# A systematic literature review of real-world treatment effectiveness and economic and humanistic burden in patients with muscle-invasive bladder cancer

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## Objectives

- This SLR evaluated real-world treatment effectiveness and economic and humanistic burden in patients with MIBC who received RC with or without NAC or AC, in order to characterize unmet need in these patients.

## Conclusions

- Patients with MIBC who receive either NAC + RC or RC alone experience a high economic and humanistic burden.
- While NAC or AC may improve outcomes for some patients, this SLR suggests that OS remains poor.
- Given its historically low uptake[4] and that not all patients can tolerate NAC,[5] together with the poor survival with NAC and AC, more effective treatments are needed.

## Background

- Muscle-invasive bladder cancer (MIBC) has a poor prognosis, with half of patients developing metastases.[1]
- National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines recommend patients with MIBC receive radical cystectomy (RC) and that patients eligible for cisplatin receive cisplatin-based neoadjuvant chemotherapy (NAC) prior to RC, as it has been shown to improve survival. Adjuvant chemotherapy (AC) may be considered for patients with high-risk pathology.[33,34]
- However, only 50% of patients with MIBC are eligible for NAC, and prior real-world studies have indicated there is a relatively low uptake of NAC and AC in patients with MIBC.[4,5]
- Improved understanding of the real-world effectiveness and burden of available treatments for patients with MIBC would help inform the development of alternative treatment options for these patients.

## Methods

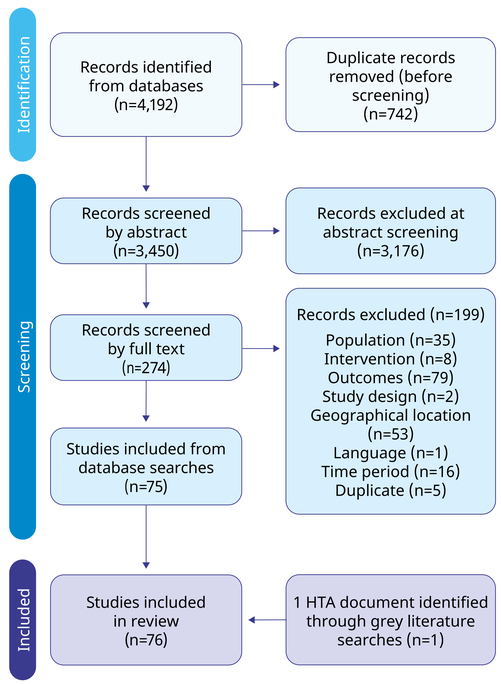
- The systematic literature review (SLR) was conducted in accordance with guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the National Institute for Clinical Excellence (NICE) Decision Support Unit guidance for evidence synthesis and decision-making.[6,7]
- Literature searches identified real-world studies of adult patients with MIBC who received RC; included studies were published in English between January 2018 and June 2023.
- Searches were performed in the following databases: Embase, MEDLINE, EconLit, PsycINFO, and Cochrane Libraries.
- A manual search of the reference lists of relevant SLRs and targeted literature reviews identified from the database searches was performed to ensure retrieval of any relevant publications not otherwise captured.
- Title, abstract, and full-text screening was conducted by 2 independent investigators, with any disagreements resolved by discussion with a third investigator.
- Abstracts and full-text publications were screened for those reporting real-world effectiveness (including median overall survival [mOS], progression-free survival [PFS], recurrence-free survival [RFS], and time to cystectomy), economic burden, and humanistic burden.
- Excluded studies were those reporting on patients who underwent bladder-sparing treatment or those where the treatment was unclear.
- Studies were restricted to those from the US, UK, Germany, France, Italy, and Spain, with a sample size of ≥100 patients.

## Results

### STUDY SELECTION

- Of 4,192 references identified, 76 were included following screening (**Figure 1**). Of these, 61 reported real-world effectiveness, 12 economic burden, and 5 humanistic burden.
- The majority of references (n=53) were from the US, 18 were from Europe (Germany, France, Italy, Spain, or UK), and 5 were multinational.

**Figure 1. Flow diagram of included studies**




HTA, health technology assessment.

### REAL-WORLD EFFECTIVENESS

- 61 studies reporting on real-world effectiveness were identified, of which 43 reported OS data.
  - The range of reported real-world OS at 3 years and 5 years and mOS for patients treated with RC alone or NAC + RC are shown in **Figure 2**.
  - In one US study, patients treated with RC + AC had worse OS than patients treated with NAC + RC (HR, 1.40; 95% CI, 1.23-1.60).[39]
- 5 studies reported on RFS, which was defined as the measure from date of RC to time of clinical recurrence or date of last follow-up. Among these studies, Boeri et al reported that 5-year RFS across patient groups was highest (56.2%) among patients who underwent >3 cycles of NAC (optimal NAC).[12]
  - 5-year RFS was 48.9% in patients who did not receive NAC and 46.8% in patients who underwent <3 cycles of NAC (suboptimal NAC).[12]
- PFS (defined as time from RC or administration of NAC until disease progression or death) was reported in 3 studies and similarly demonstrated a lower risk of progression in patients who received NAC + RC compared with RC alone.[32]
- 4 studies reported on time from the last cycle of NAC to RC.
  - Boeri et al reported that patients with time to cystectomy ≤10 weeks had significantly lower mortality than patients with time to cystectomy >10 weeks.[14]

