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Research Article

Keywords: denosumab, discontinuation, rebound fractures, zoledronic acid, cost-effectiveness analysis, osteoporosis

Posted Date: November 23rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11334919/v1

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Additional Declarations: No competing interests reported.

Managing the exit from denosumab: cost-effectiveness of a structured discontinuation pathway in the United States and China — a microsimulation and transferability analysis

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Abstract

Background: Unmanaged denosumab cessation triggers rebound fractures, yet few patients who discontinue receive follow-on therapy. We estimated the cost-effectiveness of a structured discontinuation management pathway versus usual care in the United States and China.

Methods: A lifetime microsimulation followed 70-year-old women with postmenopausal osteoporosis on denosumab under identical real-world persistence decay. The pathway delivered scheduled zoledronate bridging plus monitoring to 60% of discontinuers; usual care included spontaneous delayed sequencing. Fracture risk combined FREEDOM effects with a cessation rebound curve; bridging efficacy came from nationwide claims and trial evidence. Inputs were localized for Medicare and Chinese payer settings. Analyses were deterministic, probabilistic, one-way, scenario, subgroup, and transferability decomposition.

Results: The pathway yielded +0.0236 quality-adjusted life-years (QALYs) at +$101 per person in the United States (incremental cost-effectiveness ratio [ICER] $4,280/QALY) and +0.0144 QALYs at +¥2,260 in China (ICER ¥157,451/QALY; between 1× and 2× GDP per capita). It was more effective in 100% of draws in both settings. In patients with prior vertebral fracture, the pathway was dominant in the United States and below 1× GDP in China. No sensitivity analysis reversed the conclusion. The cross-setting gap was driven chiefly by fracture unit costs, discounting, and fracture epidemiology, partly offset by China's lower drug prices. Indefinite continuation was not cost-effective in the United States ($281,277/QALY).

Conclusions: Managing the discontinuation that already occurs in practice is high-value in the United States and cost-effective in China at conventional thresholds, prioritizing high-risk discontinuers. Uncertainty concentrates in implementation quality, not disease natural history.

Keywords: denosumab; discontinuation; rebound fractures; zoledronic acid; cost-effectiveness analysis; osteoporosis

Background

Denosumab, a human monoclonal antibody against RANKL, reduces vertebral fractures by 68% and hip fractures by 40% over three years in postmenopausal women with osteoporosis [1]. Its pharmacology, however, makes cessation hazardous: bone turnover markers rebound above pretreatment levels within months of the last dose, bone mineral density gains are rapidly lost, and case series and claims analyses report a clustering of multiple vertebral fractures 8–16 months after discontinuation, with a 3- to 5-fold higher fracture risk than under continued treatment [2, 3].

Guidelines from the Endocrine Society, ECTS, and Chinese societies converge on a clear recommendation: denosumab should not be stopped without follow-on antiresorptive therapy, with intravenous zoledronic acid typically scheduled 6–8 months after the last dose [4, 5]. Real-world practice falls dramatically short of this standard. Two-year persistence with denosumab is approximately 45%, and in a 20% sample of Medicare beneficiaries only 6.0% of discontinuers initiated any follow-on osteoporosis therapy within one year of stopping [6]; a Korean nationwide claims analysis found 22.9% [7]. For China, no post-cessation sequencing data exist at all. The population exposed to unmanaged cessation is large and growing: denosumab biosimilars launched in the United States and Europe in 2025, and denosumab is reimbursed under China's national drug list, so price-driven expansion of use will be followed by an expansion of discontinuation.

Existing economic evaluations have not engaged with this problem, because they assume perfectly executed treatment sequences. The closest prior model (China, payer perspective) restricted zoledronic acid sequencing to patients who completed three years of denosumab, assumed 100% compliance, and assigned a fixed one-year residual effect — thereby assuming away both non-adherence and the rebound phenomenon [8]. A Taiwanese evaluation compared continuation with discontinuation but was industry-funded and did not model a management program [9]. To our knowledge, no economic evaluation has asked what it is worth to manage, rather than ignore, the discontinuation that actually occurs. Nor is it known whether the answer transfers between a high-price, high-threshold system (United States) and a low-price, low-threshold one (China) — a question of practical relevance to every middle-income country adopting denosumab.

We therefore developed a lifetime microsimulation to estimate the cost-effectiveness of a structured discontinuation management pathway versus usual care among postmenopausal women who stop denosumab in routine practice, in the United States and China, with indefinite continuation as a reference arm; and we decomposed the cross-country difference in cost-effectiveness into its parameter-level drivers.

