Health-related quality of life after treatment for bladder cancer in England

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BACKGROUND: Little is known about quality of life after bladder cancer treatment. This common cancer is managed using treatments that can affect urinary, sexual and bowel function.

METHODS: To understand quality of life and inform future care, the Department of Health (England) surveyed adults surviving bladder cancer 1–5 years after diagnosis. Questions related to disease status, co-existing conditions, generic health (EQ-5D), cancer-generic (Social Difficulties Inventory) and cancer-specific outcomes (Functional Assessment of Cancer Therapy—Bladder).

RESULTS: In total, 673 (54%) patients responded; including 500 (74%) men and 539 (80%) with co-existing conditions. Most respondents received endoscopic treatment (60%), while 92 (14%) and 99 (15%) received radical cystectomy or radiotherapy, respectively. Questionnaire completion rates varied (51–97%). Treatment groups reported ≥1 problem using EQ-5D generic domains (59–74%). Usual activities was the most common concern. Urinary frequency was common after endoscopy (34–50%). Certain populations were more likely to report generic, cancer-generic and cancer-specific problems; notably those with co-existing long-term conditions and those treated with radiotherapy.

CONCLUSION: The study demonstrates the importance of assessing patient-reported outcomes in this population. There is a need for larger, more in-depth studies to fully understand the challenges patients with bladder cancer face.

INTRODUCTION
Bladder cancer (BC) is the 9th most common cancer in the United Kingdom and one of the most expensive malignancies to manage.1–3 The disease is best stratified according to the presence of muscle invasion and cellular differentiation. Most BCs are non-muscle invasive (NMIBC) and have an excellent long-term prognosis.4 NMIBC tumours are managed by endoscopic resection, intravesical chemotherapy and long-term surveillance.4,5 Following initial treatment, many patients develop local recurrence, requiring further treatments.5 Around 1/3 of tumours are muscle invasive BCs (MIBCs), requiring radical treatment if cure is to be obtained. Radical cystectomy (RC) or radiotherapy includes treatment of adjacent viscera with regional lymph nodes, and often includes systemic chemotherapy. The nature and toxicity of treatments and surveillance for BC can vary between patients, between each option and over time. There is evidence that treatment for MIBC can impact upon urinary function,6 bowel function,7 sexual function,8,9 and affects body image,10,11 which can lead to anxiety and depression.12 However, there is less evidence regarding the consequences of treatment for NMIBC and the impact on patients’ Health-Related Quality of Life (HRQL).12,13

The importance of large scale, population-level Patient-Reported Outcome Measures (PROMs) in improving healthcare design, patient experience and directing care is becoming recognised.14,15 PROMs can be used to ascertain a more comprehensive understanding of the quality of survival, alongside the impact and relevance of health care provision, and as a surrogate measure within clinical trials. Previous research in the USA used a linkage database to identify BC patients and looked at results of 620 surveys completed before diagnosis and 856 completed after by patients ≥65 years old.16 European PROMs work included 823 German patients of all ages and stages of BC.13 These cross-sectional studies used generic PROMs or generic cancer PROMs.

To date, no large-scale surveys of BC patients have been conducted in the United Kingdom. As such, in 2013 the Department of Health (DH) England designed and administered a pilot survey of patients 1–5 years following their initial treatment for BC. Here we report the results of the pilot survey, which was conducted to identify a methodology to define the HRQL of individuals in the years following their treatment and to identify potential factors associated with poor outcomes.

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Received: 18 October 2017 Revised: 21 March 2018 Accepted: 22 March 2018
Published online: 14 May 2018
Survey design
The DH methodology has been described previously for cohorts diagnosed with non-Hodgkin’s lymphoma, breast, colorectal and prostate cancer. \(^{17}\) Individuals aged 16 or older surviving 1–5 years after a diagnosis of BC were identified via the Eastern Cancer Registration and Intelligence Centre (now part of National Cancer Registration and Analysis Service, NCRAS). \(^{18}\) The sample size was chosen to match similar studies performed by the DH in other cancer sites. \(^{17}\)

Identified participants were mailed a questionnaire, with a covering letter from their treating Cancer Centre. Consent to participate was implied through return of completed questionnaires. Individuals who did not want to participate were asked to return their questionnaire uncompleted or to discard the survey. Two reminders were sent to non-responders. A Freephone helpline for patients was provided, which supported completion of the survey. Permission to approach patients without informed consent was given by the Health Research Authority (ref ECC 5-02 (FT7))/2012.

Survey content
Survey content included questions about treatment, disease status, generic HRQL (EQ-5D-5L) and BC specific outcomes (Functional Assessment of Cancer Therapy—Bladder (FACT-BL)), social problems (Social Difficulties Inventory (SDI-21)), health and well-being in the past month, experience of care and presence of other long-term conditions (LTCs) (Supplementary File 1).

The EQ-5D-5L records problems on five domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). \(^{19,20}\) The SDI-21 is a 21-item questionnaire, developed to assess everyday problems experienced by cancer patients. \(^{21}\) Questions are answered on a scale of 0 (no difficulty) to 3 (very much), with respect to the past month. Sixteen of the items form three subscales: Everyday Living, Money Matters and Self and Others. These scales form a measure of social distress (SD-16), with scores ranging from 0 to 44. \(^{22}\) The SDI-21 also comprises five single items.

