

Humanistic Burden of Radical Cystectomy (RC) Among Patients with Non-Muscle Invasive (NMIBC) or Non-Metastatic Muscle Invasive Bladder Cancer (MIBC): A Systematic Literature Review (SLR)

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Objective



Conclusions

- To evaluate the evidence on the impact of radical cystectomy (RC) in patients with bladder cancer (BC) by assessing:
 - Changes in patient-reported outcomes (PRO) from baseline (prior to RC) to post RC
 - Changes in PROs over the course of the post RC follow-up for up to 15 years
 - PROs in patients post RC compared with patients treated with bladder-sparing therapies

- Despite heterogeneity in study designs and outcomes, patients showed a decline in health-related quality of life (HRQoL) following RC compared with patients with BC who did not undergo RC.
- Physical, role, social, and sexual functions, plus fatigue, bowel, and urinary symptoms, were often affected in patients who underwent RC, and did not always fully recover in the long term.
- The PRO results are hard to interpret in the context of clinically meaningful differences because the studies did not consistently report thresholds; some studies applied thresholds inappropriately (e.g., change from baseline comparisons made); and thresholds for subdomains were not always justified.
- PROs should be more robustly and consistently assessed to inform treatment decisions and enable the development of potential strategies to mitigate impact of treatment on patient's quality of life.



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Background

- Neoadjuvant chemotherapy followed by RC is the gold-standard treatment for muscle-invasive BC (MIBC) and for very high-risk non-MIBC (NMIBC) cases. RC consists of complete removal of the bladder and the nearby lymph nodes.^{1,2}
- Although RC is a curative treatment, it is a traumatic procedure associated with high complication rates and substantial changes in daily living and HRQoL.^{3,4}
- Bladder-sparing strategies for treating MIBC have recently emerged as an alternative to surgery in appropriately selected patients; one such example is trimodal therapy, which involves maximal transurethral resection of the bladder tumor followed by concurrent chemoradiotherapy.⁵