Methods

Model overview

An individual-level state-transition microsimulation with 6-month cycles (matching the denosumab dosing interval) and a lifetime horizon (age 105 or death) was implemented in Python (NumPy). The US analysis adopted a Medicare payer perspective with 3% annual discounting; the China analysis a Chinese payer perspective with 5% annual discounting per Chinese pharmacoeconomic evaluation guidelines [10]. Costs and QALYs accrue at mid-cycle. Cohorts of 100,000 individuals per arm were simulated in the base case (10,000 per iteration in probabilistic analysis). Reporting follows the CHEERS 2022 statement [11] (checklist in Additional file 2). All parameters reside in versioned registries; no individual-level data were used. Arms within each analysis share common random numbers (variance reduction); across six independent seeds the base-case ICER varied only between $3,360 and $4,280.

Population and arms

The cohort comprised 70-year-old women with postmenopausal osteoporosis resembling the FREEDOM trial population (T-score ≤ -2.5 or prior vertebral fracture; 24% with baseline prevalent vertebral fracture), already one year into denosumab therapy. All arms share identical piecewise-annual-hazard persistence decay calibrated to published real-world rates (81% on-treatment at 1 year, 45.5% at 2 years), corroborated for year 1 in an Asia-Pacific real-world study (82.7%) [12].

Arm A (usual care). Discontinuation occurs stochastically as above. On stopping, a minority spontaneously begin a bisphosphonate after a median 12-month delay with attenuated effectiveness: 12% in the US (scenario range 6%–63% spanning Medicare, Korean, and specialist-cohort rates) and 15% in China (no national data exist; the base case is the conservative midpoint of the 6%–23% international range).

Arm B (structured discontinuation management). Discontinuation timing is identical to usual care — the program manages the consequences of cessation, not the decision to stop. At any discontinuation event, 60% (scenario range 40%–90%) receive a single zoledronic acid infusion scheduled 6 months after the last denosumab dose, delivered through a registry-and-reminder system with CTX monitoring (3 years of program cost).

Arm C (indefinite continuation; reference). Denosumab is continued for life; a sensitivity scenario applies real-world persistence to this arm.

Fracture risk engine

For each 6-month cycle, site-specific fracture incidence (clinical vertebral, hip, other major osteoporotic) is the product of (i) a baseline rate at age 70 (US: FREEDOM placebo arm [1]; China: localized — hip 150 per 100,000 per year from the national urban claims study, roughly one-third of the corresponding US white female rate [13]), scaled exponentially with age; (ii) a history multiplier (prevalent fracture ×2.2; 1.45 per subsequent vertebral fracture; post-hip ×1.3); and (iii) a treatment multiplier. While on denosumab the multiplier equals the FREEDOM relative risks (0.32, 0.60, 0.80) [1]. After cessation, a time-since-cessation rebound curve applies — 0.6, 1.3, 1.8, 1.4, 1.1 (vertebral) for 0–6, 6–12, 12–24, 24–30, and >30 months off treatment — expressed relative to the untreated baseline, reproducing a discontinuation-versus-on-treatment ratio of ~4–5.6 consistent with the Anastasilakis synthesis (3–5×) [2] and the FREEDOM discontinuation analysis (~6×) [14]. Bridging multiplies the rebound curve by a suppression coefficient: 0.40 for program-delivered zoledronate (HORIZON efficacy [15] attenuated for incomplete post-denosumab BMD protection [16, 17]) and 0.70 for spontaneous sequencing (anchored to the Korean nationwide estimate of sequencing versus no sequencing, adjusted HR 0.703, 95% CI 0.641–0.771 [7]). Suppression wanes after a 4-year zoledronate duration of effect.

Hip fracture carries a first-year excess mortality of 0.18 and vertebral fracture a 2-year excess mortality of 0.04 per year [18, 19]. Age-specific all-cause mortality follows a Gompertz approximation to national female life tables (0.020 per year at age 70 in the US, 0.018 in China, doubling every 8 years) [20]. Health-state utilities and fracture disutilities follow published estimates [21]; the Chinese baseline utility (0.93) uses EQ-5D-5L population norms [22, 23]. Costs (2025 USD; 2025 CNY) are itemized in Table 1: US fracture costs from published burden-of-illness analyses [24]; Chinese fracture costs localized from published cohorts with medical-inflation adjustment [25–28]; drug prices from current wholesale (US) and retail/reimbursement (China) data.