FACT-BL consists of the 27-item FACT-General (FACT-G) questionnaire \(^{23}\) and 13 additional items. FACT-G covers four areas; Physical well-being, Social/family well-being, Emotional well-being and Functional well-being. The 13 additional items relate to urinary issues, bowel issues, appetite and weight, sexual items, body image, a question asking if the respondent has an ostomy appliance and two questions about ostomy appliances. All items ask about the last 7 days.

These surveys were chosen for inclusion as EQ-5D-5L, SDI-21 and Functional Assessment of Chronic Illness Therapy (FACT) modules have been used in similar studies performed by the DH in other cancer sites. \(^{17,14}\) Cognitive testing of all questionnaires was performed with a group of volunteer patients and expert panel review (clinicians/methodologists). In the final version of the survey, the team designing the survey removed the ‘somewhat’ response option from FACT-BL; changing the questionnaire from five responses to four. \(^{14}\)

Data handling
All variables were derived from the survey data. Participants were asked if they had any other LTCs at the time of completing the questionnaire and to tick all conditions that they had from a list widely used in English DH surveys. This variable was categorised into none, 1, 2 or ≥3 LTCs. Information on self-reported disease status (in remission, treated but still present, not treated, recurrence, and not certain) and treatments (endoscopic/telescopic surgery with or without chemotherapy directly into the bladder, RC, chemotherapy, and radiotherapy) was taken from the questionnaire. Age was grouped into <55 years, 55–64 years, 65–74 years, 75–85 years and ≥85 years.

EQ-SD-5L responses were split into people who reported at least one problem (of any severity) on any domain and people who reported having no problems on any domain. Individual domains were categorised in this way. A validated cutoff score of ≥10 on the SD-16 scale indicates a high level of social difficulties that requires follow-up by health or social care staff. \(^{24}\) This was used in our analysis as a cutoff point (socially distressed v not socially distressed). Estimated cutoff points of 5 for the Everyday Living subscale, 2 for the Money Matters subscale and 3 for the Self and Others subscale were used in this study, as per previous research. \(^{25}\) The five single items of the SDI-21 are scored individually. \(^{22}\) As the ‘somewhat’ option was removed from the questionnaire, FACT-BL scores could not be calculated as per normal practice and thus cancer-specific questions from FACT-BL were examined separately. FACT-BL responses were grouped into those who responded ‘not at all’ or ‘a little’ and those who responded ‘quite a bit’ and ‘very much’. Outcomes pertaining to well-being, urinary items, sexual items and body image are presented here.

Statistical analysis
Descriptive statistics were used to report respondent characteristics, EQ-5D-5L responses, SDI-21 subscale scores and FACT-BL responses. Outcomes were analysed in relation to age, sex, other comorbidities and type of treatment using \(\chi^2\) tests. Statistical significance was set at the 1% level to minimise the chances of false-positive associations. Analyses were performed using Stata version 15 (Stata, College Station, TX).

RESULTS
Survey population
In total, 1252 BC patients were randomly identified and sent a questionnaire (Fig. 1). Of these, 21 (2%) died during the survey period, leaving 1231 eligible patients. Questionnaires were returned by 673 people (54% response rate), including 500 (74%) men and 162 (24%) women (Table 1). Most respondents were white (93%) and were in remission from BC (65%). Co-existing LTCs were common (80% reported ≥1 LTC and 29% reported ≥3). The most common treatment was endoscopy/telescopy (31%). Radical treatment was reported by 28% of respondents; of which 14% had undergone RC, 9% had received external beam radiotherapy and 5% had radiotherapy with intravenous chemotherapy. Other treatment combinations were given to <2% of respondents and therefore excluded from analysis. A stoma was present in 16% of respondents. Of the radical treatments, patients ≥85 years were more likely to be treated with radiotherapy (31%) (Supplementary Table 1).

Respondent and non-respondent characteristics were compared, using data from NCRAS (Supplementary Table 2). Individuals older than 85 years (RR, 39%) were less likely to participate.

Data quality
Most patients answered questions relating to sex, LTCs and treatment (<5% missing responses). Of all the PROMs, FACT-BL had the largest variety of completion rates for items and scales; with missing responses ranging from 5 to 49% (Supplementary Table 3).

Generic HRQL
Overall, 65% of respondents reported ≥1 problem on any EQ-5D-5L domain (Table 2). The percentage of respondents from treatment groups reporting ≥1 problem on any EQ-5D-5L domain ranged from 59% for endoscopy/telescopy and intravesical chemotherapy to 74% for radiotherapy. Problems with usual
activities were most commonly reported (43%). Respondents treated with radiotherapy reported more problems with mobility, self-care and usual activities compared to respondents who received other treatments. Respondents with endoscopy/telescopy were more likely to report problems with mobility than respondents treated with endoscopy/telescopy and intravesical chemotherapy (47% compared to 26%, p < 0.01).

Respondents aged ≥85 years were most likely to report some problems with mobility, self-care and usual activities. Respondents <55 years old were significantly more likely to report problems with anxiety/depression, with half of this group reporting some problems, compared to between 31–44% of other age groups (p = 0.01). Those with ≥3 LTCs reported significantly more problems on all EQ-5D-5L domains bar one (anxiety/depression).

Social difficulties
SD-16. Overall, 15% of respondents were classed as socially distressed (score ≥10, Table 3). No differences were observed by sex or age group. The respondents most likely to report significantly high social distress were those treated with radiotherapy and respondents with ≥3 LTCs; with more than a quarter of respondents from these groups meeting the criteria. Respondents with a stoma were twice as likely to be socially distressed compared to respondents without a stoma.