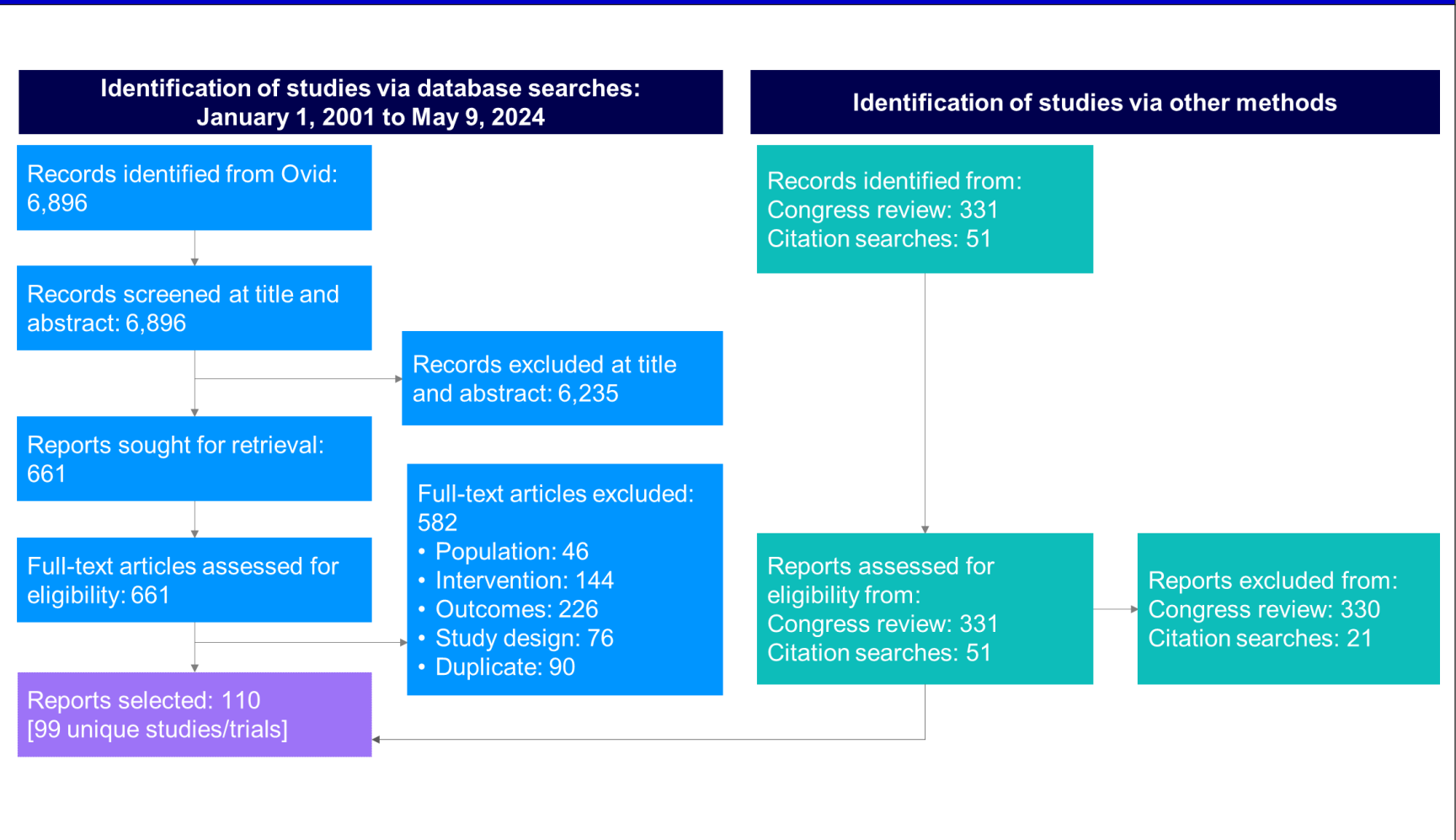
Materials and Methods

- A systematic literature review (SLR) of English-language studies published between January 1, 2001, and May 9, 2024, was conducted using the MEDLINE, Embase, Cochrane, and EconLit databases.
- The SLR identified clinical trials and real-world evidence (RWE) studies reporting HRQoL and PROs among patients with NMIBC or MIBC who underwent RC.
- Conference proceedings of the last two editions of relevant congresses were hand-searched to retrieve the latest studies not yet published in journals as full-text articles or supplementing results of previously published studies.
- Bibliographies of relevant SLRs and meta-analyses identified through database searches were also manually searched to identify key studies.

Results

- In total, 99 unique studies reported across 110 publications were included in the SLR (**Figure 1**).

