly higher on the psychological distress QoL scales using the brief symptom 18 inventory scale (higher number indicating worse distress) including higher on the depression (Rosser, mean 3.62, s.d. 4.51; Ussher, mean 4.65, s.d. 5.4) anxiety (Rosser, mean 2.57, s.d. 3.47; Ussher, mean 1.95, s.d. 2.58), and overall psychological distress scale (Rosser, mean 8.28, s.d. 8.8; Ussher, mean 10.7, s.d. 12.4) than the heterosexual validation sample[149] (n = 402, depression, mean 1.55, s.d. 2.72, P < 0.001; anxiety, mean 1.42, s.d. 2.72, P < 0.001; overall: mean 5.54, s.d. 7.9, P < 0.001).

Mental disorders and associated treatments might contribute to the development of sexual dysfunction in SMM with prostate cancer, and a review of medications and monitoring of the development of these conditions are essential in this vulnerable population.

Mitigating sexual toxicity

Preventing and managing treatment-related sexual toxicity includes communicating treatment options, the associated potential toxic effects of treatment and interventions that can help to preserve or prevent toxicity. Providing patients with this information will allow them to make an informed decision and be aware of the options for managing treatment-related sexual toxicity.

Patient-centred communication

Practitioners must enquire about sexual orientation and practices with their patients[22,150] (Fig. 6). Frameworks available to help physicians to ask about sexual orientation and sexual health include consensus reports from the National Academy of Science Engineering and Medicine (NASEM) and the British Association of Sexual Health and HIV (BASHH). The report from NASEM provides principles (inclusiveness, precision, autonomy, parsimony and privacy) for collecting sexual orientation and gender identity data and proposes specific questions to ask[151]. Key principles from the BASHH guidelines include confidentiality, communication, sexual health, documentation and specific circumstances[152]. These resources could be useful to help physicians to overcome anxiety when discussing sexuality and sexual health with SMM (Fig. 5).

However, these guidelines are not specific to patients with cancer and more research is needed to assist physicians in discussing sexual orientation and sexual practices around a cancer diagnosis. For example, a 2019 study demonstrated that only two-thirds of SMM report being out to their prostate cancer care provider[74]. In a survey from the American Urological Association, 112 adult urologists (89 males, 23 females) reported that they were significantly more comfortable discussing sexual health with heterosexual patients (80%) than with SMM (64%). Additionally, 63% of respondents do not ask patients about sexual orientation and 26% assume the patient to be heterosexual[153]. Furthermore, a survey of ASCO members revealed that less than half of providers ask about sexual orientation, and that 17% of respondents thought that collecting sexual orientation data was not important[154]. This study cited health-care provider discomfort, institutional culture, and lack of training, resources and time as barriers to collection of sexual orientation data. Similarly, a systematic review revealed that health-care professionals might fail to discuss sexual health-related issues with patients owing to time constraints, lack of education, concern about offending the patient and personal discomfort[155].

Nevertheless, on the masculine self-esteem scale, SMM patients who disclosed their sexual orientation had significantly higher self-esteem (77, s.d. 18) than those who did not disclose their orientation (62, s.d. 20). This openness is likely to improve the physician–patient relationships, which can promote better sexual and disease-related outcomes[156]. The lack of discussion regarding sexual orientation and preference might be related to the reported reduced satisfaction with prostate cancer care among SMM patients, whereby SMM describe significantly lower levels of satisfaction with treatment than heterosexual men[53].

When considering prostate cancer treatments and their associated toxic effects, asking about role-in-sex, in addition to sexuality and sexual practices, is important (Fig. 2 and Fig. 4). Knowing the role-in-sex of a patient might influence treatment recommendations, guide conversations and affect shared decision-making in this population, as the adverse effects of treatment differ and the specific interests of men might differ[157] (Fig. 4). For example, a qualitative interview with a prostate cancer survivor who identified as a bottom noted that treatment-related ED was not distressing owing to the lack of importance his erection has on his sexual life and identity[132]. Thus, a bottom or vers might be more interested in learning about problematic RAI, including anodyspareunia, dysorgasmia and prostate sensation after prostate cancer treatment, whereas men who identify as a top or vers might be more interested in learning how specific therapies affect erection firmness and penile shape and/or length, and those who consider themselves a side might be interested in learning about climacturia and anejaculation[22]. By appropriately guiding conversations, patients will be able to make an informed decision, which could help to decrease the rate of sexual identity change in this patient population. Considering the entire patient is essential when discussing

treatment options and treatment-related sexual dysfunction, especially in SMM (Fig. 5).

Sexual rehabilitation and devices

Sexual devices and medications can help patients to restore their capacity to experience arousal and orgasm by altering physiology and increasing sensation[48]. Such devices to support sexual rehabilitation, restoration and assistance are important to SMM with prostate cancer[48]. A 2019 qualitative study identified that significantly more SMM prostate cancer survivors than heterosexual patients are likely to try an assistive sexual aid[158]. Such aids include oral medications, penile injections and/or implants, vacuum pumps and vibrators. Furthermore, although both SMM and heterosexual men were dissatisfied with sexual aids, SMM were more likely to seek information and support about sexual rehabilitation from the internet, therapists and support groups[158]. This point further illustrates the openness of SMM to using sexual assistive devices and the need for cancer-care providers to discuss sexual rehabilitation with this population.

Information regarding sexual assistive devices should be provided to patients with prostate cancer at an initial consultation, in order to help guide discussion of treatment options and future sexual rehabilitation[159]. SMM treated for prostate cancer report that limited information is provided on sexual restoration at consultation. This lack of education about sexual rehabilitation might delay treatment and lead to worse sexual outcomes[160–162].