SDI-21 subscales. Difficulties with Everyday Living (score ≥5) were reported by 21% of respondents (Table 3). Respondents treated with radiotherapy and those who had ≥3 LTCs reported a higher level of difficulty with Everyday Living (both 41%). Comparatively fewer patients receiving other treatments reported difficulties (≤25%). When comparing patients who did not have radical treatments, significantly more respondents with endoscopy/telescopy reported difficulties with Everyday Living than respondents treated with endoscopy/telescopy and intravesical chemotherapy (23% compared to 11%, p < 0.01). Difficulties with Everyday Living did not vary by sex, age group or stoma status.

Difficulties with Money Matters (score ≥2) were reported by 14% of respondents. This difficulty was significantly more likely to be reported by respondents who were <55 years of age (42% compared to between 3 and 23% of other age groups, p < 0.01). Differences were not found for treatment type, disease status, stoma status, LTCs or sex (Table 3).

Difficulties with Self and Others (score ≥3) were reported by 17% of respondents. Reporting of significant difficulties with Self and Others was high in respondents <55 years of age, where more than a third (34%) reported difficulties (Table 3).

SDI-21 single items. The most commonly reported difficulty was with travelling or plans to take a holiday; reported by 33% of respondents. Respondents with a stoma were significantly
Table 2. EQ-5D-5L number of generic health problems and domain responses by demographic

| Demographic | Problems on any EQ5D domain | Mobility | Self-care |
|-------------|-----------------------------|----------|-----------|
|              | No problems | Problems | p-value | No problems | Problems | p-value | No problems | Problems | p-value |
| Age, years  |              |          |         |              |          |         |              |          |         |
| <55         | 21 41.2     | 30 58.8 | 0.226   | 40 76.9     | 12 23.1  | 0.01     | 45 88.2     | 6 11.8   | 0.01     |
| 55–64       | 43 32.6     | 89 67.4 |          | 101 74.3    | 35 25.7  |          | 119 87.5    | 17 12.5  |          |
| 65–74       | 92 39.5     | 141 60.5 |        | 164 68.3    | 76 31.7  |        | 210 87.1    | 31 12.9  |        |
| 75–84       | 54 30.9     | 121 69.1 |        | 88 49.2     | 91 50.8  |        | 141 77.0    | 42 23.0  |        |
| ≥85         | 9 26.5      | 25 73.5 |          | 12 34.3     | 23 65.7  |        | 23 67.7     | 11 32.3  |        |
| Sex         |              |          |         |              |          |         |              |          |         |
| Male        | 170 35.6    | 308 64.4 |        | 310 63.7    | 177 36.3 |        | 410 83.5    | 81 16.5  |        |
| Female      | 51 33.6     | 101 66.4 |          | 98 61.2     | 62 38.8  |          | 133 83.1    | 27 16.9  |          |
| No. of long-term conditions |          |         |         |              |          |         |              |          |         |
| None        | 57 53.3     | 50 46.7 | 0.01    | 94 86.2     | 15 13.8  | 0.01     | 107 98.2    | 2 1.8    | 0.01     |
| 1           | 84 43.5     | 109 56.5 |        | 155 78.3    | 43 21.7  |        | 181 91.0    | 18 9.0   |        |
| 2           | 41 30.1     | 95 69.9 |        | 84 60.4     | 55 39.6  |        | 120 86.3    | 19 13.7  |        |
| ≥3          | 31 17.1     | 150 82.9 |        | 63 33.3     | 126 66.7 |        | 120 62.8    | 71 37.2  |        |
| Disease status |            |          |         |              |          |         |              |          |         |
| Remission   | 170 40.4    | 251 59.6 | 0.01    | 288 66.8    | 143 33.2 | 0.01     | 371 85.9    | 61 14.1  | 0.01     |
| Treated but cancer still present |            |          |         |              |          |         |              |          |         |
| Recurrence  | 8 26.7      | 22 73.3 |          | 20 66.7     | 10 33.3  |          | 25 83.3     | 5 16.7   |          |
| Not certain | 15 19.2     | 63 80.8 |          | 39 48.1     | 42 51.9  |          | 60 74.1     | 21 25.9  |          |
| Treatment   |              |          |         |              |          |         |              |          |         |
| Endoscopy/telescopy | 68 34.5 | 129 65.5 | 0.16    | 108 53.5    | 94 46.5  | 0.01     | 166 81.0    | 39 19.0  | 0.01     |
| Endoscopy/telescopy with chemotherapy directly into the bladder | 80 41.5 | 113 58.5 |          | 145 74.0    | 51 26.0  |          | 177 89.9    | 20 10.1  |          |
| Radical cystectomy | 27 30.7 | 61 69.3 |          | 62 68.9     | 28 31.1  |          | 74 82.2     | 16 17.8  |          |
| Radiotherapy and Intravenous chemotherapy | 10 30.3 | 23 69.7 |          | 20 57.1     | 15 42.9  |          | 31 88.6     | 4 11.4   |          |
| Radiotherapy | 16 26.2     | 45 73.8 |          | 26 41.3     | 37 58.7  |          | 41 66.1     | 21 33.9  |          |
| Stoma status |              |          |         |              |          |         |              |          |         |
| Stoma       | 31 29.5     | 74 70.5 | 0.19    | 70 66.0     | 36 34.0  | 0.02     | 86 81.1     | 20 18.9  | 0.40     |
| No stoma    | 152 36.4    | 266 63.6 |          | 271 63.5    | 156 36.5 |          | 365 84.5    | 67 15.5  |          |
| Demographic                  | Usual activities | Pain/Discomfort | Anxiety/Depression |
|------------------------------|------------------|-----------------|-------------------|
|                              | No problems      | Problems        | p-value           |
| N %                          | N %              | N %             | N %              |
| Age, years                   |                  |                 |                   |
| <55                          |                  |                 |                   |
| 35  67.3  17  32.7           |                  |                 |                   |
| 84  62.7  50  37.3           |                  |                 |                   |
| 151 63.2  88  36.8           |                  |                 |                   |
| 87  47.5  96  52.5           |                  |                 |                   |
| ≥85                          |                  |                 |                   |
| 12  35.3  22  64.7           |                  |                 |                   |
| Sex                          |                  |                 |                   |
| Male                         | 291  59.4  199  40.6 | 300  61.2  190  38.8 | 317  64.6  174  35.4 |
| Female                       | 81  51.3  77  48.7 | 107  67.3  52  32.7 | 99  63.9  56  36.1 |
| No. of long-term conditions  |                  |                 |                   |
| None                         | 87  79.1  23  20.9 | 87  79.8  22  20.2 | 79  71.8  31  28.2 |
| 1                            | 133 67.2  65  32.8 | 140 69.7  61  30.3 | 132 67.0  65  33.0 |
| 2                            | 78  56.1  61  43.9 | 82  59.9  55  40.1 | 91  65.9  47  34.1 |
| ≥3                           | 62  33.0  126  67.0 | 86  45.5  103  54.5 | 103 54.8  85  45.2 |
| Disease status               |                  |                 |                   |
| Remission                    | 271 63.3  157  36.7 | 292 67.9  138  32.1 | 301 70.2  128 29.8 |
| Treated but cancer still present | 20  48.8  21  51.2 | 21  52.5  19  47.5 | 19  47.5  21  52.5 |
| Recurrence                   | 16  53.3  14  46.7 | 16  53.3  14  46.7 | 15  50.0  15  50.0 |
| Not certain                  | 31  38.3  50  61.7 | 37  45.7  44  54.3 | 44  55.0  36  45.0 |
| Treatment                    |                  |                 |                   |
| Endoscopy/telescopy          | 123 60.0  82  40.0 | 144 70.6  60  29.4 | 132 65.4  70  34.6 |
| Endoscopy/telescopy with chemotherapy directly into the bladder | 131 66.8  65  33.2 | 130 66.7  65  33.3 | 129 65.5  68  34.5 |
| Radical cystectomy           | 41  46.1  48  53.9 | 51  56.0  40  44.0 | 53  59.6  36  40.4 |
| Radiotherapy and Intravenous chemotherapy | 17  50.0  17  50.0 | 16  47.1  18  52.9 | 20  57.1  15  42.9 |
| Radiotherapy                 | 26  41.9  36  58.1 | 33  53.2  29  46.8 | 41  67.2  20  32.8 |
| Stoma status                 |                  |                 |                   |
| Stoma                        | 51  47.7  56  52.3 | 54  50.5  53  49.5 | 67  62.6  40  37.4 |
| No stoma                     | 260 60.7  168  39.3 | 277 64.6  152 35.4 | 276 63.9  156 36.1 |
Table 3. Social Difficulties Inventory: SD-16 and SDI-21 subscale results by demographic

