Cost-Effectiveness Analysis of Denosumab for the Treatment of Bone Metastases: A Systematic Literature Review

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INTRODUCTION

Bone metastases develop in approximately 65–75% of patients with breast and prostate cancer and 15–40% of those with lung cancer, colon cancer or multiple myeloma, causing skeletal-related events (SREs): pathological fractures, spinal cord compression, and the need for radiotherapy or surgery.

SREs carry a heavy clinical and economic burden. Bisphosphonates (zoledronic acid, ZA) and denosumab are the main agents used to prevent SREs, but the cost-effectiveness of denosumab remains uncertain and depends on local prices, dosing and comparators. [1,3]

OBJECTIVE

To systematically review the published economic evidence on denosumab for SRE prevention in adults with solid or haematological cancers and bone metastases.

Population: Adults with cancer and bone metastases

Intervention: Denosumab vs comparators (e.g. ZA)

Outcome: Total cost, total QALY, incremental cost, incremental QALY, ICER

METHOD

1. **Search**
Embase, PubMed and Google Scholar; original articles 2016–2026. Keywords: cost-effectiveness analysis, denosumab, bone metastases, multiple myeloma, ICER, QALY
2. **Screen**
Two reviewers independently, following Cochrane and PRISMA guidance
3. **Extract**
Two reviewers independently extracted study, model, cost and outcome data
4. **Appraise**
Quality assessed with the 36-item Drummond checklist

RESULTS

8
evaluations: 6 solid tumour, 2 multiple myeloma

USA: 3 · Canada: 1 · India: 1
Czech Republic: 1 · Malaysia: 1
Multiple countries: 1

Markov models: 5
Partitioned survival: 1
Partitioned survival + Markov: 1
Decision tree: 1

≥80%
of Drummond criteria met by all 8 studies

Table 1. Characteristics of included studies (n=8)

Study	Setting / perspective	Comparator	Model	Horizon
Cristino 2017[5]	Czech Republic; payer	ZA	Markov	Lifetime
Farhana 2019[7]	Malaysia; Ministry of Health	Usual care, ZA q12w	Markov	Lifetime (~7 years)
Raje 2018[8]	USA; societal and payer	ZA q4w	Partitioned survival	Lifetime
Shapiro 2017[2]	USA; payer	ZA monthly, ZA q3m	Markov	2 years
Stopeck 2020[1]	USA; societal and payer	ZA, no treatment	Markov	Lifetime
Terpos 2019[6]	Austria, Belgium, Greece, Italy; national healthcare system	ZA q4w	Partitioned survival semi-Markov	Lifetime
Tu 2021[4]	Canada; healthcare system	4- vs 12-weekly BTA	Decision tree	1 year
Wadhwa 2024[3]	India; societal	ZA q4w, ZA q12w	Markov	Lifetime

Table 2. Key cost-effectiveness findings (n=8)

Study	Key quantitative result	Conclusion
Cristino 2017[5]	ICER 382,673–608,133 CZK/QALY; ΔQALY 0.0423–0.0926	Denosumab cost-effective across tumor types
Farhana 2019[7]	ΔQALY 0.17; ICER RM 114,068/QALY vs ZA (WTP RM 42,688)	Not cost-effective vs ZA; ZA q12w most cost-effective
Raje 2018[8]	ΔQALY 0.244; ICER $107,939 societal and $120,569 payer	Denosumab cost-effective (WTP $150,000/QALY; multiple myeloma)
Shapiro 2017[2]	ΔCost $47,910–$51,533; ΔQALY −0.02 to −0.03	ZA q3m dominates
Stopeck 2020[1]	ΔQALY 0.128; ICER $70,730 societal and $104,778 payer	Denosumab cost-effective
Terpos 2019[6]	ΔQALY ≈0.18–0.25; ICER €6,982 (Greece) to €27,228 (Italy)/QALY	Denosumab cost-effective in all 4 countries (multiple myeloma)
Tu 2021[4]	ΔCost −C$3,293.75; ΔQALY +0.008; INB C$3,681	12-weekly BTA dominates 4-weekly treatment
Wadhwa 2024[3]	ΔQALY 0.01–0.02; ICER ₹30.9M–₹45.4M/QALY vs ZA q12w	Not cost-effective; ZA q12w preferred