Outcomes and analyses

Total discounted cost, QALYs, and fracture counts per person; ICERs for B versus A (primary) and C versus A (reference); net monetary benefit at $50,000, $100,000, and $150,000 per QALY (US) and at 1×, 2×, and 3× GDP per capita (China; 2025 official ¥99,665 [29]), the latter

bracketing published opportunity-cost-based threshold estimates [30]. Analyses: deterministic base case; probabilistic sensitivity analysis (PSA; 500 draws); one-way sensitivity analysis of 15 parameters; scenario analyses (biosimilar pricing, bridging coverage, rebound magnitude, spontaneous sequencing rate, reference-arm persistence); subgroup analyses by starting age (65/70/75) and prevalent vertebral fracture; and a transferability decomposition in which parameter groups (discount rate, fracture epidemiology, fracture unit costs, intervention costs, utility/mortality, spontaneous sequencing) were swapped from the Chinese base case to US levels (costs converted at 7.2 CNY per USD) one at a time and cumulatively.

Validation

The model was checked against external anchors before analysis in both settings: (1) two-year persistence 45% by construction; (2) ratio of the vertebral fracture rate in the 0–2 years after cessation to the on-treatment rate, target 3–6 (US 3.95; China 3.83); (3) spontaneous-sequencing versus no-sequencing rate ratio, anchor 0.703 (simulated 0.79 US, 0.81 China) — simulated ratios sit slightly above the anchor's 95% CI because the modeled 12-month sequencing delay leaves the first post-cessation year largely unprotected by construction, whereas the claims-based anchor captures all-cause protection including early sequencers; (4) lifetime hip fracture accumulation 13.8% (US) and 8.1% (China, consistent with the ~3-fold lower Chinese hip incidence); (5) remaining life expectancy 15.8 (US) and 16.7 (China) years. A model-consistency check applied real-world persistence to the continuation arm and reproduced usual care exactly ($\Delta = 0$).

Results

Base cases

Table 2 summarizes base-case and probabilistic results. **United States.** Usual care accumulated $16,277 and 9.310 QALYs per person. The pathway cost $101 more and yielded 0.0236 more QALYs — an ICER of $4,280 per QALY — while averting 7.5% of clinical vertebral, 4.3% of hip, and 6.8% of other major fractures. Indefinite continuation gained 0.118 QALYs over usual care at an incremental $33,172 (ICER $281,277/QALY).

China. Usual care accumulated ¥10,244 and 9.464 QALYs per person. The pathway cost ¥2,260 more and yielded 0.0144 more QALYs — an ICER of ¥157,451 per QALY, between 1× GDP

(¥99,665; NMB −¥829) and 2× GDP (¥199,330; NMB +¥601) per capita — while averting 6.5% of clinical vertebral and 3.6% of hip fractures. Indefinite continuation cost ¥149,535/QALY, similar to the pathway, reflecting China's low denosumab price (¥624 per dose).

Probabilistic analysis

In the US, median incremental cost was $103 (IQR −$47 to $249; 31.6% probability of cost savings) and median incremental QALY 0.0224; the pathway was more effective in 100% of draws, and the probability of positive net benefit was 99.6%, 100%, and 100% at $50,000, $100,000, and $150,000 per QALY (Fig. 1). In China, median incremental cost was ¥2,230 (IQR ¥1,687–2,773; no cost-saving draws) and median incremental QALY 0.0136 (100% of draws positive); the probability of positive net benefit was 21.8%, 64.2%, and 86.2% at 1×/2×/3× GDP (Fig. 3). In both countries, uncertainty is effect-sided in magnitude but never crosses into harm.

One-way and scenario analyses (US)

Across low–high ranges of 15 parameters, incremental net monetary benefit at $100,000/QALY remained positive throughout ($954–$3,721) (Fig. 2). The three most influential parameters were all implementation characteristics: zoledronate duration of effect (2–6 years), bridging coverage (40%–90%), and program bridging suppression (0.30–0.55). All 13 scenarios produced ICERs between dominance and $19,713/QALY: the pathway was dominant at 90% coverage and at high rebound magnitude, and the worst case was 40% coverage ($15,933). Biosimilar price reductions (−15% to −50%) left B-versus-A economics exactly unchanged, because identical persistence in both arms cancels the drug price. Applying real-world persistence to the continuation arm reproduced usual care exactly; improving adherence without managing cessation worsened continuation's ICER to $282,512.

Subgroups

Table 3 gives subgroup ICERs. **US:** $9,385 (age 65), $4,280 (70), and dominant (75) per QALY; $11,385 without prior vertebral fracture; and dominant in women with prior vertebral fracture (−$245 and +0.039 QALYs at age 70; −$459 and +0.041 at age 75). **China:** ¥168,913 (65) and ¥155,954 (75); ¥204,152 without prior fracture (above 2× GDP); and below 1× GDP in women with prior vertebral fracture — ¥79,357 (70) and ¥72,266 (75). In both countries, the group bearing the rebound burden is where the program is unambiguously worth funding.