| Demographic     | Social Distress | Everyday Living | Money Matters | Self and Others |
|-----------------|-----------------|-----------------|--------------|-----------------|
|                 | SD % | No SD % | SD % | No SD % | SD % | No SD % | SD % | No SD % | SD % | No SD % |
| Age, years      |      |        |      |        |      |        |      |        |      |        |
| <55             | 14   | 26.4   | 39   | 73.6   | 13   | 24.5   | 40   | 75.5   | 22   | 41.5   |
| 55–64           | 23   | 17.3   | 110  | 82.7   | 22   | 16.3   | 113  | 83.7   | 31   | 23.3   |
| 65–74           | 29   | 12.0   | 212  | 88.0   | 44   | 18.1   | 199  | 81.9   | 23   | 9.5    |
| 75–84           | 23   | 13.8   | 144  | 86.2   | 43   | 24.0   | 136  | 76.0   | 11   | 6.5    |
| ≥85             | 5    | 16.1   | 26   | 83.9   | 12   | 35.3   | 22   | 64.7   | 1    | 3.0    |
| Sex             |      |        |      |        |      |        |      |        |      |        |
| Male            | 71   | 14.8   | 410  | 85.2   | 93   | 18.9   | 400  | 81.1   | 74   | 15.3   |
| Female          | 24   | 16.1   | 125  | 83.9   | 42   | 26.9   | 114  | 73.1   | 14   | 9.3    |
| No. of long-term conditions |      |        |      |        |      |        |      |        |      |        |
| None            | 6    | 5.7    | 100  | 94.3   | 9    | 8.3    | 99   | 91.7   | 11   | 10.4   |
| 1               | 23   | 11.9   | 170  | 88.1   | 25   | 12.3   | 178  | 87.7   | 25   | 12.8   |
| 2               | 18   | 13.4   | 116  | 86.6   | 25   | 18.1   | 113  | 81.9   | 17   | 12.7   |
| ≥3              | 48   | 26.1   | 136  | 73.9   | 77   | 41.0   | 111  | 59.0   | 34   | 18.3   |
| Disease status  |      |        |      |        |      |        |      |        |      |        |
| Remission       | 43   | 10.3   | 376  | 89.7   | 71   | 16.5   | 359  | 83.5   | 48   | 11.4   |
| Treated but cancer still present | 10   | 24.4   | 31   | 75.6   | 12   | 29.3   | 29   | 70.7   | 4    | 9.8    |
| Recurrence      | 6    | 20.7   | 23   | 79.3   | 6    | 20.7   | 23   | 79.3   | 6    | 20.7   |
| Not certain     | 20   | 26.0   | 57   | 74.0   | 27   | 33.7   | 53   | 66.3   | 15   | 19.2   |
| Treatment       |      |        |      |        |      |        |      |        |      |        |
| Endoscopy/telescopy | 23   | 11.6   | 176  | 88.4   | 47   | 23.1   | 156  | 76.9   | 23   | 11.6   |
| Endoscopy/telescopy with chemotherapy directly into the bladder | 16   | 8.5    | 173  | 91.5   | 21   | 10.8   | 174  | 89.2   | 22   | 11.6   |
| Radical cystectomy | 21   | 23.6   | 68   | 76.4   | 23   | 25.3   | 68   | 74.7   | 17   | 19.1   |
| Radiotherapy and Intravenous chemotherapy | 7    | 20.0   | 28   | 80.0   | 7    | 20.0   | 28   | 80.0   | 7    | 20.0   |
| Radiotherapy    | 16   | 28.1   | 41   | 71.9   | 24   | 40.7   | 35   | 64.3   | 4    | 6.9    |
| Stoma status    |      |        |      |        |      |        |      |        |      |        |
| Stoma           | 24   | 22.6   | 82   | 77.4   | 25   | 23.1   | 83   | 76.9   | 20   | 18.9   |
| No stoma        | 48   | 11.2   | 379  | 88.8   | 81   | 18.7   | 353  | 81.3   | 52   | 12.1   |