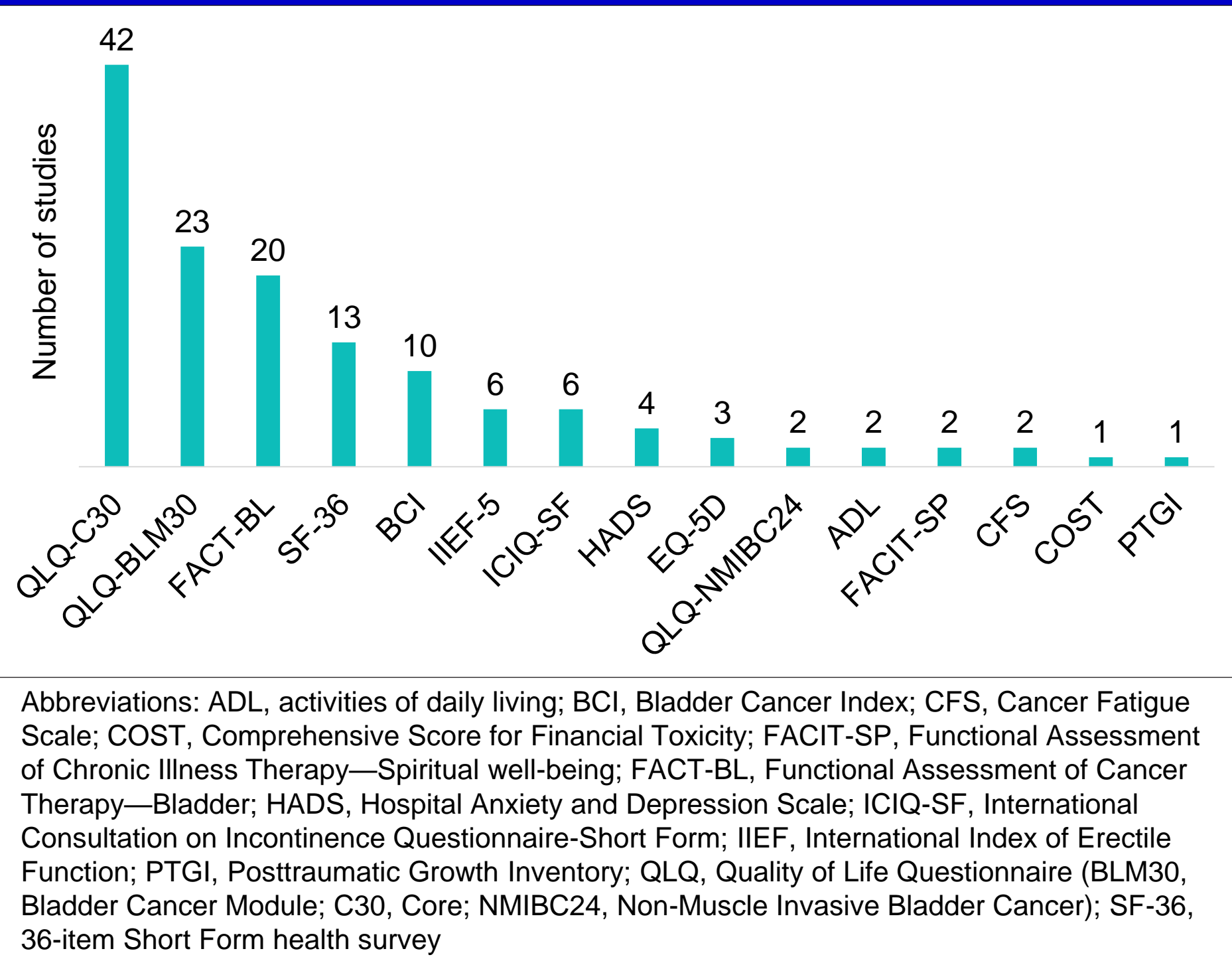
Figure 1. Literature attrition diagram



- Among the 99 included studies, 89 were RWE studies and 10 were randomized controlled trials.
- Populations included NMIBC (seven studies), MIBC (43), and mixed NMIBC/MIBC (49).
- The majority of studies were conducted in Europe (49%).
- The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core (EORTC QLQ-C30) was the most common instrument used across the studies (**Figure 2**).

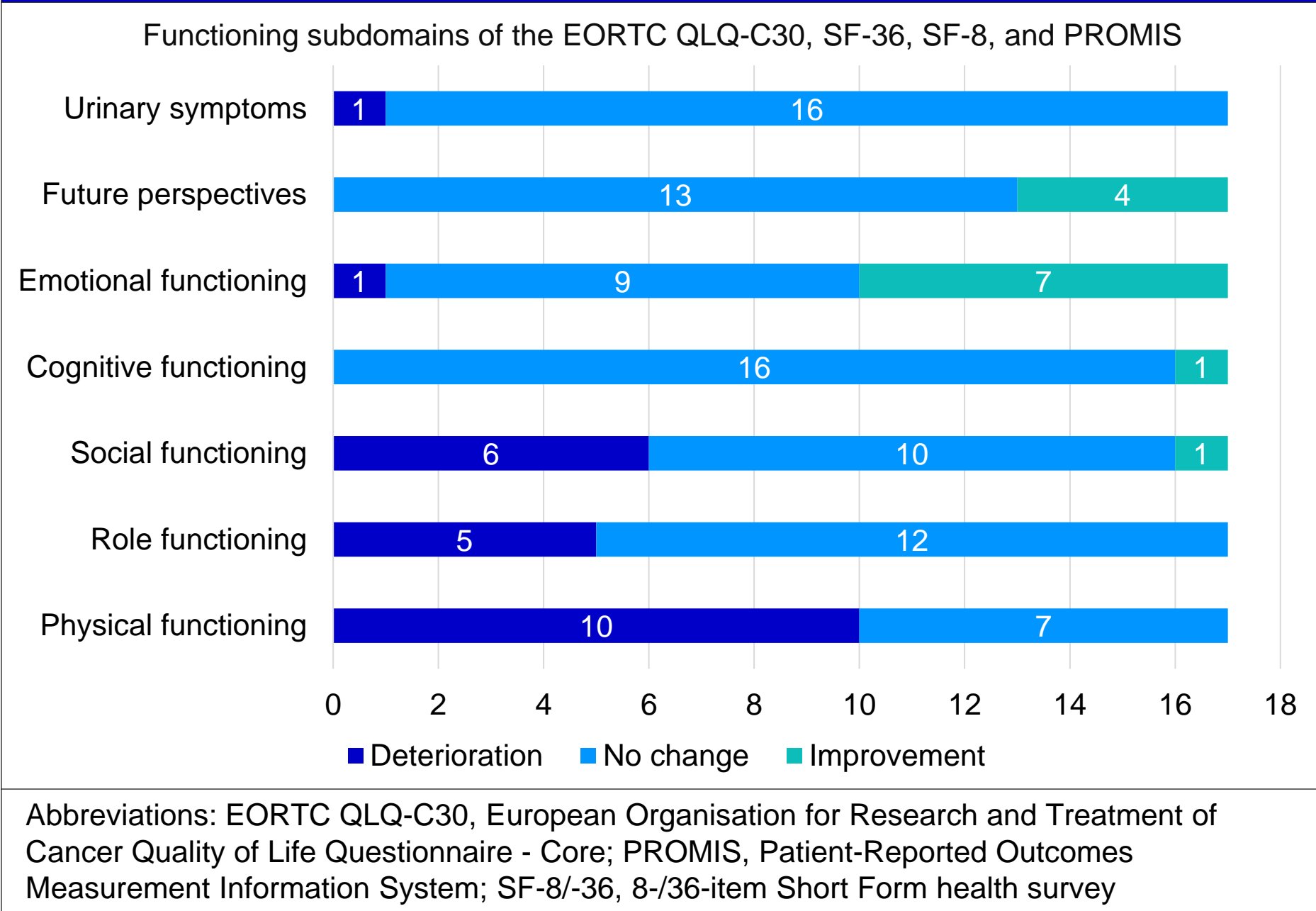
Results (cont.)

