Healthcare Cost, Resource Use, and Economic Models of Cisplatin-Ineligible Muscle-Invasive Bladder Cancer Patients (MIBC)

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Introduction & Objective

- Muscle-invasive bladder cancer (MIBC) is characterized by high mortality and relapse, with limited treatment options due to toxicity of standard therapies and poor outcomes from surgery alone in cisplatin-ineligible patients.[1,2]
- **Objective**: To conduct a systematic literature review (SLR) evaluating direct and indirect costs, healthcare resource utilization (HRU), and cost-effectiveness among patients with cisplatin-ineligible MIBC.

Methods

- The SLR was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, the Centre for Reviews and Dissemination, and the Cochrane Collaboration guidelines.[3,4]

Eligibility Criteria

- Eligibility criteria were defined using the PICOS (Patients, Interventions, Comparators, Outcomes, Study Design) framework

Table 1. Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria
Population	Adult patients (≥18 years) with cisplatin-ineligible MIBC	Non-MIBC populations
Intervention/ Comparator	NA	NA
Outcomes	ICERs, QALYs, cost per QALY gained, healthcare costs, and resource use	Studies not reporting relevant outcomes
Study Design	Observational studies and economic models	Non-observational and non-economic model designs
Other	English-language publications from the US, Canada, and EU-5, published between 2015–2025	Non-peer-reviewed publications and out-of-scope geographies

Abbreviations: EU-5, European Union 5 (France, Germany, Italy, Spain, United Kingdom); ICER, Incremental Cost-Effectiveness Ratio; MIBC, Muscle-Invasive Bladder Cancer; NA, Not Applicable; QALY, Quality-Adjusted Life Year; US, United States

Information Sources

- Searches were conducted in Embase, MEDLINE, EconLit through the OVID platform, using free-text and controlled vocabulary.

Study Selection

- Abstracts were independent screened by two reviewers, with inclusion determined by consensus. The same process was applied for full-text screening.

Data Extraction and Critical Appraisal

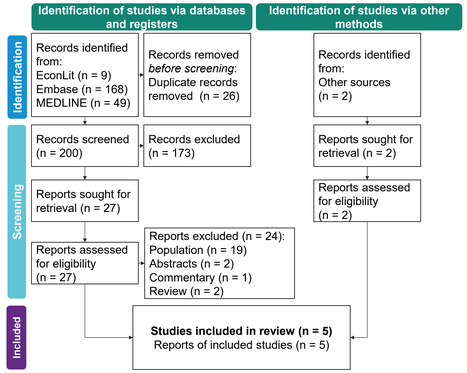
- Data were extracted into standardized templates capturing costs, HRU, and economic outcomes, with independent validation.
- Critical appraisal was conducted using the Drummond Checklist.[5]

Results

Literature Search Findings

- 226 records identified (Dec 9, 2025); 26 duplicates removed (n = 200 screened), 173 excluded, 27 full-text assessed, 24 excluded (population n = 19; secondary literature n = 5), **5 studies included** (3 database[6,7,10], 2 additional sources[8,9] [Google Scholar]).

Figure 1. PRISMA Flow Diagram



Included Studies and Study Characteristics

- **5 studies included**: 4 cost-effectiveness models and 1 US claims-based analysis
- 4 studies reported costs; 1 reported HRU only

Table 2. List of Included Studies

Study & Country	Study Design	Model Type	Reference Year (Currency)	Drummond Checklist
Squires 2025 (US)	Cohort (claims database)	NA	2022 (USD)	NA
Khaki 2021 (US)	CEA	Decision analytic simulation	2020 (USD)	9
Cheung 2025 (Canada)	CUA	Microsimulation (Canadian policy)	NR (CAD)	7
Hale 2020 (US)	CUA	3-state partitioned survival	2018 (USD)	9
Wu 2025 (UK)	CUA	Markov model	2024 (GBP)	9

Abbreviations: CAD, Canadian Dollar; CEA, Cost-effectiveness analysis; CUA, Cost-utility analysis; GBP, Great Britain Sterling; NA, Not Applicable; NR, Not reported; UK, United Kingdom; US, United States; USD, United States Dollar

HealthCare Costs

- Immune checkpoint inhibitors **(ICIs) had higher costs than chemotherapy** in the US[8]
- Enfortumab vedotin + pembrolizumab (**EV+P**) had **substantially higher costs versus** gemcitabine + cisplatin (**GCIs**)[9,10]
- **BC-related costs** were **higher in patients with versus without recurrence** ($3,649 vs $766 PPPY).