χ² tests for categorical variables:

- Age, years: χ²(4, N=250) = 26, p < 0.01
- Sex: χ²(1, N=250) = 0.2, p = 0.688
- No. of long-term conditions: χ²(4, N=250) = 64.7, p < 0.01
- Disease status: χ²(3, N=250) = 18.8, p = 0.008
- Treatment: χ²(4, N=250) = 27.7, p < 0.01
- Stoma status: χ²(1, N=250) = 3.3, p = 0.068

Note: p-values are approximate and may require further statistical analysis.
Table 4. Cancer-specific patient-reported outcomes by treatment group

| Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|---------------------------------------------------------------|---------------------|-------------------|---------------------------------------------|----------------------|---------|
| Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much |
| N | % | N | % | N | % | N | % |

**Physical well-being**

| Item | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|------|---------------------------------------------------------------|---------------------|-------------------|---------------------------------------------|----------------------|---------|
|      | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|      | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much |
| N | % | N | % | N | % | N | % | N | % |

**Social/family well-being**

| Item | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|------|---------------------------------------------------------------|---------------------|-------------------|---------------------------------------------|----------------------|---------|
|      | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|      | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much |
| N | % | N | % | N | % | N | % | N | % |

**Emotional well-being**

| Item | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|------|---------------------------------------------------------------|---------------------|-------------------|---------------------------------------------|----------------------|---------|
|      | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|      | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much |
| N | % | N | % | N | % | N | % | N | % |

**Functional well-being**

| Item | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|------|---------------------------------------------------------------|---------------------|-------------------|---------------------------------------------|----------------------|---------|
|      | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|      | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much |
| N | % | N | % | N | % | N | % | N | % |

**Bladder cancer-specific items**

| Item | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|------|---------------------------------------------------------------|---------------------|-------------------|---------------------------------------------|----------------------|---------|
|      | Endoscopy/telescopy with chemotherapy directly into the bladder | Endoscopy/telescopy | Radical cystectomy | Radiotherapy and Intravenous chemotherapy | Radiotherapy | p-value |
|      | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much | Not at all/somewhat | Quite a bit/very much |
| N | % | N | % | N | % | N | % | N | % | N | % |

*For men only* I am able to have and maintain an erection 91 66.4 46 33.6 76 59.8 51 40.2 52 94.5 3 5.5 17 89.5 2 10.5 34 89.5 4 10.5 NA
Table 5. Cancer-specific patient-reported outcomes by number of long-term conditions (LTCs)