Transferability decomposition

Table 4 shows the decomposition. Starting from the Chinese base case (¥157,451/QALY), swapping parameter groups to US levels one at a time moved the ICER to ¥127,218 (discount rate 5%→3%); ¥102,914 (US fracture epidemiology); ¥52,766 (US fracture unit costs — the largest single step); ¥247,265 (US drug/intervention prices — worsening, i.e., China's low drug prices are an advantage); ¥178,115 (US utility/mortality); and ¥152,670 (US spontaneous sequencing). The cumulative swap reproduced the US ICER exactly after currency conversion (¥31,116 = $4,322 × 7.2), confirming model coherence. The US–China gap is thus not one effect but a structural bundle: higher fracture costs and a lower discount rate favor the intervention in the US, while China's intervention-cost advantage partially offsets its lower fracture costs, lower hip incidence, and steeper discounting.

Threshold analyses (China)

If China's true fracture costs exceed the direct medical estimates by 2.5-fold (a societal-perspective upper bound), the pathway meets 1× GDP for the whole population; at 5-fold it becomes dominant (−¥184, +0.0144 QALYs). Conversely, covering only prior-fracture patients meets 1× GDP with no cost re-estimation at all.

Discussion

Main findings

Managing the discontinuation that already happens in practice is a high-value strategy in both a high-price/high-threshold system and a low-price/low-threshold one, but for nearly opposite reasons. In the US, the program is near-costless (+$101) because expensive fractures are averted; in China the same bundle costs ¥2,260 net because fractures are cheap to the payer, yet still clears 2× GDP per capita — and clears 1× GDP outright in women with prior vertebral fracture. Indefinite continuation, the intuitive alternative, is not cost-effective in the US ($281,277/QALY) and offers no advantage over managing discontinuation in China (¥149,535/QALY).

Relation to prior work

Our results invert the framing of prior economic evaluations, which asked whether denosumab should be started or continued under perfect execution. Under realistic persistence, the policy-relevant margin is not "more treatment versus less" but "managed versus unmanaged cessation"

— and improving adherence without managing cessation is worse still ($282,512/QALY). For China specifically, the prior model [8] assumed away the rebound problem entirely; with rebound included, we find the Chinese answer is more favorable than the classic low-cost-of-fracture squeeze would suggest, because the intervention itself is cheap in China (denosumab ¥624, generic zoledronate ¥500–650) while the rebound hazard is unchanged — a finding of growing relevance as China's osteoporotic fracture burden becomes the world's largest [31].

Implementation, not epidemiology, drives uncertainty — in both settings

The one-way analysis located decision-relevant uncertainty in three implementation parameters in the US, and the same effect-sided structure held in China (100% probability of benefit). Additional observational studies of rebound epidemiology are unlikely to change either decision; program design — coverage achieved at discontinuation, bridging quality, and zoledronate effect durability — determines where the realized ICER sits. The pathway resembles a fracture liaison service applied to pharmacological cessation, and FLS experience suggests that coverage is the binding constraint in routine practice [32].

What the decomposition adds

Transferability studies of osteoporosis economics typically re-run models with local inputs and stop there. The group-wise decomposition shows why the answer differs: fracture unit costs dominate, followed by the discounting convention and hip-fracture epidemiology, with drug prices acting in the opposite direction. Two practical corollaries follow. First, Chinese payers applying a societal cost perspective (fracture costs ×2.5) should find the pathway cost-effective at 1× GDP for the entire discontinuing population. Second, other middle-income settings can approximate their answer by locating themselves on the same parameter axes rather than rebuilding the model.

Rebound-fracture evidence base

The effectiveness input for bridging rests on observational causal inference (HR 0.703 for sequencing versus no sequencing, Korean nationwide claims) and RCT evidence that zoledronate attenuates but does not abolish post-denosumab bone loss. No completed RCT has fracture endpoints for post-denosumab zoledronate; the ongoing SAFE-Z trial (NCT06767150) will provide them [33], and the model is designed to be re-estimated when SAFE-Z reports. The near-

zero cost side (US) and low absolute program cost (China) make the downside of early implementation small.