Figure 2. PRO instruments used across the included studies



- Overall, 84% of studies reported deterioration in HRQoL and an increased symptom burden post RC vs. pre-RC baseline. HRQoL decline often partially or fully recovered post RC.
- Physical, social, and role functioning declined, while emotional functioning, cognitive functioning, and future perspectives improved or remained constant vs. preoperative values (**Figure 3**). Studies consistently reported a decline in sexual function post RC that did not fully recover during follow-up.

Figure 3. Studies reporting changes in functional domains post-RC



- Scores on all functional domains of the EORTC QLQ-C30 were with clinically meaningful improvements higher at >1 year vs. ≤1 year of follow-up post RC: role, emotional and cognitive functioning (**Figure 4a**).
- For the EORTC QLQ-C30 global health status/quality of life (QoL) subscale, mean scores for the general populations in the United States, Canada, and Europe range from 63.9 to 66.1 (standard deviation ~20).
- For the global health status / QoL subscale of EORTC QLQ-C30 which measures overall health, the median score in study participants at ≤1 year of follow-up post RC was lower (63.7) but similar to that of the general population in N America/Europe (range 63.9-66.1 [standard deviation ~20])⁶ (**Figure 4a**).
- At >1 year follow-up, median global health status/QoL score (68.2) was higher vs. ≤1 year, indicative of an overall improvement in health over time post RC.
- The highest symptom burden at ≤1 year and >1 year follow-up was observed for the fatigue subdomain; the lowest burden was reported for the nausea/vomiting subdomain. Symptom subdomains with clinically meaningful improvements at >1 year post RC vs. ≤1 year post RC were fatigue, appetite loss, diarrhea and insomnia diarrhea after. (**Figure 4b**).
- The median scores for the constipation domain were numerically higher at >1 year compared with ≤1 year post RC follow-up but below the MID threshold. Scores for pain, dyspnea, and nausea/vomiting were comparable (**Figure 5**).
- On the BC module of the EORTC QLQ (EORTC QLQ-BLM30), the median scores with clinically meaningful improvements during >1 year post RC compared with ≤1 year post RC were catheter use and future perspectives.
- The subdomains with clinically meaningful deteriorations in score over time post RC were urostomy symptoms and body image domains and remained constant for the sexual functioning domain (**Figure 5**).