|                              | No LTC | 1 LTC | 2 LTCs | ≥3 LTCs | p-value |
|------------------------------|--------|-------|--------|--------|---------|
|                              | N %    | N %   | N %    | N %    |         |
| Physical well-being          |        |       |        |        |         |
| I have a lack of energy      | 97 91.5 | 9 8.5 | 170 85.9 | 28 14.1 | 98 76.0 | 31 24.0 | 101 55.5 | 81 44.5 | $\chi^2 = 66, \ p < 0.001$ |
| Because of my physical       | 104 98.1 | 2 1.9 | 170 91.9 | 15 8.1 | 116 94.3 | 7 5.7 | 132 80.0 | 33 20.0 | $\chi^2 = 298, \ p < 0.001$ |
| condition, I have trouble    |        |       |        |        |         |
| meeting the needs of my      |        |       |        |        |         |
| family                        |        |       |        |        |         |
| I have pain                  | 101 97.1 | 3 2.9 | 175 94.6 | 10 5.4 | 109 87.2 | 16 12.8 | 138 81.2 | 32 18.8 | $\chi^2 = 24.9, \ p < 0.001$ |
| Social/family well-being     |        |       |        |        |         |
| I feel close to my friends   | 26 27.4 | 69 72.6 | 64 35.4 | 117 64.6 | 46 39.3 | 71 60.7 | 66 41.0 | 95 59.0 | $\chi^2 = 53, \ p = 0.150$ |
| My family has accepted my    | 14 13.6 | 89 86.4 | 25 13.8 | 156 86.2 | 20 16.3 | 103 83.7 | 18 10.8 | 148 89.2 | $\chi^2 = 1.8, \ p = 0.609$ |
| illness                      |        |       |        |        |         |
| I am satisfied with my sex   | 39 56.5 | 30 43.5 | 71 61.7 | 44 38.3 | 48 75.0 | 16 25.0 | 67 76.1 | 21 23.9 | $\chi^2 = 10, \ p = 0.018$ |
| life                         |        |       |        |        |         |
| Emotional well-being         |        |       |        |        |         |
| I feel sad                   | 70 94.6 | 4 5.4 | 128 94.1 | 8 5.9 | 74 88.1 | 10 11.9 | 86 76.1 | 27 23.9 | $\chi^2 = 22.9, \ p < 0.001$ |
| I am satisfied with how I am | 16 20.8 | 61 79.2 | 31 21.8 | 111 78.2 | 22 23.7 | 71 76.3 | 47 36.2 | 83 63.8 | $\chi^2 = 9.5, \ p = 0.023$ |
| coping with my illness       |        |       |        |        |         |
| I feel nervous               | 73 97.3 | 2 2.7 | 133 94.3 | 8 5.7 | 84 93.3 | 6 6.7 | 95 79.2 | 25 20.8 | $\chi^2 = 24.9, \ p < 0.001$ |
| I worry about dying          | 69 90.8 | 7 9.2 | 132 93.6 | 9 6.4 | 85 94.4 | 5 5.6 | 104 83.9 | 20 16.1 | $\chi^2 = 96, \ p = 0.023$ |
| I worry that my condition    | 91 85.8 | 15 14.2 | 166 86.5 | 26 13.5 | 113 87.6 | 16 12.4 | 145 81.0 | 34 19.0 | $\chi^2 = 3.3, \ p = 0.348$ |
| will get worse               |        |       |        |        |         |
| Functional well-being        |        |       |        |        |         |
| I am able to work (include   | 18 18.0 | 82 82.0 | 38 21.3 | 140 78.7 | 53 42.7 | 71 57.3 | 87 53.7 | 75 46.3 | $\chi^2 = 55.6, \ p < 0.001$ |
| work at home)                |        |       |        |        |         |
| My work (include work at home) is fulfilling | 20 21.5 | 73 78.5 | 44 26.0 | 125 74.0 | 43 36.8 | 74 63.2 | 77 51.3 | 73 48.7 | $\chi^2 = 312, \ p < 0.001$ |
| I am able to enjoy life      | 16 15.0 | 91 85.0 | 29 14.7 | 168 85.3 | 25 19.4 | 104 80.6 | 60 33.7 | 118 66.3 | $\chi^2 = 243, \ p < 0.001$ |
| I am sleeping well           | 23 21.9 | 82 78.1 | 52 26.8 | 142 73.2 | 44 33.1 | 89 66.9 | 75 41.9 | 104 58.1 | $\chi^2 = 155, \ p < 0.001$ |
| I am enjoying the things I   | 16 15.7 | 86 84.3 | 31 16.2 | 160 83.8 | 34 27.2 | 91 72.8 | 79 45.4 | 95 54.6 | $\chi^2 = 47.7, \ p < 0.001$ |
| usually do for fun           |        |       |        |        |         |
| I am content with the quality | 22 20.4 | 86 79.6 | 28 14.6 | 164 85.4 | 38 29.9 | 89 70.1 | 67 74.2 | 112 26.7 | $\chi^2 = 1.8, \ p = 0.150$ |
| of my life right now         |        |       |        |        |         |
| Bladder cancer-specific      |        |       |        |        |         |
| items                        |        |       |        |        |         |
| I have control of my         | 14 13.3 | 91 86.7 | 30 15.3 | 166 84.7 | 27 20.3 | 106 79.7 | 45 25.0 | 135 75.0 | $\chi^2 = 8.3, \ p = 0.04$ |
| bowel's                       |        |       |        |        |         |
| I urinate more frequently    | 73 70.9 | 30 29.1 | 117 63.6 | 67 36.4 | 87 70.7 | 36 29.3 | 99 55.6 | 79 44.4 | $\chi^2 = 10, \ p = 0.019$ |
| than usual                   |        |       |        |        |         |
| I have a good appetite       | 13 12.1 | 94 87.9 | 31 16.0 | 163 84.0 | 21 15.8 | 112 84.2 | 50 26.9 | 136 73.1 | $\chi^2 = 13, \ p < 0.001$ |
| It burns when I urinate      | 99 98.0 | 2 2.0 | 174 92.6 | 14 7.4 | 120 94.5 | 7 5.5 | 153 89.0 | 19 11.0 | $\chi^2 = 85, \ p = 0.036$ |
| I am interested in sex       | 52 54.2 | 44 45.8 | 98 58.0 | 71 42.0 | 82 69.5 | 36 30.5 | 130 77.8 | 37 22.2 | $\chi^2 = 21.8, \ p < 0.001$ |
| (For men only) I am able to  | 42 61.8 | 26 38.2 | 87 66.4 | 44 33.6 | 75 78.1 | 21 21.9 | 107 82.9 | 22 17.1 | $\chi^2 = 15.1, \ p < 0.001$ |
| have and maintain an         |        |       |        |        |         |
| erection                     |        |       |        |        |         |
more likely to report ‘quite a bit’ or ‘very much’ difficulty with this item than those without a stoma (29% compared to 15%, \( p < 0.01 \)). Difficulties with sexual matters were reported ‘quite a bit’ or ‘very much’ by 15% of respondents. This difficulty was significantly more likely to impact on men, 17% of whom reported ‘quite a bit’ or ‘very much’ difficulty compared to 5% of females (\( p < 0.01 \)).