Limitations

First, bridging effectiveness is surrogate-anchored and observational; we bound it with a suppression coefficient and wide sensitivity ranges, and the SAFE-Z trial will eventually supersede these inputs. Second, the rebound curve's time-shape is a literature-anchored piecewise approximation rather than an individual-data reconstruction. Third, Chinese parameters are unevenly evidenced: fracture incidence is urban-claims-based and rural rates are likely lower; no Chinese persistence or post-cessation sequencing data exist, so we used Korean/Taiwanese hazards and a conservative midpoint sequencing rate (both scenario-tested); and the EQ-5D-5L baseline (0.93) reflects the instrument's known ceiling effect in Chinese general-population samples. Fourth, treatment re-initiation after discontinuation, oncology indications, caregiver costs, and bisphosphonate maintenance after bridging are not modeled; the first and last are conservative against the intervention. Fifth, prices are 2025–2026 list/retail-based; confidential rebates are unobservable and were handled by scenario. Finally, the Chinese reimbursement environment is moving (volume-based procurement of zoledronate, provincial denosumab pricing); the decomposition indicates the conclusion is robust to plausible drug-price movement because intervention cost acts in China's favor.

Conclusions

A structured discontinuation management pathway for denosumab — scheduled zoledronate bridging with monitoring, delivered to the discontinuation events that routine practice already generates — is a near-costless, high-value intervention in the United States and is cost-effective in China at conventional thresholds, with prior-fracture patients the unambiguous priority group in both. Because the decisive uncertainties are implementable rather than epidemiological, the pathway's value is a policy choice. In a biosimilar era enlarging both the treated and the discontinuing populations in both countries, managing the exit from therapy deserves the same attention as the entry into it.

List of abbreviations

BMD: bone mineral density; CHEERS: Consolidated Health Economic Evaluation Reporting Standards; CI: confidence interval; CTX: C-terminal telopeptide of type I collagen; FLS: fracture liaison service; GDP: gross domestic product; HR: hazard ratio; ICER: incremental cost-effectiveness ratio; IQR: interquartile range; NMB: net monetary benefit; PSA: probabilistic sensitivity analysis; QALY: quality-adjusted life-year; RR: relative risk; WAC: wholesale acquisition cost.

Declarations

Ethics approval and consent to participate

Not applicable. This study is a model-based economic evaluation that used only published aggregate data; no human participants, human tissue, or individual-level data were involved. Clinical trial number: not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The parameter registries, model outputs, and full result tables supporting the conclusions of this article are included within the article and its additional files. The Python model source code and analysis scripts are available from the corresponding authors on reasonable request and will be deposited in a public repository upon acceptance.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contributions

Z.L., Q.H., and J.D. contributed to study conception and interpretation of results; T.F. developed the microsimulation model, performed all analyses, and wrote the first draft of the manuscript; J.Z., T.Y., and P.Y. contributed to parameter sourcing and interpretation of results; X.M. and

R.W. contributed to data curation and validation; X.S. and Y.X. supervised the study and critically revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

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Figure legends

Fig. 1 Cost-effectiveness plane (A) and cost-effectiveness acceptability curve (B) for the structured discontinuation management pathway versus usual care, United States, 500 probabilistic draws; dashed rays mark $50k/100k/150k per QALY.

Fig. 2 Tornado diagram: one-way sensitivity analysis of incremental net monetary benefit at $100,000/QALY, United States.

Fig. 3 Cost-effectiveness plane (A) and cost-effectiveness acceptability curve (B), China; dashed rays and marked points at 1×/2×/3× GDP per capita (¥99,665/199,330/298,995).

Tables

Table 1 Key model inputs, by setting (selected; full registries in Additional file 1: Table S1)

Parameter	US	China	Source
Baseline clinical vertebral rate (age 70, /yr)	0.0042	0.0042	[1]
Baseline hip rate (/yr)	0.0030	0.0015	[1, 13]
Denosumab RR vertebral / hip / other	0.32 / 0.60 / 0.80	same	[1]
Rebound RR (vertebral) peak / recovery	1.8 / 1.1	same	[2, 14]
Bridging suppression program / spontaneous	0.40 / 0.70	same	[7, 15–17]
Spontaneous sequencing rate	12%	15%	[6, 7]; China blank (midpoint)
Bridging coverage	60%	60%	Assumption (40–90% scenarios)
Denosumab per dose	$1,875	¥624	WAC 2025; China retail 2025–26
Zoledronate infusion (event)	$250	¥1,200	CMS ASP+6%; China generic + administration
Program cost	$180/yr × 3 y	¥900/yr × 3 y	FLS-analogue costing
Hip fracture year-0 cost	$46,000	¥40,000	[24–26]
Clinical vertebral event cost	$6,500	¥30,000	[24, 25, 27]
Baseline utility	0.82	0.93	[21–23]
Discount rate	3%	5%	US convention; [10]
Willingness-to-pay	$50k–150k	1×–3× GDP (¥99,665–298,995)	[29, 30]

Table 2 Base-case and probabilistic results (per person, discounted)