Figure 4. Median EORTC-QLQ-C30 scores following RC according to follow-up duration for functional domains (a) and symptom domains and items (b)

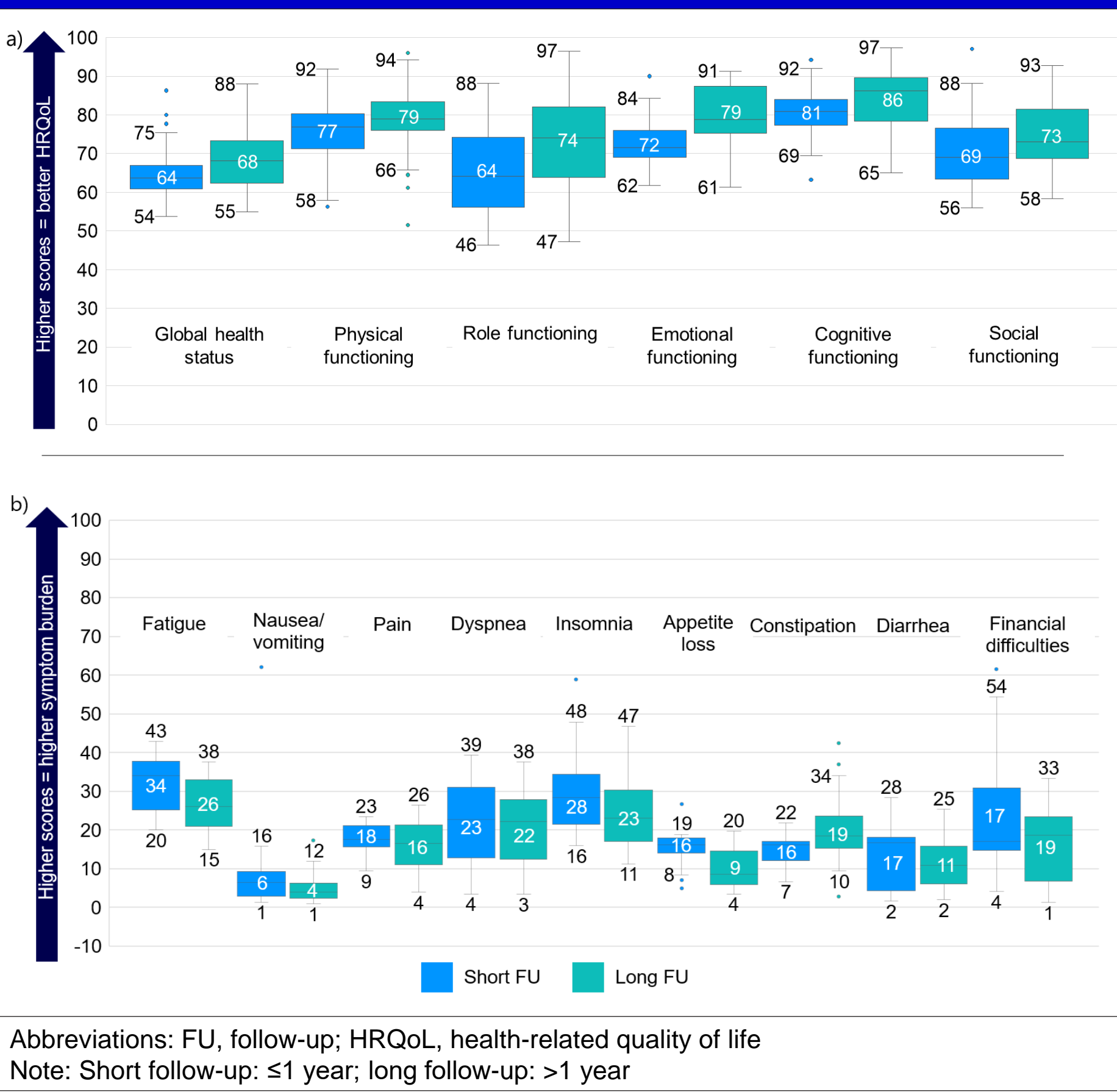
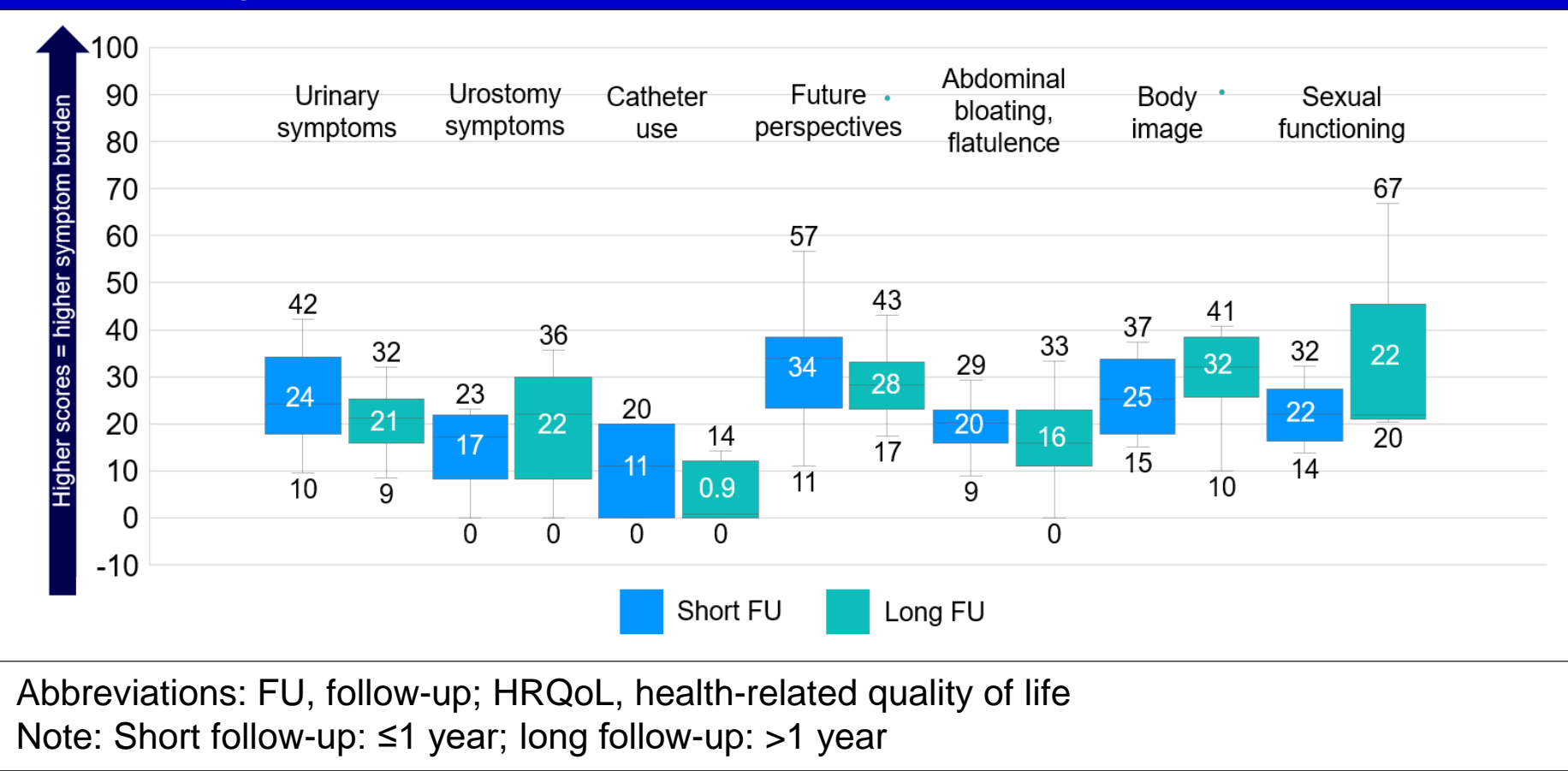
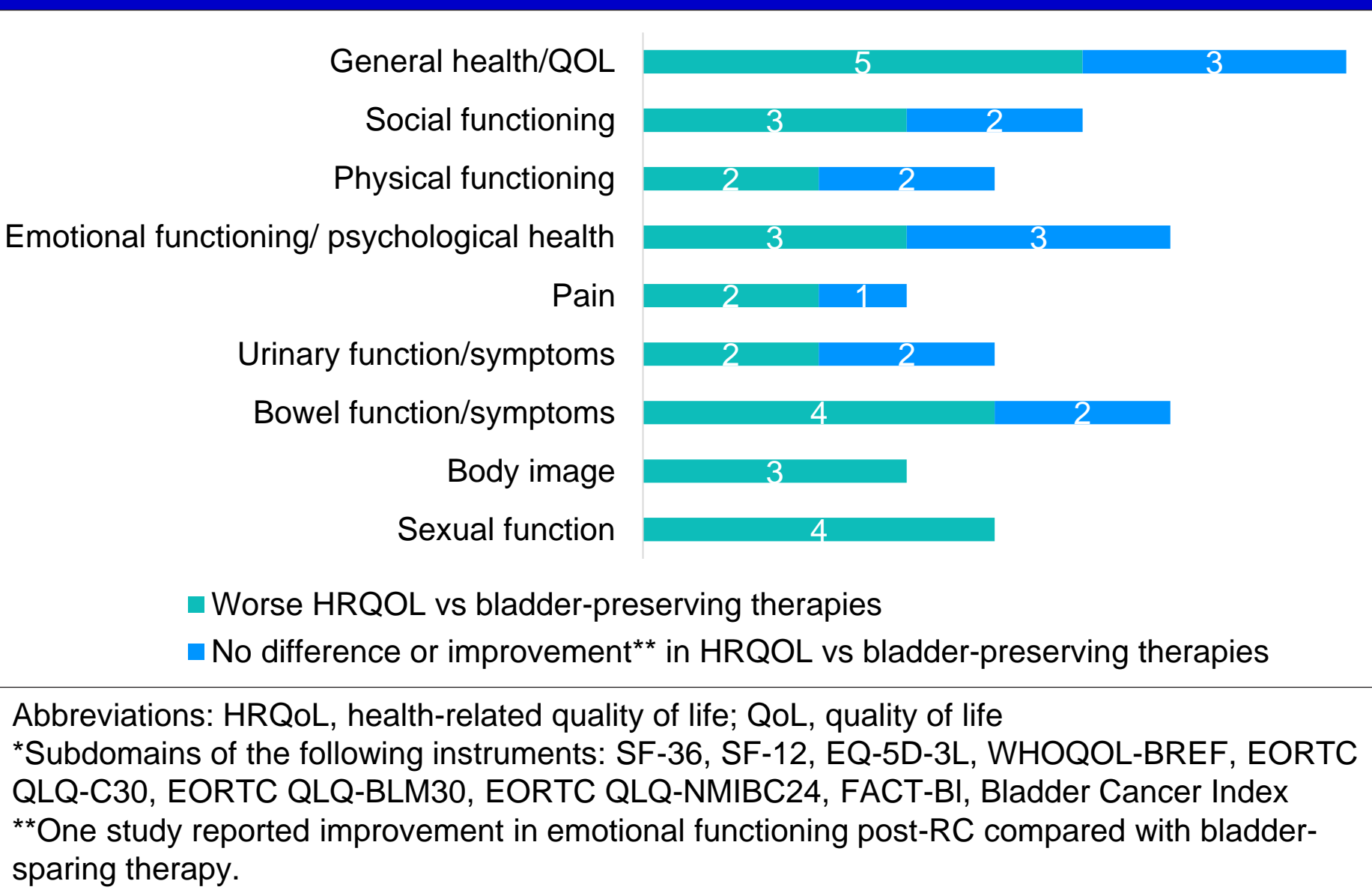


Figure 5. Median EORTC-QLQ-BLM30 score following RC according to follow-up duration



- More studies reported worse HRQoL among patients with RC vs. those treated with bladder-sparing therapies, particularly for sexual function, fatigue, bowel symptoms, pain, body image, social functioning, and general health/QoL, whereas physical and emotional functioning were similar or improved (**Figure 6**).

Figure 6. Studies comparing HRQoL across subdomains* in patients with RC vs. patients treated with bladder-sparing therapies



Limitations

- Some studies were published as abstracts only, providing limited data.
- Studies were highly heterogenous regarding instruments used and methods of assessing and reporting changes in PROs. Therefore, comparisons between studies should be cautioned.
- Some studies did not perform or provide a formal statistical analysis for the PROs assessments and conclusions on improvement or deterioration for PROs were purely descriptive.
- Changes and differences in PROs were often not presented in the context of clinically meaningful MID thresholds.



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