ED rehabilitation

Sexual restoration after prostate cancer treatment has been primarily focused on improving erectile function. Common treatments for ED following prostate cancer treatment include phosphodiesterase 5 (PDE5) inhibitors (such as tadalafil and sildenafil), penile injection therapy, penile implants and vacuum erectile devices (VED)[160,163,164]. In the general prostate cancer population, ~50% of prostate cancer survivors use a rehabilitation method for penile erection restoration, but although penile rigidity increases, ~73% of general patients discontinue these rehabilitation methods[158,160]. SMM are more likely to use oral medications (66% versus 38%, $P < 0.001$), penile injections (26% versus 13%, $P < 0.001$), vacuum pumps (27% versus 11%, $P < 0.001$) and penile constriction rings (36% versus 16%, $P < 0.001$) than heterosexual patients[158] (Table 1).

In the general population, sildenafil has been found to help with ED. Initiating sildenafil therapy before radiation and continuing it during radiation has been demonstrated to improve erectile function[165]. Additionally, in a randomized controlled crossover study, 36% of men responded to sildenafil but not to placebo[166]. Similarly, starting sildenafil after radical prostatectomy helps to improve ED and starting sildenafil early improves rehabilitation[167]. In addition to PDE5 inhibitors, VEDs might help with ED following radiation therapy and surgery. This approach is especially important in patients who might have a contraindication to PDE5 inhibitors owing to a concomitant medication or comorbidity[168,169].

Penile stretching

As well as assisting with ED, VEDs and PDE5 inhibitors might have a role in the restoration of penile length, girth and shape following prostate cancer treatment (Table 1). Trials have investigated the use of VEDs for penile changes after radical prostatectomy. In a cohort of 28 patients, VED use was found to preserve penile length when treatment was started 1 month after surgery[170]. Additionally, the use of VEDs was associated with smaller decreases in penile size than no treatment[169]. Although the association between penile shortening and changes with radiation treatment is not as strong, ongoing studies are attempting to understand how VEDs can be used to prevent penile shrinkage during radiotherapy[168]. Moreover, PDE5 inhibitors might also help with changes in penile length. In a randomized study investigating the effect of tadalafil 5 mg daily, tadalafil 20 mg as needed, or placebo after radical prostatectomy showed that 5 mg tadalafil helped to preserve penile length compared with placebo[171].

Climacturia rehabilitation

Climacturia rehabilitation includes pelvic floor exercises, blood flow restriction and surgical intervention (Table 1). Additionally, emptying one's bladder before intercourse and using condoms might also help to manage climacturia[89]. In a randomized controlled trial, patients who underwent prostatectomy had significantly less climacturia events after the use of pelvic floor exercises compared with those who had surgery and did not participate in pelvic floor exercises ($P = 0.004$)[172]. In addition to pelvic floor exercises, blood flow restriction might help decrease climacturia. Penile constriction rings (cock rings) work in a similar manner to VEDs by preventing blood flow out of the penile vasculature. They can be a helpful intervention for patients with mild erectile difficulties, increase pleasure during orgasm[48], and help to reduce symptoms of climacturia[173].

Constriction bands have been investigated for treatment in the general population for patients with climacturia after radical prostatectomy. In a study of 14 men who underwent radical prostatectomy, the addition of a cock ring resulted in a reduction of the frequency of climacturia at 6 months — in fact, 48% of patients experienced no climacturia with use of a cock ring at 6 months after surgery[173]. Notably, cock rings should not be left on for more than 20 min (ref. 48).

Surgical management is another intervention that can be used to help to alleviate climacturia. In a cohort of patients who had undergone radical prostatectomy, patients who received an artificial urinary sphincter or sling placement had an improvement in sexual urinary symptoms and QoL[174]. More recently a mini-jupette, a sling placed and sutured over the urethra, has been used to help climacturia[175]. In a cohort of 38 patients with ED, a mini-jupette was placed and, among 30 patients who had previously reported climacturia, 92.8% noticed an improvement in symptoms[176].

Treatment of orgasm changes

Hardly any studies have identified possible treatments for issues with orgasm (Table 1). In the general population, tamsulosin might help with dysorgasmia following radical prostatectomy and, in one study, dysorgasmia pain improved in 77% of patients after tamsulosin initiation[105]. In a retrospective study of 131 men in the general population with orgasm disorders, cabergoline — a potent dopamine D_2 receptor agonist and prolactin inhibitor — helped to improve dysorgasmia. A subset of men in this population had previously undergone and responded positively to the treatment[177]. However, more studies are required to understand how to restore orgasms in SMM after prostate cancer treatment, especially in patients participating as the receptive partner in RAI.

Receptive anal intercourse rehabilitation

Understanding how other sexual assistive devices such as vibrators, dildos, lubricants, might help SMM prostate cancer survivors' problematic RAI, including anodyspareunia, remains an unmet need (Table 1). Ussher et al. observed that SMM are more likely to use vibrators and

dildos than heterosexual men (36% versus 16%, $P < 0.001$)[158]. Moreover, the *Restore*-1 study identified that although erectile-enhancing drugs, pelvic floor exercises, penile injections and vacuum pumps were the most commonly discussed treatment options with SMM, in practice surgical implants, referral to a sexual counsellor and the use of dildos, butt plugs or anal dilators received higher satisfaction ratings among SMM prostate cancer survivors. This discrepancy highlights the critical need to investigate ways to restore pleasurable RAI[178].

Treatment for other cancers, such as cervical cancer, have demonstrated that sexual devices, including dilators and vibrators, can assist in sexual rehabilitation in patients with reduced sensation or arousal following treatment. In a pilot study of 15 patients with cervical cancer, a clitoral therapy device significantly improved sexual desire, arousal, orgasm, sexual satisfaction and decreased associated pain, with an increase in Female Sexual Function Index score from 17 to 29.4 after 3 months of treatment (maximum score of 36; $P < 0.001$). Gynaecological examinations revealed an improvement in vaginal elasticity and mucosal colour, a decrease in bleeding and ulceration, and an increase in moisture[179]. Additionally, vaginal dilators are commonly used after pelvic cancer therapy to prevent stenosis and stretch the vagina[180].