Setting / arm	Cost	QALYs	Vertebral fx	Hip fx	ICER vs usual care
US — A usual care	$16,277	9.310	0.135	0.138	—
US — B pathway	$16,378	9.333	0.125	0.132	**$4,280/QALY**
US — C continuation	$49,449	9.428	0.040	0.084	$281,277/QALY
China — A usual care	¥10,244	9.464	0.142	0.081	—
China — B pathway	¥12,504	9.479	0.133	0.078	**¥157,451/QALY**
China — C continuation	¥17,286	9.511	0.043	0.048	¥149,535/QALY

PSA (B vs A): US — Δcost median $103 (IQR −$47 to $249), P(effective) 100%, P(cost-saving) 31.6%, P(NMB>0) 99.6–100% at $50k–150k. China — Δcost median ¥2,230 (IQR ¥1,687–2,773), P(effective) 100%, P(NMB>0) 21.8% / 64.2% / 86.2% at 1×/2×/3× GDP.

Table 3 Subgroup ICERs (B vs A)

Subgroup	US ($/QALY)	China (¥/QALY)
Age 65 / 70 / 75	9,385 / 4,280 / dominant	168,913 / 157,451 / 155,954
No prior vertebral fracture	11,385	204,152
Prior vertebral fracture, age 70	dominant (−$245, +0.039)	79,357 (<1× GDP)
Prior vertebral fracture, age 75	dominant (−$459, +0.041)	72,266 (<1× GDP)

Table 4 Transferability decomposition (China base → US parameter levels; costs converted at 7.2 CNY/USD)

Parameter group swapped (one at a time)	ICER (¥/QALY)	Δ vs China base (¥)
China base case	157,451	—
Discount rate 5%→3%	127,218	−30,233
Fracture epidemiology (hip/other → US)	102,914	−54,537

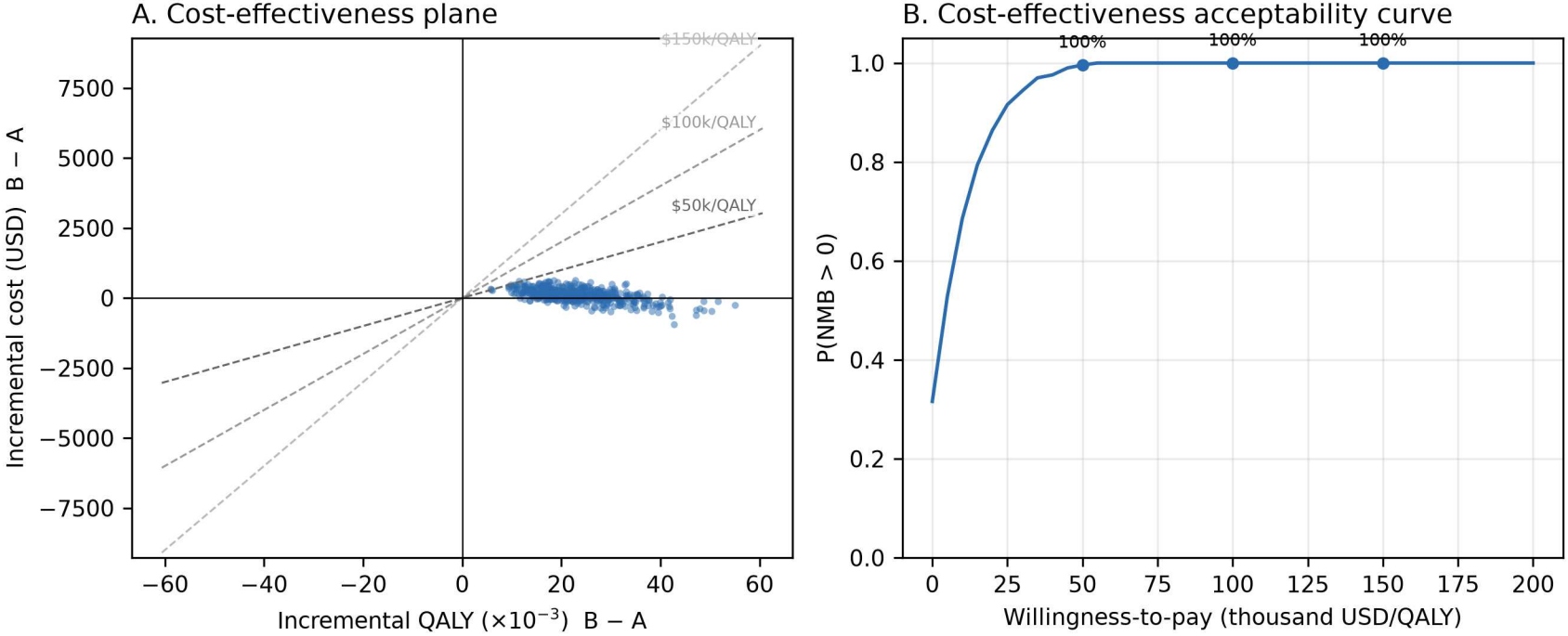
Parameter group swapped (one at a time)	ICER (¥/QALY)	Δ vs China base (¥)
Fracture unit costs → US	52,766	−104,685
Intervention costs → US	247,265	+89,814
Utility / mortality → US	178,115	+20,664
Spontaneous sequencing 15%→12%	152,670	−4,781
All groups (cumulative)	31,116	equals US ICER × 7.2

