

Supportive medications and interventions received by prostate cancer survivors: results from the PiCTure study

Frances J Drummond, PhD,^{a*} Anna T Gavin, MB, BCH, BAO, MSc,^b and Linda Sharp, PhD^c

^aDepartment of Epidemiology and Public Health, University College Cork, Cork, Ireland; ^bNorthern Ireland Cancer Registry, Queens University Belfast, Belfast, United Kingdom; and ^cNewcastle University, Newcastle-upon-Tyne, United Kingdom

Background Prostate cancer treatments are associated with after-effects that adversely affect men's health-related quality of life long into survivorship.

Objective To investigate the use of supportive medications and interventions in a population-based study of prostate cancer survivors

Methods A cross-sectional postal questionnaire was sent to 6,559 prostate cancer survivors (ICD10 C61) who were 2-18 years post diagnosis, identified through population-based cancer registries in Ireland. Information was sought on after-effects that had been experienced at any time after treatment and any medication or intervention received to alleviate symptoms. The Decisional Regret Scale was used to measure survivors' regret over their entire treatment experience. Chi-square tests were used to investigate variations in receipt of these medications or interventions.

Results In a population-based study of prostate cancer survivors (n = 3,364), use of supportive medications/interventions was low. Younger men more often used medications/interventions for impotence and depression, older men for bowel problems and incontinence. 35.6% of survivors reported any decisional regret, significantly higher among those taking supportive medications/interventions for impotence.

Limitations The study is descriptive, survivors were not asked if the supportive care received matched their needs and whether they were satisfied with their supportive care.

Conclusions This study documents, for the first time, population-based data on patient-reported use of supportive medications and interventions to alleviate adverse effects of prostate cancer and its treatment. Increased use of medications/interventions for treatment after-effects could improve survivor quality of life.

Funding/sponsorship Health Research Board (HRA_HSR/2010/17) and Prostate Cancer UK (NI09-03 & NI-PG13-001). Supplemental funding, NI Public Health Agency and National Cancer Control Programme in the RoI.

Prostate cancer treatments are associated with various physical after-effects, including urinary, sexual, and bowel symptoms.¹ These after-effects can have an impact on survivors' health-related quality of life (HRQoL).² Pharmaceutical and surgical interventions are available to manage or ameliorate many of these after-effects (eg, sildenafil citrate taken during and after radiotherapy improves sexual function),³ and their receipt has a positive impact on HRQoL.⁴

However, studies of clinicians suggest that such interventions may not be used widely.^{5,6} Patient-reported data on this topic is lacking. Therefore, we investigated the use of supportive medications and interventions in this population-based study of prostate cancer survivors.

Methods

The PiCTure (Prostate Cancer Treatment, *Your Experience*) study methods have been described elsewhere.⁷ Briefly, 6,559 prostate cancer survivors 2-15 years after diagnosis (diagnosed during January 1, 1995-March 31, 2010, and alive in November 2011), identified from population-based cancer registries in the Republic of Ireland and Northern Ireland, were invited to complete a postal survey. Information was sought on after-effects (incontinence, impotence, gynaecomastia, hot flashes/sweats, bowel problems, depression) that had been experienced at any time after treatment. For each after-effect, men were asked if they had received any medication or interventions to alleviate symptoms, and, if so, what they had received; examples of common interven-

Accepted for publication November 21, 2017. Correspondence: Frances J Drummond, PhD; francesjdrummond22@gmail.com. Disclosures: Dr Sharp has previously received an unrestricted grant from Sanofi-Aventis to investigate treatment patterns in prostate cancer. Drs Drummond and Gavin report no disclosures or conflicts of interest. JCSO 2017;15(6):e309-e313. ©2017 Frontline Medical Communications. doi: <https://doi.org/10.12788/jcso.0384>

TABLE 1 Responders and nonresponders were compared by chi-squared tests for each characteristic