Like vaginal dilators, anal dilators might be useful for SMM who have survived prostate cancer and who are receiving radiation. Acutely, radiation can cause irritation, pain and friability owing to inflammation[181]. As these changes are mediated by the inflammatory response, fibromuscular tissue and adhesions can develop and lead to anal stenosis[182] (Fig. 4b). To help shape the anal canal and prevent anal stenosis, anal dilators can be useful after radiation treatment[183–185]. The use of dilators can prevent the formation of scar tissue and help to break down existing scar tissue[183–185], which will in turn help the anus and rectum to become more elastic[186,187]. Studies are needed to investigate the feasibility and outcome of anal dilators to help mitigate anodyspareunia in SMM with prostate cancer.

Prostate massage vibrators might be a useful recommendation for sexual dysfunction restoration in SMM after prostate cancer. Prostate massage vibrators can help men to achieve orgasm via stimulation of the prostate gland and, even if the prostate is removed or damaged, the surrounding sensory nerves might be stimulated and enhanced by a prostate massage vibrator. In the general population, prostate massage vibrators can alleviate overall prostate pain: two studies including a total of 115 participants showed a statistically significant decrease in prostatic pain score with prostate massage vibrators compared with no intervention[188,189]. Thus, these massagers might be a useful intervention for SMM with prostate cancer experiencing problematic RAI, although more studies are required to confirm their benefit. These interventions to help restore and preserve pleasurable RAI might help SMM who have survived prostate cancer to preserve their role-in-sex identity in RAI.

Poppers. Of important note to clinicians is the recreational use of alkyl nitrites (poppers) in the SMM community[190]. Poppers are inhalants used to circumvent anodyspareunia via the upregulation of cyclic guanosine monophosphate (cGMP), which promotes relaxation of musculature, including the anal sphincters, assisting with accommodation of a partner's penis[191,192]. One study reported that ~46% of 1,745 SMM had used alkyl nitrites in the last 6 months, primarily to facilitate penetration[193]. Inquiring about and counselling patients on the use of poppers are essential when prescribing a PDE5 inhibitor (such as sildenafil or tadalafil), as the combination of these drugs can cause haemodynamic instability, hypotension and syncope[191] (Fig. 5).

Maintaining sexual health

In addition to discussing treatment options, treatment outcomes and interventions for treatment-related toxicity at consultation, follow-up appointments are important to monitor the toxic effects of treatment. Within the SMM community specifically, following up on aspects relevant to RAI, in addition to erectile function, is essential.

Questionnaires to monitor toxicity

Currently, many centres monitor the toxic effects of prostate cancer treatment using standardized questionnaires, including the Male Sexual Health Questionnaire (MSHQ)[194], EPIC[195], IIEF[196], and Sexual Health Inventory for Men (SHIM), an abbreviated version of the IIEF (IIEF-5)[197]. However, these questionnaires focus on erectile function necessary for vaginal intercourse and omit information related to anal intercourse, neglecting the needs of many SMM[198]. Additionally, these questionnaires were developed in cohorts with uniform sexual orientation and gender representation, limiting the validity and usefulness within a sexually diverse patient population[198]. The IIEF was modified to IIEF-MSM for HIV-positive SMM, and this version contains information relevant to insertive and receptive anal intercourse, but still focuses on erectile function[199]. Additionally, the score was developed for the HIV-positive population and has not been validated among patients with prostate cancer who might experience different sexual toxicities from people living with HIV.

However, new questionnaires are being developed with more inclusive questions to address the needs of SMM. In a group of 53 SMM who had undergone prostate cancer treatment, 64% reported a belief that the prostate is a source of sexual pleasure ($P < 0.0001$) and 53% felt that measuring sexual satisfaction after receptive anal intercourse is important ($P < 0.01$)[200]. A new questionnaire created in 2022 consists of 13 domains, including libido, ejaculation, erection, orgasm, receptive and/or insertive anal intercourse, masturbation, oral sex, urinary incontinence or climacturia, and other general sexual questions encompassing a wider range of sexual practices[198]. This questionnaire covers the broader SMM sexual experience; however, further analysis is necessary for its validation[198]. Another inclusive QoL questionnaire for SMM called the Sexual Minorities and Prostate Cancer Scale (SMACS) was developed using patient data from the *Restore*-2 study[51,96,201,202]. The questionnaire contains three sections — behaviour/desire, problems and role-in-sex — as well as five validated subscales — sexual satisfaction, sexual confidence, frequency of issues, urinary incontinence in sex and problematic receptive anal intercourse. The scale is reliable and can be used in conjunction with other existing scales. These questionnaires must be implemented into daily clinical practice and research.

Receptive anal intercourse resumption after treatment

Men who engage in RAI ('bottoms'), must be counselled on the safe resumption of RAI following treatment. The UK has developed guidance based on a panel of 15 clinical oncologists and 11 urologists using a modified Delphi technique to understand the timing for when patients can resume RAI[203]. However, no clear consensus was reached for many of the interventions, and further research is required to define the time interval necessary before intercourse can safely be resumed. Even so, 91% of panel members agreed that patients should refrain from RAI after surgery, which allows the vesicourethral anastomosis to heal and reduces the risk of leakage and urinary incontinence. Additionally, radical prostatectomy might weaken the rectal wall, leaving it susceptible to trauma from receptive anal intercourse, which could prolong recovery or cause perforation.

Glossary

Anodyspareunia
Painful receptive anal intercourse.

Bottom
The receptive partner in anal intercourse; although this term has also been generalized in sexual minority culture to include the receptive partner in oral intercourse.