Table 3. Healthcare Costs

Study & Country	Treatment / Group	Total Cost	Incremental Cost
Cheung 2025 (Canada)	GCis	$261,296	Reference
	N+GCis	$455,513	$194,217
	EV+P	$769,262	$507,966
Hale 2021 (US)	GCarb	$66,773	Reference
	Pembro	$225,334	$158,561
Squires 2025 (US)	With recurrence	$10,324	NR
	Without recurrence	$3,662	
Wu 2025 (UK)	Platinum-based chemo	£40,875	Reference
	EV+P	£121,214	£80,339

Abbreviations: EV+P, enfortumab vedotin + pembrolizumab; GCarb, gemcitabine-carboplatin; GCis, gemcitabine-cisplatin; N, nivolumab; NR: Not Reported; Pembro, Pembrolizumab

Quality-Adjusted Life Years (QALY)

- **EV+P** showed **the highest QALY gains** (+1.24–1.35 **versus chemotherapy**, UK/Canada)[9,10]
- **Pembrolizumab gained +2.01 QALYs versus GCarb** in the US[8]

Table 4. QALY by Study

Study & Country	Treatment	QALY	QALY Gain
Cheung 2025 (Canada)	GCis	1.57	Reference
	N+GCis	1.96	0.39
	EV+P	2.92	1.35
Hale 2021 (US)	GCarb	0.90	Reference
	Pembro	2.91	2.01
Wu 2025 (UK)	Chemo	1.41	Reference
	EV+P	2.65	1.24

Abbreviations: EV+P, Enfortumab vedotin + pembrolizumab; GCarb, Gemcitabine + Carboplatin; GCis, Gemcitabine + Cisplatin; N, Nivolumab; Pembro, Pembrolizumab; QALY, Quality Adjusted Life years

Incremental Cost-Effectiveness Ratio (ICER)

- **EV+P ICERs**: **$375,170** (Canada) and **£64,772** (UK)[9,10]
- In the US, **atezolizumab was dominant versus ddMVAC**; **pembrolizumab achieved $78,925/QALY versus GCarb**; others exceeded thresholds.[6,8]

Table 5. ICER by Study

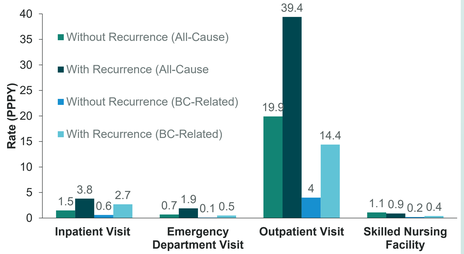
Study & Country	Treatment	ICER
Cheung 2025 (Canada)	GCis	Reference
	N+GCis	$499,448
	EV+P	$375,170 (*extended dominance over N+GCis*)
Khaki 2021 (US)	ddMVAC	Reference (Primary Analysis)
	GCis	Reference (Secondary Analysis)
	Pembro	$552,143 / $1,225,058
	ATZ	Dominant / Secondary: $1,629,855
	N+I	$1,464,119 / $1,662,327
Hale 2021 (US)	GCarb	Reference
	Pembro	$78,925/QALY gained vs GCarb
Wu 2025 (UK)	Chemo	Reference
	EV+P	£64,772

Abbreviations: ATZ, Atezolizumab; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin (adriamycin), and cisplatin; EV+P, Enfortumab vedotin + pembrolizumab; GCarb, Gemcitabine + Carboplatin; GCis, Gemcitabine + Cisplatin; I, Ipilimumab; ICER, Incremental Cost- Effectiveness Ratio; N, Nivolumab; Pembro, Pembrolizumab

Healthcare Resource Utilization

- **Recurrent MIBC had higher HRU compared** with those **without recurrence** (e.g., inpatient 2.7 vs 0.6 PPPY)[7]

Figure 2. Healthcare Resource Utilization by Recurrence Status



Abbreviations: Abbreviations: BC, Bladder cancer; PPPY, per patient per year

Key Findings

- EV+P provides the highest QALYs
- Cost-effectiveness varies by country
- Only ATZ is cost-effective in the US
- EV+P has higher costs vs chemotherapy
- Recurrence increases HRU and costs

Limitations

- Study heterogeneity (model, data sources, time horizons, currencies) limits comparability
- Differences in modeling approaches (partitioned survival, Markov, microsimulation) reduce consistency
- Heavy reliance on trial-based inputs for cost and utility (e.g., KEYNOTE) limits real-world relevance
- Long-term extrapolation introduces structural uncertainty
- Lack of head-to-head comparisons increases ICER uncertainty
- Limited evidence base (n=5; US/UK/Canada) restricts generalizability

Conclusions

- EV+P showed the highest QALY gains, but cost-effectiveness varied by jurisdiction
- ICI and ADC regimens improved economic outcomes vs chemotherapy
- In the US, only atezolizumab was cost-effective; others exceeded thresholds
- Recurrence drove higher HRU, highlighting the burden of progression
- Standardized models and real-world data are needed to improve future analyses

References

Scan the following QR code for the reference list:

Disclosure and Acknowledgements

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