Cancer-specific HRQL

Physical well-being. Overall, 25% of the cohort responded that they experienced a lack of energy ‘quite a bit’ or ‘very much’, but this was higher in respondents treated with radiotherapy (43%) (Table 4). Pain was reported ‘quite a bit’ or ‘very much’ by 10% of respondents and was higher in respondents with ≥3 LTCs (19%) (Table 5).

Social/family well-being. Of the 51% who answered this item, two thirds (67%) reported dissatisfaction with their sex life (‘not at all’ or ‘a little’ satisfied with their sex life). Dissatisfaction was significantly more likely to be reported by patients who underwent RC surgery compared to those who had other treatments (Table 4). A higher percentage of females reported that they were ‘quite a bit’ or ‘very much’ satisfied with their sex life (51% compared to 31% of males, \( p < 0.01 \)).

Emotional well-being. Respondents across the cohort reported a lack of satisfaction with how they were coping with their illness, as almost three-quarters of respondents reported that they were ‘not at all’ or ‘a little’ satisfied. Feeling ‘quite a bit’ or ‘very much’ nervous was reported by 10% of respondents; particularly by females (18% compared to 7% of males, \( p < 0.01 \)), and those with ≥3 LTCs (Table 5).

Functional well-being. Around a third of respondents (35%) answered ‘not at all’ or ‘a little’ about their ability to work. Respondents treated with radiotherapy were less likely to be able to work compared to respondents receiving other treatments (Table 4).

Although three quarters of respondents reported that they were content with the quality of their life right now (reporting ‘quite a bit’ or ‘very much’), respondents with ≥3 LTCs were significantly more likely to report that they were not content (Table 5).

Bladder cancer-specific items

Urinary items: Urinating more frequently than usual was common after endoscopy (reported ‘quite a bit’ or ‘very much’ in 34–37%) and radiotherapy (reported ‘quite a bit’ or ‘very much’ in 44–50%) (Table 4).

Sexual items: Disinterest in sex was reported by 66% of respondents and had a good response rate of 85%. Disinterest in sex was significantly higher in females than males, with 86% of females saying they were ‘not at all’ or only ‘a little’ interested in sex, compared to 60% of males (\( p < 0.01 \)). This difference was observed (but not significant due to small numbers) when restricted to those who had a stoma, with 89% of females saying they were ‘not at all’ or only ‘a little’ interested. Ability to maintain an erection was less likely in males who had a stoma, with 96% reporting ‘not at all’ or ‘a little’ to this item, though the result was not significant due to small numbers.

Body image: Just under half of respondents said that they didn’t like their body appearance at all, or only liked it a little (48%). Respondents with a stoma were more likely to report not liking their body at all or only liking it a little (60% compared to 46% of respondents without a stoma, \( p = 0.01 \)).

DISCUSSION

Here we report HRQL in individuals between 1 and 5 years post diagnosis for BC. While modest in size compared to PROMs studies in other cancer sites, this work represents the largest UK study to date and demonstrates this methodology is feasible in this population. We have identified that reduced HRQL is common in patients following BC treatment, that there are differences according to treatment modality and patient characteristics, and that further more focused studies are warranted.

Several key findings deserve discussion. First, our results highlight the need to support people who have pre-existing health conditions and a new diagnosis of BC. Respondents with LTCs were much more likely to report poor HRQL across all EQ-5D-5L items, all domains apart from Money Matters on the SD-21, SD-16 and on multiple items of FACT-BL. The design and methodology used in this survey limits our ability to investigate this further and to understand whether this reflects the impact of BC on other LTCs, or the impact of other LTCs on HRQL. This is an important area for future studies to focus on.

Second, while we do not know details of each tumour (i.e., stage or grade), most patients (60%) received only endoscopic surgery. To date, most BC HRQL reports have focused upon MIBC and cystectomy outcomes. As such, our data are the first to look at HRQL in MIBC and NMIBC outcomes across a UK population. When comparing NMIBC treatments, overall, respondents receiving endoscopic surgery with intravesical chemotherapy had higher HRQL and fewer everyday living difficulties than those receiving only endoscopic surgery. This may reflect recall bias (guidelines suggest that most patients should have received intravesical chemotherapy), \(^{31}\) performance status (unfit patients did not receive intravesical chemotherapy), treatment differences (intravesical chemotherapy improves disease outcomes) or service design (perhaps better designed services are more guideline compliant and more likely to support patients through treatment). Support for patient selection has shown that for many domains the HRQL was superior for combined treatment rather than just endoscopic surgery.