Neoclitoris
A reconstructed or created clitoris.

Neovagina
A reconstructed or created vagina.

Outercourse
A subjective term usually referring to sexual intimacy and pleasure that does not include penetration.

Poppers
Alkyl nitrites, which are inhalants used to relax anal musculature used for receptive anal intercourse.

Role-in-sex
The role a person identifies with during sexual intercourse (for example, top, bottom, versatile, side).

Sexual and gender minority
Individuals who identify as lesbian, gay, bisexual, transgender, gender diverse, asexual, queer and intersex as well as those who do not but whose sexual orientation, gender identity or reproductive development varies from traditional, societal, cultural or physiological norms.

Sexual identity
Refers to a person's identity more broadly in terms of sexual intercourse and relationships.

Side
A sexual minority man who does not engage in anal intercourse or identify with 'top', 'bottom' or 'vers'.

Top
The insertive partner in anal intercourse; although this term has been generalized in sexual minority culture to also include the insertive partner in oral intercourse.

Vers
Or verse, short for 'versatile', a person who engages in both the receptive and the insertive role in intercourse.

Thus, the recommended time to avoid RAI after surgery is 2 weeks. Additionally, 73% of panel members agreed that patients should abstain from intercourse after EBRT, providing time to allow the inflammation from radiation to subside. Without allowing sufficient time to heal, trauma to this area could exacerbate inflammation and radiation-induced proctitis. Patients should refrain from anal intercourse for 6 weeks following EBRT. All panellists recommended abstinence from RAI after brachytherapy (both high-dose-rate (HDR) and low-dose-rate (LDR)). Following HDR brachytherapy, patients should abstain for 2 months and following LDR brachytherapy patients should abstain from anal intercourse for 1–2 months[203]. This period allows prostatic and rectal inflammation to subside and decreases potential exposure to the patient's partner.

Similarly, a study investigating abstention periods for RAI and sustained cuddling ('spooning') after LDR brachytherapy concluded that patients treated with ^{125}I should avoid spooning for 2 months, whereas those treated with ^{103}Pd do not need to avoid spooning after treatment. The authors of this study also recommend that patients should avoid RAI for 6 months after ^{125}I seed placement and for 2 months after ^{103}Pd seed placement[204]. The results of this study differ from the UK panel consensus, demonstrating that further research is needed. Additionally, as ^{103}Pd can be given in combination with EBRT, patients should be encouraged to avoid anal intercourse for 2 months after the last day of treatment with brachytherapy or EBRT (Fig. 2).

Sexual practices after treatment

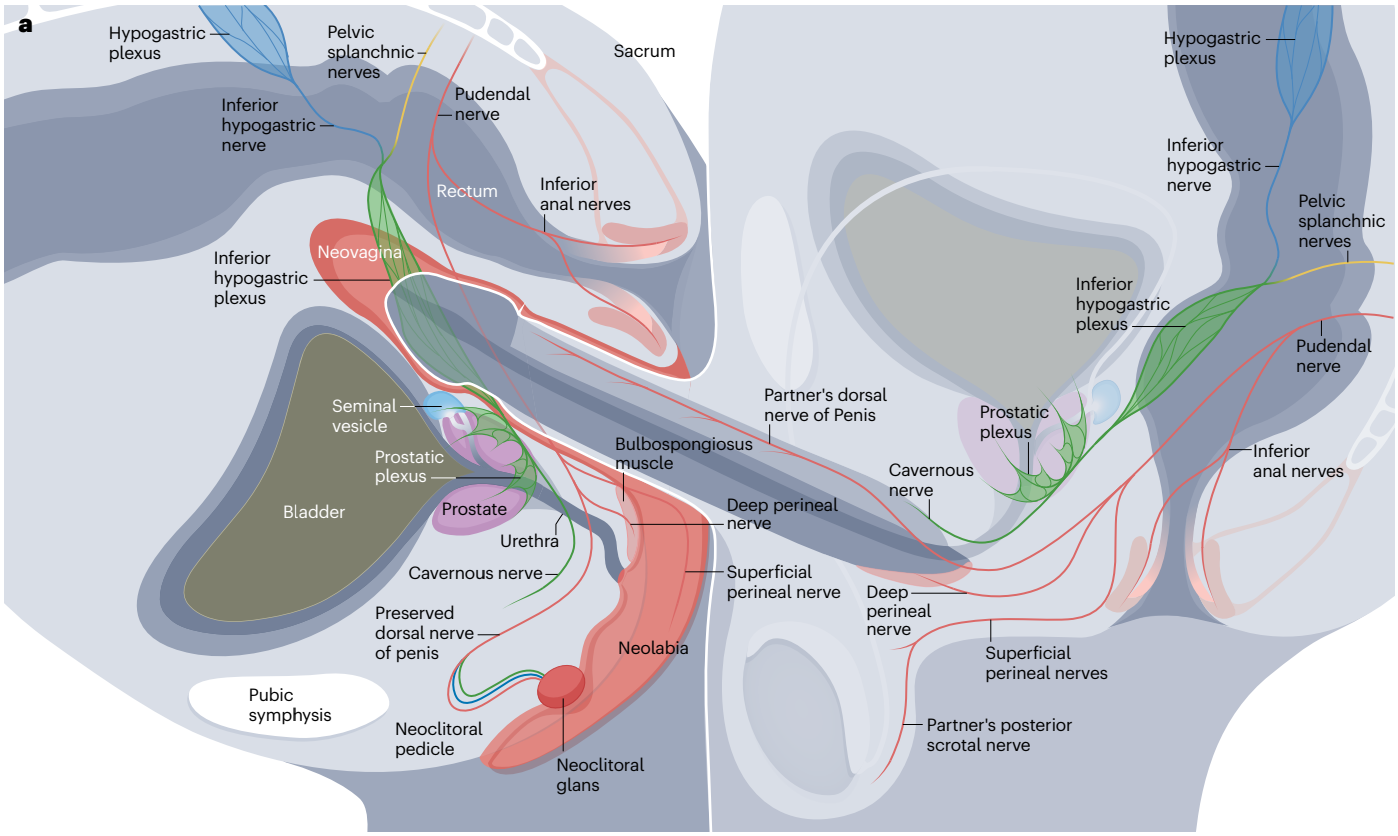
Patients should be counselled on common sexual practices to be avoided after treatment during initial consultation and again after treatment. For example, in any male receiving LDR brachytherapy, a condom should be used to avoid ejecting a radioactive seed into their partner. However, specific recommendations should be made to men who participate in RAI, as anal intercourse and vaginal intercourse are associated with different sets of risks. Anal mucosa is less compliant and accommodating than vaginal mucosa, resulting in a higher risk of contracting sexually transmitted infections (STIs) and/or HIV during anal intercourse owing to mucosal tear and damage[205–207]. Condom use is already uncommon within the SMM community — in a cohort of 121 SMM with prostate cancer, ~22% of participants (n = 26) reported unprotected insertive anal intercourse in the prior 3 months[74]. Thus, health-care providers must counsel patients on condom use following prostate cancer treatment to decrease the risk of HIV and/or STI acquisition (Fig. 2).