Characteristic	All men eligible to be sent a questionnaire (N = 6,559)	Responders (n = 3,348)	Nonresponders (n = 3,299)
Age at diagnosis, y			
<60	1,329 (20)	799 (24)	546 (17)
60-69	2,939 (45)	1,631 (49)	1,345 (41)
≥70	2,291 (35)	918 (27)	1,408 (43)*
Time since diagnosis (years)			
<5	3,101 (47)	1,614 (48)	1,532 (46)
5-10	2,114 (32)	1,075 (32)	1,066 (32)
≥10	1,344 (20)	659 (20)	701 (21)*
Gleason grade			
Low (2-6)	913 (14)	212 (6)	268 (8)
Medium (7-8)	3,658 (55)	2,186 (65)	1,472 (45)
High (8-10)	1,072 (16)	625 (19)	447 (13)
Unknown	1,437 (22)	325 (10)	1,112 (34)*
Stage			
I	111 (2)	110 (3)	160 (5)
II	3,706 (57)	2,015 (60)	1,582 (48)
III	947 (14)	612 (18)	348 (10)
IV	267 (4.0)	141 (4.2)	124 (4)
Unknown	1,530 (23%)	470 (14%)	1,085 (33%)*
Jurisdiction			
Republic of Ireland	4,537 (68)	2,338 (70)	2,203 (67)
Northern Ireland	2,106 (32)	1,010 (30)	1,096 (33)*

* $P < .001$

tions were provided. Men were also asked if they had been told they may become infertile and, if so, whether they had preserved their sperm. The Decisional Regret Scale⁸ was used to measure survivors' regret over their entire treatment experience. This 5-item scale, rated on a 5-point Likert scale from 1 (strongly agree) to 5 (strongly disagree) was summed and standardized to a value of 0-100, with higher scores reflecting higher levels of decisional regret.⁸ This scale has good psychometric properties⁸ and strong reliability in our sample (Cronbach's alpha = 0.85). Responders were categorized as having any regret (score ≥1) or no regret (score = 0).

The number of men who reported receiving an intervention was expressed as a percentage of survey responders and of men who reported ever having the relevant after-effect. Chi-square tests were used to investigate variations in receipt by: age at diagnosis (≤59, 60-69, ≥70 years); time since diagnosis (≤5, 5-10, >10 years); jurisdiction (Republic of Ireland, or Northern Ireland); and primary treatment(s)

received (radical prostatectomy [RP], external beam radiotherapy [EBRT] with androgen deprivation therapy [ADT], EBRT without ADT, brachytherapy, ADT [without other therapies], and active surveillance/watchful waiting). Among survivors who ever experienced an after-effect, chi-square tests were used to investigate whether the percentage who reported decisional regret differed depending on whether or not they received the relevant supportive intervention.

Ethics approval was from the Irish College of General Practitioners (Republic of Ireland) and the Office for Research Ethics Committee Northern Ireland.

Results

In all, 3,348 survivors participated in the survey (adjusted response rate, 54%). Compared with nonresponders, responders were more often from the Republic of Ireland ($P = .007$), <70 years at diagnosis ($P < .001$), 5-10 years post diagnosis ($P < .001$), with low or medium Gleason grade

TABLE 2 After-effects experienced by prostate cancer survivors and receipt of medications and other interventions

After-effect/ Intervention	Ever experi- enced after- effect, n (%)	Receipt of intervention		Any decisional regret	
		n (%)	% reporting after-effect	% receipt of intervention	% no intervention
Incontinence					
Artificial sphincter	1,253 (37)	70 (2)	6	51	41
Medication (eg, tolterodine)		266 (8)	21	41	42
Impotence					
Medication (eg, sildenafil citrate, tadalafil)	2,351 (70)	666 (20)	28	47	39*
Penile implants/pumps		78 (2)	3	51	41
Alprostadil injections		155 (5)	7	56	41*
Gynaecomastia					
Treatment (eg, tamoxifen, radiotherapy)	624 (19)	78 (2)	13	47	45
Hot flashes/ sweats					
Medication (eg, venlafaxine, paroxetine)	1,348 (40)	105 (3)	8	44	39
Depression					
Medication (eg, fluoxetine)	603 (18)	167 (5)	28	51	46
Bowel problems^b					
Medication (eg, loperamide-simethicone, laxatives)	537 (23)	190 (8)	35	39	43

^aExpressed as a percentage of men who responded to the survey and responders who 'ever' reported experiencing the relevant after-effect; and percentage of men who 'ever' experienced an after-effect and who reported any decisional regret stratified by receipt of the relevant intervention. ^bQuestion asked in the Republic of Ireland only; 2,338 responders.