Third, around 30% of respondents received radical therapy, including 16% who had a stoma and 9% who had received radiotherapy. The latter were most likely to report low HRQL problems with mobility, self-care and usual activities. They were also more likely to be socially distressed (score ≥10 on SD-16), have high levels of difficulty with everyday living, report a lack of energy and an inability to work. Patients treated with radiotherapy were also more likely to report needing to urinate more frequently than usual. While these findings may reflect outcomes from radiotherapy, when compared to RC, it is more likely they reveal treatment patterns and pre-existing fitness.\(^{26}\) Evidence to support this is that most of these measures were better for patients who received both radiotherapy with chemotherapy (for which higher fitness is needed). Indeed outcomes from RC and radiotherapy with chemotherapy were broadly comparable to each other and to patients receiving only endoscopy/telescopy.\(^{27}\) Finally, overall there were some encouraging findings with social distress generally being low in respondents, as 85% were below the cutoff point, and perfect health (i.e., no problems on EQ-5D-5L) was reported by 35% of respondents.

This study has a number of key limitations. Response rates were marginally lower than for UK surveys in other cancer sites (63% for colorectal cancer)\(^{14}\) and 68% overall for a pilot study of individuals diagnosed with non-Hodgkin’s lymphoma (62%), breast (68%), colorectal (64%) and prostate cancer (69%)).\(^{17}\) This may reflect the BC population (i.e., typically more deprived, more manual workers and lower literacy rates than other cancers).\(^{28}\) While respondents were willing to answer personal questions, response rates for sexual items were lower than for other domains. Details of disease stage were not available and treatment details were self-reported.
(and not verified from other sources) thereby reducing ability to interpret data in detail.

A major limitation was the removal by the survey developers of the ‘somewhat’ response option from the FACT-BI questionnaire, which meant that composite scores could not be calculated, thus affecting the interpretation of results. Although the removal of response options from validated measures is not considered good measurement practice, we were still able to gain important information about patients who had few or no problems and patients who had severe problems with individual items. Despite this limitation, it was considered important to present the findings as there is a lack of large-scale studies looking at all BC populations. A further limitation was that, as it was a pilot study, the sample was randomly identified, rather than population-based.

The results have been presented descriptively and multivariable analysis was not undertaken. The small number of respondents in some subgroups (e.g., in some of the treatment groups) and the lack of information on important confounders (such as a measure of socioeconomic deprivation) make it difficult to obtain robust, meaningful results.

Although more detailed analysis could not be carried out in this study, it is important that future studies aim to incorporate this. In particular, quantifying the impact of treatment-related issues (e.g., urinary, bowel, sexual problems or fatigue) on HRQL and social distress is hugely important, as this will further highlight the support and care needs of this group of patients, and indicate where there are gaps in service provision.

Recent qualitative work highlighted gaps in the understanding of HRQL of BC patients (particularly patients with NMIBC). Important themes included post-treatment experiences in terms of family/friend support networks, dealing with incontinence, voiding and catheterising, the ‘new normal’ (e.g., coping with their post-surgery body), changing sexuality and living with the lifelong threat of cancer. Although the authors recommend longitudinal qualitative work with BC patients, based on the results of the DH study, there is also a need to undertake quantitative work to understand how HRQL changes in BC patients over time. Future work should aim to identify both high risk groups and treatment-related items with the biggest impact on HRQL. This could potentially lead to PROMs being used as part of routine practice, with risk factors for low HRQL monitored in clinic.

A further recommendation for future BC PROMs work using FACT-BI is to include some validation work within the analysis. Although FACT-G is widely considered to be a reliable and valid tool to use with cancer patients, the bladder cancer-specific items require psychometric analysis to understand how useful these items are for use with BC populations. Alternatively, clinicians and researchers may choose other BC specific measures, such as the Bladder Cancer Index (BCI), or the European Organisation for Research and Treatment of Cancer (EORTC) NMIBC and MIBC modules.

These data represent the largest PROMs study to use BC specific PROMs. The results have highlighted groups at high risk of significant adverse consequences following BC diagnosis. However, there is a need to carry out larger in-depth population-based HRQL studies of BC patients to fully understand the extent of the morbidity burden experienced by survivors of BC.

ACKNOWLEDGEMENTS
We thank all the individuals who participated in this study and the National Cancer Registration and Analysis Service. The survey was administered by Picker Institute, Europe. This article is based in part on information collected and quality assured by Public Health England and NHS England. The data collection was funded by the Department of Health, England. Subsequent analysis was funded by Yorkshire Cancer Research (Award reference number: 5385—The Yorkshire Cancer Research Bladder Cancer Patient-Reported Outcomes Survey).

AUTHOR CONTRIBUTIONS
Study concept and design: J.C., M.R., and A.W.G.; acquisition of data: L.H.; analysis and interpretation of data: S.J.M., A.D., P.W., L.H., J.W.C., and A.W.G.; drafting of the manuscript: S.J.M., A.D., P.W., S.E.B., J.W.C., and A.W.G.; revised the manuscript: S.J.M., A.D., P.W., S.E.B., J.W.C., and A.W.G.; approved the manuscript: all authors.

ADDITIONAL INFORMATION
Supplementary information is available for this paper at https://doi.org/10.1038/s41416-018-0084-z.

Competing interests: The authors declare no competing interests.

Ethics approval and consent to participate: Permission to approach patients without informed consent was given by the Health Research Authority (ref ECC S-02 (FT7)/2012). Consent to participate was implied through return of completed questionnaires.

Availability of data and materials: The aggregated results of data analysis, STATA files and output for data extraction are available from the authors on request. Individual patient-level data used to generate results are not freely available, but may be applied for through the PHE Data Release (ODR).

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