Both the *Restore*-1 (ref. 74) and *Restore*-2 (ref. 202) studies showed that patients became infected with HIV or other STIs after prostate cancer treatment. In *Restore*-2 (ref. 202), ~11.4% of patients became infected with an STI, including syphilis (4.3%), gonorrhoea (2.8%), chlamydia (2.5%) and HIV (1%, n = 4)[202]. Similarly, in *Restore*-1 (ref. 74), 3 of the 171 at-risk patients (1.8%) became infected with HIV following prostate cancer treatment. Risk factors for HIV and STI acquisition after prostate cancer therapy can include changes in role-in-sex (for example, a switch from top to bottom can increase the risk of STIs and HIV)[74,135], varied relationships and reduced condom use[208]. Thus, providers must discuss safe sex practices including HIV and STI risk, the importance of condoms, and HIV pre-exposure prophylaxis (PrEP) with SMM diagnosed with prostate cancer (Fig. 4).

Providers might also want to discuss the use of an appropriate lubricant to help with RAI after prostate cancer treatment, as it can help with accommodation of the partner's penis into the rectum during anal intercourse and can help to intensify and prolong sexual intercourse[209]. For RAI, silicone-based lubricants have the advantage of persisting on the mucous membranes and, after treatment, silicone lubricant can adhere to scar tissue, reducing shear stress on the scar during penetration[48,209].

In addition to lubricant, counselling SMM on safe RAI preparation is also recommended after prostate cancer treatment. Given the presence of faecal matter in the rectum, many patients will cleanse the rectal vault with douches or enemas before engaging in RAI[210]. In fact, in a large survey study of 5,000 SMM, ~88% of patients who have RAI practice anal douching[211]. Men might use regular water, soapy water, salt water, or commercial products such as saline solution, sodium phosphates, mineral oils/glycerin and laxatives[211].

However, douching can damage the rectal lining and cause bleeding, which in turn leads to an increased risk of HIV and STI infection[212,213]. Additionally, douching can alter the rectal microbiome[213], which is essential for maintaining the rectal epithelium and host immunity[214], as well as preventing surgical and procedural complications[215]. Furthermore, the microbiome has been implicated in acute radiation proctitis. Synbiotics or mixtures of probiotics (gut bacteria) and prebiotics (non-digestible compounds for probiotic growth assistance), have been shown to help reduce the risk of acute proctitis[216]. Future research is needed to understand how to safely cleanse before RAI as well as the role of the microbiome in mediating toxicity. Although research is ongoing[217], patients must be counselled on the risks of vigorous anal douching following prostate cancer treatment and to consider


a
Hypogastric plexus
Pelvic splanchnic nerves
Sacrum
Pudendal nerve
Inferior hypogastric nerve
Rectum
Inferior anal nerves
Neovagina
Inferior hypogastric plexus
Seminal vesicle
Prostatic plexus
Bladder
Prostate
Urethra
Cavernous nerve
Preserved dorsal nerve of penis
Pubic symphysis
Neoclitoral pedicle
Neoclitoral glans
Bulbospongiosus muscle
Partner's dorsal nerve of Penis
Deep perineal nerve
Superficial perineal nerve
Neolabia
Hypogastric plexus
Inferior hypogastric nerve
Pelvic splanchnic nerves
Inferior hypogastric plexus
Pudendal nerve
Prostatic plexus
Cavernous nerve
Inferior anal nerves
Deep perineal nerve
Superficial perineal nerves
Partner's posterior scrotal nerve