* $P \leq .001$

(Gleason scores of ≤ 6 [good prognosis] and 7, respectively; $P < .001$), and clinical stage II-IV ($P < .001$; Table 1).

Impotence (70%) was the most commonly reported after-effect, followed by hot flashes/sweats (40%), incontinence (37%), bowel problems (23%), gynaecomastia (19%), and depression (18%; Table 2).

Of responders, 2% received an artificial sphincter, representing 6% of men who ever experienced incontinence post diagnosis (Table 2). This percentage was significantly higher in participants diagnosed longer ago, from the Republic of Ireland, and who received RP (Table 3). Incontinence medication was received by 8% of participants (21% of those who experienced incontinence). Use varied significantly by age, jurisdiction, and treatment. For impotence, medications were more commonly used (20% of participants; 28% with impotence) than were injections (5% and 7%, respectively) or penile implants/pumps (2% and 3%, respectively). Use of all 3 types of intervention was highest in men who had RP; injections and implants/pumps were significantly more common among younger men. Of those experiencing gynaecomastia, 13% received interventions; receipt was highest in men who had EBRT with ADT, were <5 years post diagnosis and from Northern Ireland. For hot flashes/sweats, 3% of participants (8% who experienced symptoms) received medications; this was higher in

men who had EBRT. Of those who reported depression, 28% received medication; receipt was highest in younger men and in Northern Ireland. Medication for bowel problems was used by 35% of men who experienced these; use was highest in older men, those diagnosed more recently, and those who had EBRT. Sixty percent of men reported having been told they would become infertile; 11 (0.3% of participants) preserved their sperm, 7 from the Republic of Ireland and 4 from Northern Ireland.

A total of 35.6% of survivors reported any decisional regret. Among survivors who ever had an after-effect, a higher percentage of those who used a supportive intervention reported decisional regret compared with those who did not; this was only statistically significant for those using medication or alprostadil injections for impotence (Table 2).

Discussion

This study documents, for the first time, population-based data on patient-reported use of supportive medications and interventions to alleviate adverse effects of prostate cancer and its treatment. Among survivors who experienced after-effects, use was highest for bowel problems, impotence, and depression, but even for those, only 28%–35% of men took medication. Although it is possible that some survivors

TABLE 3 Receipt of medications and other interventions among prostate cancer survivors, by age at diagnosis, time since diagnosis, jurisdiction and primary treatment(s) received; numbers and percentages expressed as a percentage of survey responders, with significant chi square tests indicated