Figure 1. Czech Republic: denosumab vs ZA, ICER by tumour type vs WTP threshold (CZK '000/QALY)

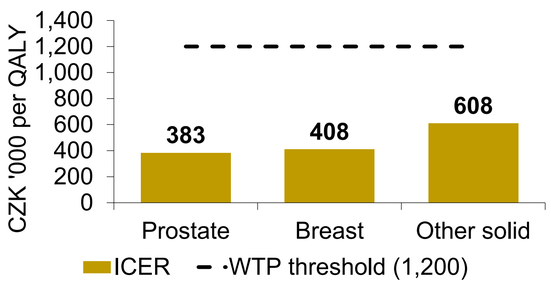


Figure 2. India: denosumab q4w vs ZA q12w, ICER by breast cancer subtype (₹ million/QALY)

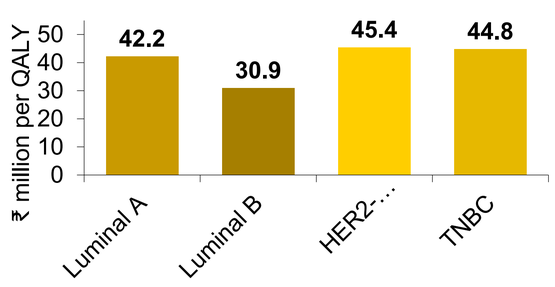


Figure 3. Drummond checklist: methodological quality (Yes responses, % of 36 items). *Estimated from extracted data

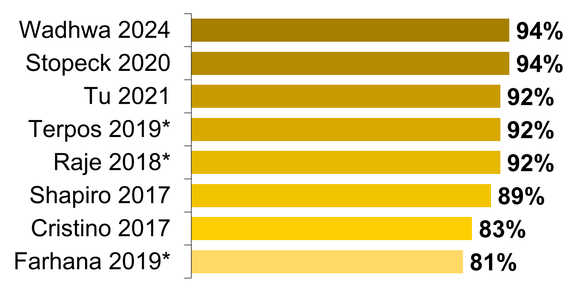
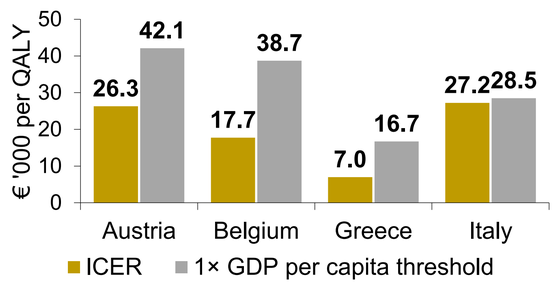


Figure 4. Multiple myeloma (Terpos 2019): denosumab vs ZA, ICER vs 1× GDP per capita threshold (€ '000/QALY)



CONCLUSIONS

- **Denosumab's cost-effectiveness for preventing SREs was highly context-dependent** across 8 evaluations (6 solid tumour, 2 non-solid tumours/haematological malignancies, specifically multiple myeloma), varying by country, comparator, dosing strategy and willingness-to-pay threshold.
- **Denosumab was cost-effective vs ZA in 4 of 8 evaluations** (USA, Czech Republic, and multiple myeloma in the USA and four European countries), but **not in India or Malaysia** at the reported thresholds; in a second US analysis, ZA every 3 months dominated denosumab.
- **Extended-interval ZA (every 12 weeks)** emerged as a potentially cost-effective alternative to more frequent dosing in selected settings (India, Malaysia, Canada).
- Despite generally **high methodological quality** (all studies met ≥80% of Drummond criteria), inconsistencies in reporting productivity costs and statistical uncertainty highlight areas for improvement in future economic evaluations.

Abbreviations: BTA, bone-targeted agent; CZK, Czech koruna; ICER, incremental cost-effectiveness ratio; INB, incremental net benefit; QALY, quality-adjusted life-year; SRE, skeletal-related event; WTP, willingness to pay; ZA, zoledronic acid.

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