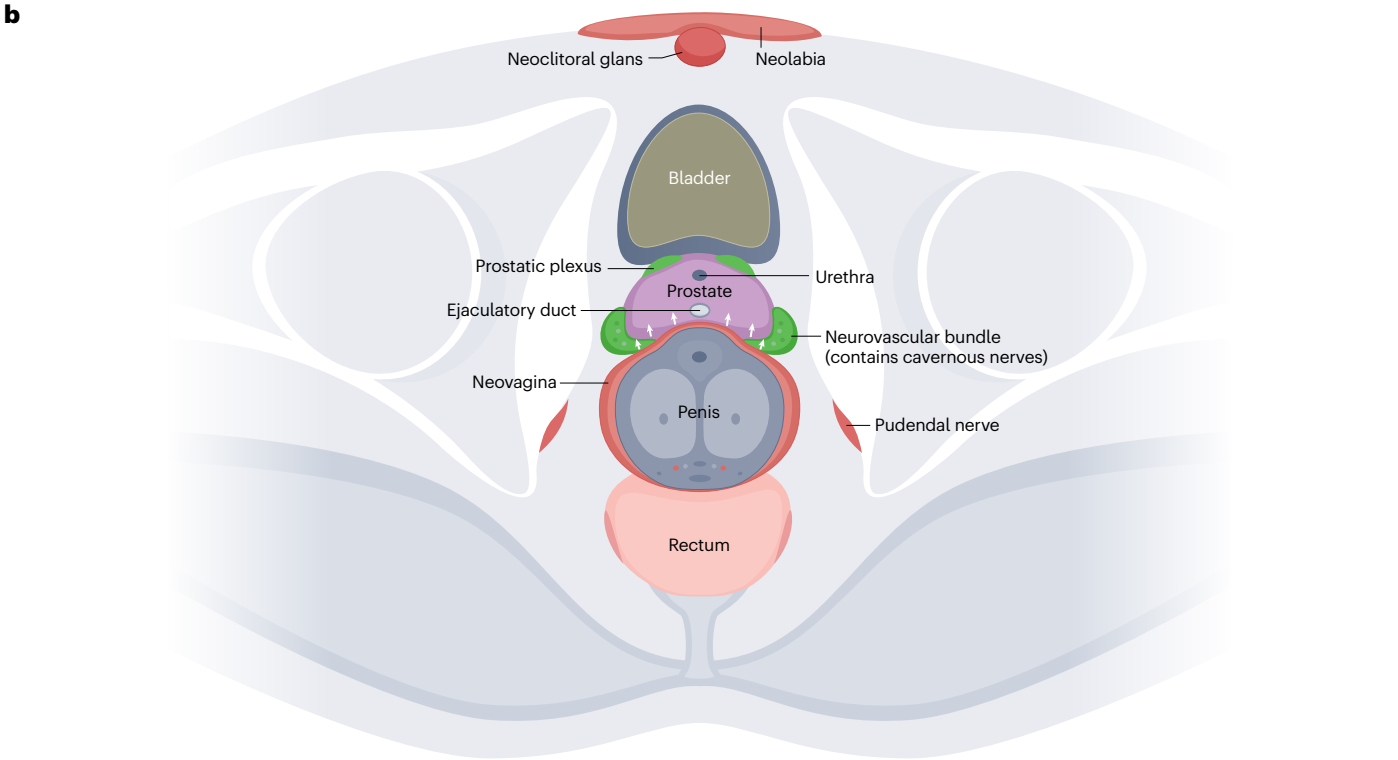

b
Neoclitoral glans
Neolabia
Bladder
Prostatic plexus
Urethra
Prostate
Ejaculatory duct
Neurovascular bundle (contains cavernous nerves)
Neovagina
Penis
Pudendal nerve
Rectum

Fig. 7 | Anatomy of pleasurable neovaginal intercourse. a, Representative sagittal image of pleasurable neovaginal intercourse, gender minorities are a heterogenous cohort with a range of anatomy with a diverse sexual script. People who have undergone feminizing pelvic affirmation surgery are likely to have a neoclitoris with or without a neovagina (as a clitoroplasty can be performed without accompanying vaginoplasty, known as zero-depth vaginoplasty). During clitoroplasty, a sensate neoclitoris is reconstructed and consists of the neoclitoris glans, tissue from the glans penis, and the neoclitoris pedicle, preserved neurovasculature containing the dorsal penile nerves[20,222]. **b**, Representative axial image of pleasurable receptive neovaginal intercourse. The prostate is located anteriorly to the neovagina, analogous to its location in receptive anal intercourse in cisgender men. During receptive neovaginal intercourse, a partner's penis and body can stimulate the surrounding nerves of the neovagina, prostate and neoclitoris, eliciting pleasure and orgasm for both partners.

alternatives, including high-fibre diets with external gentle shower rinsing, before intercourse.

Gender minorities with prostate cancer

Although research is emerging regarding SMM with prostate cancer, little information exists regarding gender minority patients with prostate cancer, including TGW and trans feminine people in general, or people who are recorded male at birth with feminine gender identities. Notably, issues surrounding gender minorities can be subsumed within discussions of sexual identity, meaning that this population's specific needs might become neglected.

Gender minorities are a diverse cohort

Contributing to the nuance of this population is that gender minorities are a heterogenous cohort with a range of anatomy and hormonal milieu with a diverse sexual script. Physicians might care for TGW who are just beginning their use of GAHT or for those who have been using GAHT for extended periods of time. Additionally, physicians might care for TGW who have undergone, plan to undergo, do not plan to undergo, or are undecided about receiving feminizing gender-affirming genital reconstruction, or gender-affirming surgery (GAS). These various factors contribute to the individual patient profile and the resultant need for personalized treatment discussions for TGW with prostate cancer. Health-care professionals must be sensitive and aware of the range of transgender experiences and presentations when managing TGW with prostate cancer, as 48% of transgender patients avoid or delay care owing to medical insensitivity[218].

Epidemiology and presentation of prostate cancer in gender minorities

With a lifetime prevalence of 12.1%, prostate cancer is the most common non-dermatological malignancy in cisgender males, including SMM[1]; however, the prevalence and incidence of prostate cancer in TGW is likely to be significantly lower[14,219]. One of the largest studies to date — a cohort study of 2,281 TGW in the Netherlands — concluded that women receiving androgen deprivation therapy and oestrogens were at a substantially lower risk of prostate cancer than the general male population[13]. The low incidence and prevalence of prostate cancer in TGW is multifactorial: contributory factors might include barriers to care for these patients[220], the use of oestrogen-supplementing GAHT, which might be protective against prostate cancer[221], and lower detectable PSA, as well as younger overall mortality for TGW compared with cisgender men[222,223].