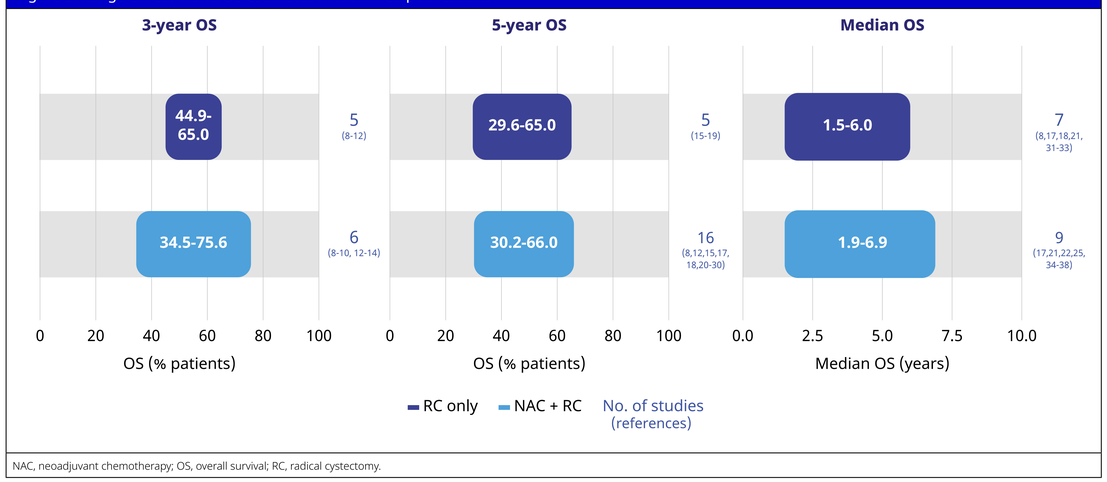
### ECONOMIC BURDEN

- 12 studies reported economic burden (9 were from the US), with 7 reporting direct costs and 5 length of hospital stay following treatment.
- 7 studies reported direct costs associated with MIBC for patients who underwent RC.
  - Costs associated with RC in the US are shown in **Figure 3**,[40-42] with inpatient costs post-RC reported to make up a large component of total costs.[40]
  - Négrier et al reported mean overall costs of a first RC hospital stay of patients with MIBC or upper tract urothelial cancer in France as €11,756.[43]
- The median length of hospital stay for patients undergoing RC ranged from 3.0 to 9.6 days.[24,44-47]
  - Posielski et al reported median length of stay of 9.6 days with RC only, compared with 8.5 days with NAC + RC among patients aged ≥70 years.[24]

### HUMANISTIC BURDEN

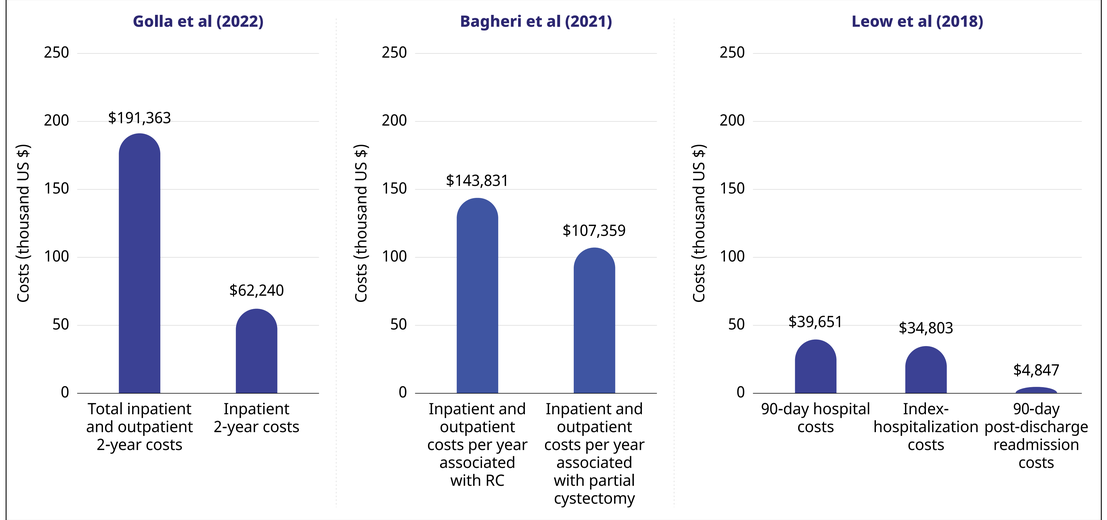
- Humanistic burden was reported in 5 cohort studies: 1 in the US and 4 in Germany.
- Health-related quality of life decreased following either NAC + RC or RC alone during a follow-up period of 1 to 12 years, with fatigue, nausea, and appetite loss among the common symptoms affecting patient quality of life.[48-52]
- Among patients undergoing RC, those treated with NAC had better emotional and mental health than patients who did not receive NAC.[48]

**Figure 2. Range of real-world OS estimates in identified publications**




NAC, neoadjuvant chemotherapy; OS, overall survival; RC, radical cystectomy.

**Figure 3. Economic burden—costs associated with RC in the US**




RC, radical cystectomy.

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