After-effect/ Intervention, n (%)	Age at diagnosis, y			Time since diagnosis, y			Jurisdiction		Primary treatment(s) received					
	≤59	60-69	≥70	<5	5-10	>10	Rep. of Ireland	N. Ireland	RP	EBRT+ ADT	EBRT- ADT	BT	ADT	AS/ WW
Incontinence														
Artificial sphincter	23 (3)	35 (2)	12 (1)	13 (1)	30 (3)	27 (4)***	59 (3)	11 (1)**	48 (69)	0	17 (25)	1 (1)	2 (3)	2 (3)***
Medication	53 (7)	123 (8)	90 (11)*	130 (9)	89 (9)	47 (8)	201 (10)	65 (7)*	61 (24)	49 (19)	95 (37)	19 (7)	24 (9)	9 (4)*
Impotence														
Medication	297 (25)	235 (25)	134 (24)	288 (24)	231 (25)	128 (23)	483 (24)	164 (23)	406 (62)	79 (12)	118 (18)	35 (5)	7 (1)	8 (1)***
Penile implants/ pumps	41 (6)	33 (2)	5 (1)***	29 (2)	28 (3)	21 (4)	51 (3)	27 (3)	63 (82)	4 (5)	5 (1)	0	1 (1)	1 (1)***
Alprostadil injections	92 (13)	58 (4)	5 (1)***	63 (5)	48 (5)	44 (7)	112 (6)	43 (5)	138 (90)	3 (2)	9 (6)	0	3 (2)	1 (1)***
Gynaecomastia														
Treatment	26 (4)	35 (3)	17 (2)	49 (4)	16 (2)	13 (2)**	12 (1)	66 (7)**	8 (10)	35 (45)	29 (37)	1 (1)	5 (6)	13 (2)***
Hot flashes/ sweats														
Medication	27 (4)	50 (4)	28 (4)	45 (4)	37 (4)	23 (4)	65 (4)	40 (4)	15 (14)	27 (26)	41 (39)	2 (2)	37 (4)	0***
Depression														
Medication	59 (8)	77 (5)	31 (4)***	70 (5)	67 (6)	30 (5)	96 (5)	71 (7)**	57 (35)	28 (17)	57 (35)	1 (1)	17 (10)	5 (3)
Bowel problems ^a														
Medication	32 (7)	83 (9)	75 (15)***	93 (13)	61 (9)	36 (8)**	—	—	47 (25)	31 (16)	86 (46)	5 (3)	18 (10)	1 (1)***

ADT, androgen deprivation therapy; AS, active surveillance; BT, brachytherapy; EBRT, external beam radiotherapy; RP, radical prostatectomy; WW, watchful waiting

^aQuestion asked in the Republic of Ireland only; 2,338 responders.

* $P < .01$; ** $P < .005$; *** $P < .001$

declined medications or other interventions, these low levels of use strongly suggest that not all survivors who might benefit from supports receive them.

There was little evidence that utilisation was higher in survivors diagnosed more recently. This suggests that, although the number of prostate cancer survivors has grown, and there is greater focus on survivorship issues in clinical practice, this has not translated into more men receiving support to manage after-effects. Care is needed to ensure that the newer models of post-cancer follow-up being considered or adopted in many settings,⁹ do not exacerbate this issue.

As expected, patterns of utilisation varied by treatment(s) received. Higher use of surgical and pharmaceutical interventions to alleviate incontinence among survivors in the Republic of Ireland than in Northern Ireland is likely owing to the higher rate of radical prostatectomy in the Republic of Ireland, whereas greater use of treatments for gynaecomastia in Northern Ireland reflects higher use of hormone therapy there.¹⁰ Other variations in intervention use were more surprising. Younger men were significantly more likely to report using supportive interventions for depression and impotence, the latter finding being consistent with findings in a Swedish population-based study.¹¹ Older men were significantly more likely to report interventions for incontinence and bowel problems. Although those trends could be explained by differences in treatment receipt by age, it is possible that men of different ages may be more likely to seek, or be offered, help for certain types of after-effects. With the exception of interven-

tions for bowel problems, a higher percentage of men who received intervention(s) for an after-effect reported decisional regret. There are a number of possible explanations: these men may have experienced more severe after-effects, which required interventions; they may have been less satisfied with their posttreatment function and/or more proactive about recovering or treating their after-effects. This requires further investigation.

This is a large, international, population-based study, the first such study to describe patient-reported use of supportive care following a range of prostate cancer treatments. Although this study is novel, there are a number of limitations. It is a cross-sectional, descriptive study. We did not ask survivors whether the supportive interventions received matched their needs and wants, and whether they were satisfied with the supportive care received. Furthermore, although the response rate is comparable with other similar studies,^{12,13} it is possible that the supportive care of non-responders was different to that of responders.

Our study included men from 2 jurisdictions with separate health care systems, suggesting that low use of supportive interventions may be common across systems. There is a need for further research into patient and health care system factors associated with the receipt of supportive interventions and how satisfied men are with these, in this and other health care settings. Presently, it is clear that more needs to be done in the clinical setting to support prostate cancer survivors manage treatment after-effects; this in turn could improve survivors' HRQoL.

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