Notably, despite a lower relative incidence and prevalence, studies suggest that prostate cancer might have a more aggressive presentation in TGW, which could also be due to late presentation in these patients. A non-systematic review of the literature identified 10 case reports of TGW with prostate cancer and found that 6 patients presented with metastatic disease, 3 with local or locally advanced disease and 1 with unknown disease[224]. In TGW, the development of prostate cancer has been debated, as oestrogen–testosterone balance has a role in prostate cancer development. In TGW, oestrogen is administered to suppress endogenous testosterone levels. This combination has been shown to increase the risk of prostate cancer in rats, with incidence of prostate cancer increasing from 35–40% in rats treated with exogenous testosterone alone to 90–100% in rats treated with combination exogenous testosterone and oestrogen[225,226]. Furthermore, TGW who begin their transition at an older age might be at a greater risk of prostate cancer than those who transitioned at a younger age, who would presumably have had prolonged exposure to oestrogen therapy.

Prostate cancer in TGW might develop in the setting of medical or surgical castration from GAHT or feminizing GAS; thus, prostate cancer in transgender patients is likely to be castration resistant[224]. Castration resistance portends worse outcomes in patients with prostate cancer with a median overall survival ranging from 9 to 36 months depending on the extent of metastatic disease[227–230]. Thus, if TGW are at risk of prostate cancer and potentially develop more aggressive castration-resistant disease, the treatment course might need to be more aggressive[231–233], leading to more severe sexual health-related side effects. To help to improve disease and survival outcome as well as avoid iatrogenic treatment-related sexual dysfunction for this patient population, prostate cancer screening, such as the PSA cut-off point, should likely be refined and adjusted for TGW[234].

Sexual health and dysfunction in gender minorities

Little information exists regarding the management of sexual dysfunction in TGW with prostate cancer. Several important factors should be considered when managing sexual dysfunction in TGW in general. A systematic review evaluating sexual dysfunction in transgender people identified that feminizing GAHT might decrease libido in the short term, whereas feminizing genital reconstruction surgery can increase libido and arousal[235]. However, decreased libido might not be a concern for TGW and, in one study with 45% of patients experiencing decreased libido, only 20% reported it as a dysfunction whereas 25% reported that it was not causing distress[236].

The prostate and receptive intercourse after feminizing pelvic GAS. TGW might engage in pleasurable receptive anal and/or neovaginal intercourse. An individual's decision to undergo genital GAS as well as the type of genital GAS will determine the spatial relationship of the prostate with other pelvic anatomy and its subsequent role in facilitating pleasure during receptive intercourse (Fig. 7). For example, a patient who has undergone zero-depth vaginoplasty[237] might engage in pleasurable RAI in which the prostate will play an important role in facilitating pleasure and orgasm (Fig. 1 and Fig. 2), whereas a patient who has undergone a full-depth vaginoplasty might engage in both pleasurable receptive neovaginal and anal intercourse, with the prostate facilitating pleasure and orgasm in receptive neovaginal intercourse[238,239] (Fig. 2 and Fig. 7).

The standard procedure for neovaginal creation in feminizing genital GAS is penile inversion vaginoplasty, and the resulting

neovagina may not self-lubricate[240]. In cases where penoscrotal tissue is insufficient or when penile inversion has failed, bowel segment[241] or peritoneal flap[242] vaginoplasty can be performed. The neovagina is constructed anterior to the rectoprostatic fascia located between the prostate and rectum and, thus, analogous to the location and role of the prostate in RAI, the prostate is located anterior to the neovagina[237]. Moreover, the preserved neurovascular bundle remains posterolateral to the prostate, and likely both the prostate and surrounding neurovasculature contribute to orgasm and pleasure in receptive neovaginal intercourse[239]. Moreover, during feminizing genital GAS, the pelvic floor muscles are dissected to allow for neovaginal creation with the resultant ischiocavernosus muscles located laterally to the neovagina in addition to the bulbospongiosus muscle located anteriorly to the neovagina in a similar relationship to the urethra[21,237].

Additionally, a reconstructed neurovascular pedicle flap for neoclitoris sensation containing the preserved dorsal nerve of the penis as well as a reconstructed neolabia from scrotal and penile skin, with the dorsal nerve of the penis and posterior scrotal nerve innervation being sensate structures that can facilitate pleasurable intercourse for patients with a zero-depth and full-depth neovaginas[238,239].

Direct stimulation of the prostate, located anteriorly to the neovagina, and the surrounding nerves by a penis, as well as stimulation of the neoclitoris and neolabia, will elicit afferent sensory impulses through branches of the pudendal, pelvic splanchnic and hypogastric nerve networks with reflex efferent motor impulses causing contraction of the pelvic floor muscles — the bulbospongiosus and ischiocavernosus muscles[238] (Fig. 2b). This will lead to resultant pressure on the insertive partner's penis, which in turn will lead to increased erectile firmness and pleasure for the insertive partner[35]. Through these neural pathways, both partners will have pleasurable intercourse through sustained sensory neurocircuits that can lead to an orgasm. Overall, TGW report more sexual encounters after GAHT and GAS, suggesting that neoclitoral and neovaginal creation increase confidence, comfort[20,243] and happiness[235,244].

When considering sexual dysfunction in TGW with prostate cancer, sexual toxicities must be approached differently compared with sexual dysfunction in SMM with prostate cancer. For example, TGW might experience dyspareunia through neovaginal intercourse[20] and/or anodyspareunia through anal intercourse. Additionally, within this population, questions and questionnaires must be customized, as TGW might experience orgasm and sexual arousal from the neoclitoris, rather than, or in addition to, the prostate through receptive neovaginal or anal intercourse[245] (Fig. 7a,b). It is important to understand the anatomy and nerves responsible for pleasurable neovaginal and anal intercourse (Fig. 2) when counselling TGW with prostate cancer as this can help to facilitate treatment discussions and recommendations (Fig. 6).

Recognizing sexual and anatomical diversity among transgender women. Understanding the diversity of sexuality and anatomy among trans feminine individuals is important. A physician might make the well-intentioned assumption that a transgender woman would have a similar sexual script to other women and that they would not want to involve their penis as part of their sexual pleasure; however, some TGW might wish to use their penis in a range of sexual activities, including being insertive partners[246,247].

Treatment-related sexual dysfunction with gender minorities

TGW must be counselled regarding sexual dysfunction and treatment options for prostate cancer at consultation and at follow-up appointments (Fig. 6). Managing sexual dysfunction in transgender patients with prostate cancer depends on whether the patient has already undergone, or might later undergo, pelvic GAS[224]. For those who have not undergone GAS, discussion must include the patient's desire to have GAS surgery in the future. If a TGW wishes to pursue GAS after prostate cancer treatment, further discussions are necessary before definitive cancer management. Analogous to breast reconstruction following breast cancer management, multidisciplinary discussion must include the surgical oncologist, radiation oncologist and reconstructive surgeon[248]. A more nuanced and detailed conversation should then ensue regarding sexual practices and relevant toxicities. Careful consideration should be given to safety and effectiveness of the cancer treatment as well as the feasibility and cosmesis of future pelvic GAS. This conversation will enable fully informed treatment decisions. For example, although a labiaplasty might be feasible after radical prostatectomy, EBRT, or brachytherapy, vaginoplasty after treatment might carry an increased risk of fistula formation, urethral meatus stenosis and incontinence[224].

For TGW who have already undergone GAS, prostate cancer treatment can be complex, as radical prostatectomy can lead to fistula formation and EBRT and brachytherapy can lead to neovaginal stenosis requiring rehabilitation with dilators[180]. As such, treating surgeons and radiation oncologists must be aware of anatomical changes[249] and evolving technologies. For example, a radiation oncologist might consider using neovaginal hydrogel spacing to limit the dose to the neovagina, similar to using a hydrogel spacer to limit dose to the rectum in cisgender men during prostate cancer treatment[250]. In addition, as many patients might be surgically or chemically castrated, management might follow castration-resistant prostate cancer guidelines[231–233]. Although decisions in this population focus on disease eradication, as treatments for castration-resistant prostate cancer advance[251], conversations surrounding sexual health might move to the forefront. Further research is necessary to understand how treatment should be modified and, ideally, personalized for TGW with prostate cancer.

Conclusions

Data regarding the effects of prostate cancer therapies on sexual health outcomes in SMM and TGW are scarce. Existing studies illustrate differences in the sexual health outcomes of SMM and TGW compared with cisgender heterosexual men. Treatment-related sexual dysfunctions experienced by SMM include problematic RAI, including anodyspareunia and altered pleasurable sensation, ED, climacturia, anejaculation and changes in penile size and shape. At consultation, patients should be asked about sexual orientation, gender identity and role-in-sex, and patients should be counselled on treatment-related toxic effects tailored to their role-in-sex (top, bottom, versatile, or side). Additionally, physicians should ask gender minority patients about hormones and pelvic GAS. Understanding the patient as a whole will enable informed patient conversations at consultation and shared decision-making, when appropriate, for prostate cancer treatment selection.

Although the roles of the prostate and the surrounding neurovasculature are well known in pleasurable receptive anal intercourse and are recognized in neovaginal intercourse; more research is needed to understand the pathophysiology and mechanism of damage to surrounding anatomical structures from prostate cancer treatment and the resultant sexual dysfunction. Understanding the mechanism of treatment-related damage to the prostate and surrounding structures will enable researchers to develop novel ways of alleviating treatment-related damage to the prostate and surrounding tissues as well as,

potentially, restore prostate sensation. These advances would help to further correct the inequities in scientific and biomedical research.

Sexual health QoL questionnaires for patients with prostate cancer are beginning to incorporate domains and questions relevant to SMM patients, especially related to RAI. Information from more inclusive questionnaires will empower clinicians with evidence when discussing anatomy, physiology and pathophysiology of organ function related to sexual pleasure in SMM and TGW with prostate cancer. Additionally, these data could empower the sexual and gender minority community to advocate for more equitable care and further research. Further information from validated questionnaires on sexual dysfunction and research regarding the ways in which prostate cancer treatments affect SMM and TGW would also enable scientific advances in technologies to prevent and mitigate these toxicities.

Prostate cancer providers should commit to understanding the management of sexual health and dysfunction in sexual and gender minorities following prostate cancer treatment. Urologists, radiation oncologists, medical oncologists and clinical oncologists must move beyond a narrow definition of sexual activity and sexual pleasure focused on heterosexual intercourse and reproductive ability in patients with prostate cancer. Health-care providers should incorporate the functional, physiological and anatomical basis of sexual pleasure in all patients with prostate cancer, regardless of sexual or gender identity.

Published online: 22 May 2023

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Acknowledgements
Research reported in this publication was supported by the Office of The Director, National Institutes of Health under Award Number DP5OD031876. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions
D.R.D., B.R.S.R. and D.C.M. researched data for the article. D.R.D. wrote the manuscript. All authors made a substantial contribution to the discussion of content and reviewed and edited the article before submission.

Competing interests
M.D.G. declares research funding from Bristol Myers Squibb, Novartis, Dendreon, AstraZeneca, Merck and Genentech and is a paid advisory board consultant for Bristol Myers Squibb, Merck, Genentech, AstraZeneca, Pfizer, EMD Serono, SeaGen, Janssen, Numab, Dragonfly, GlaxoSmithKline, Basilea, UroGen, Rappta Therapeutics, Alligator, Silverback, Fujifilm and Curis. The other authors declare no competing interests.

Additional information
Peer review information *Nature Reviews Urology* thanks Findlay Macaskill and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

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