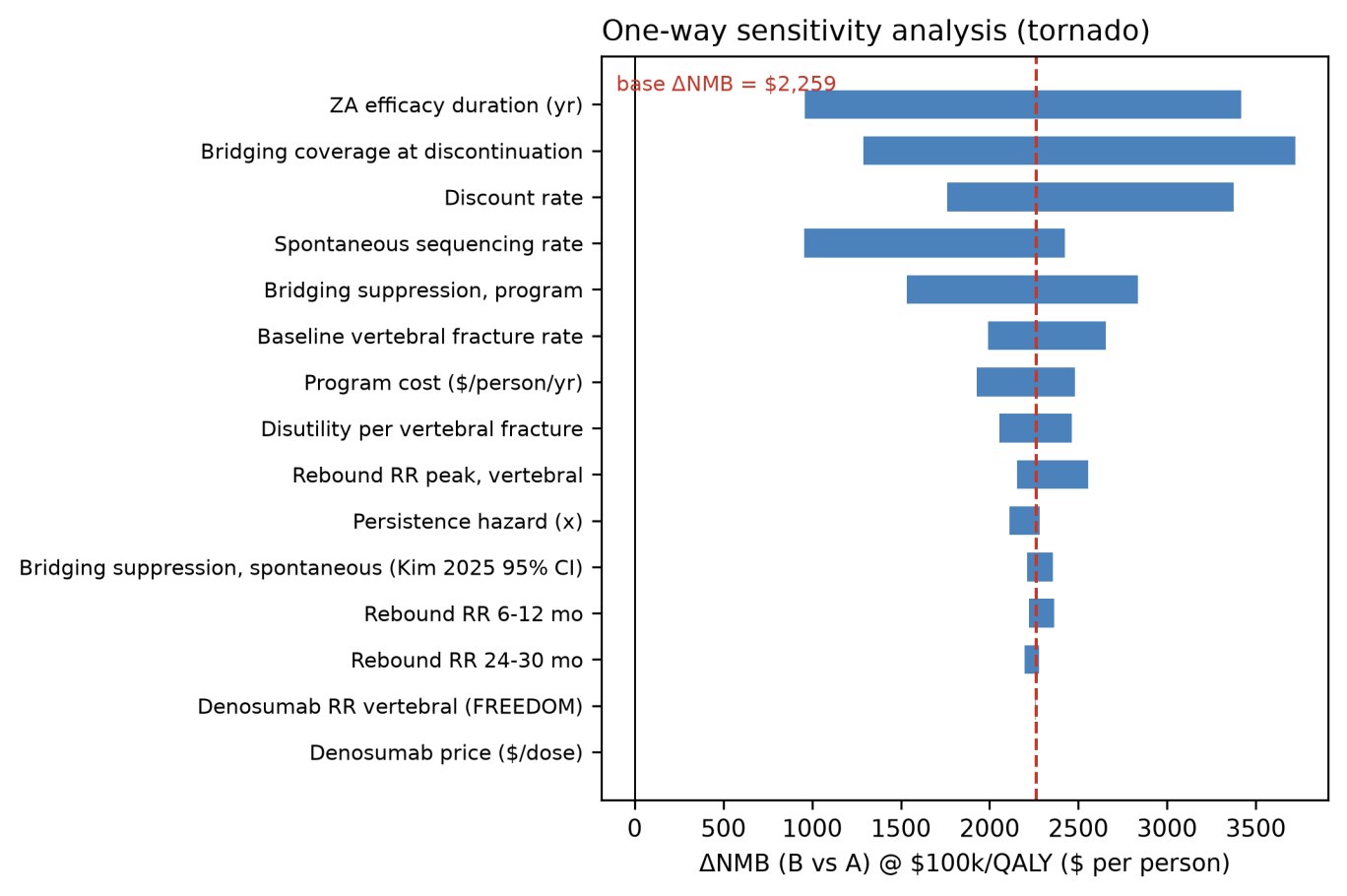
Additional file 1

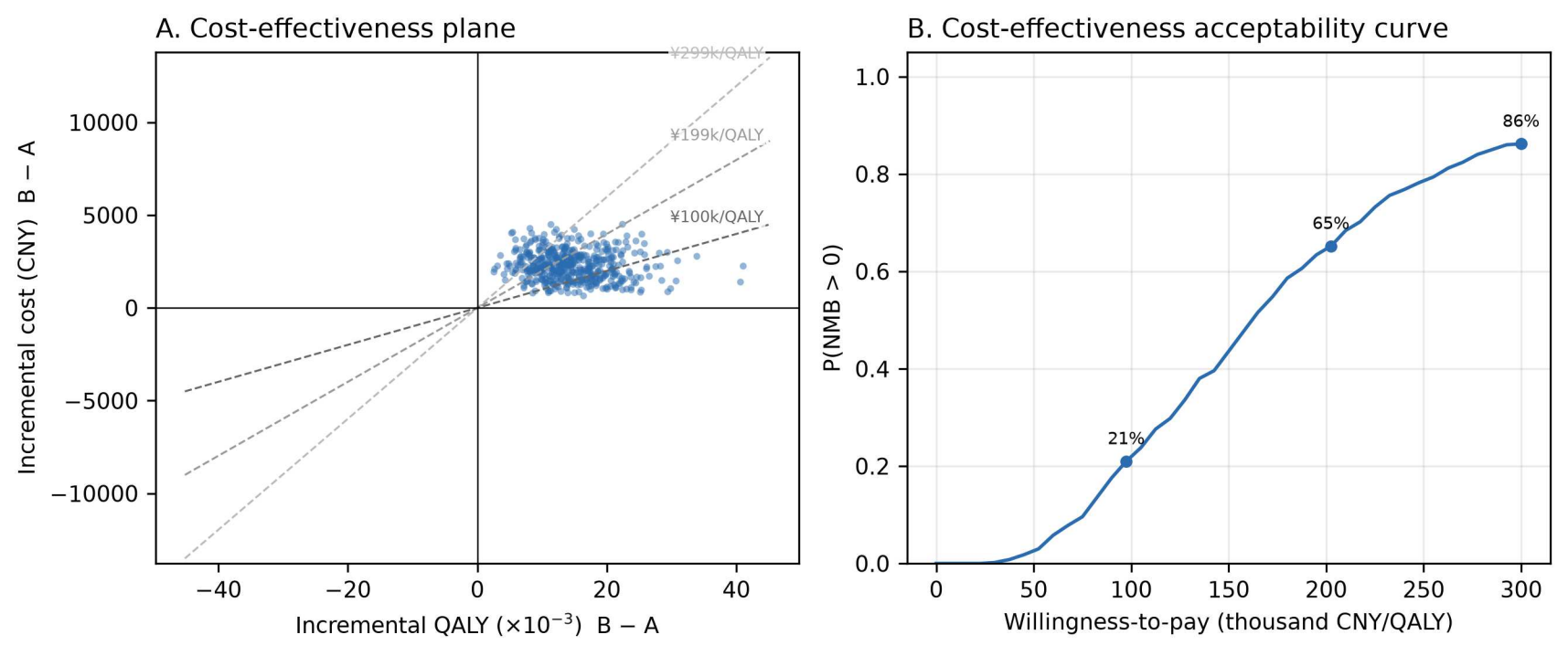
Additional file 1: Supplementary methods and results. Parameter registry (Table S1), model validation against external anchors (Table S2), full scenario and subgroup results (Table S3).

Additional file 2

Additional file 2: CHEERS 2022 (Consolidated Health Economic Evaluation Reporting Standards) checklist for this study.


A. Cost-effectiveness plane
$150k/QALY
$100k/QALY
$50k/QALY
Incremental cost (USD) B − A
7500
5000
2500
0
−2500
−5000
−7500
−60
−40
−20
0
20
40
60
Incremental QALY (×10⁻³) B − A
B. Cost-effectiveness acceptability curve
100%
100%
100%
P(NMB > 0)
1.0
0.8
0.6
0.4
0.2
0.0
0
25
50
75
100
125
150
175
200
Willingness-to-pay (thousand USD/QALY)


One-way sensitivity analysis (tornado)
base ΔNMB = $2,259
ZA efficacy duration (yr)
Bridging coverage at discontinuation
Discount rate
Spontaneous sequencing rate
Bridging suppression, program
Baseline vertebral fracture rate
Program cost ($/person/yr)
Disutility per vertebral fracture
Rebound RR peak, vertebral
Persistence hazard (x)
Bridging suppression, spontaneous (Kim 2025 95% CI)
Rebound RR 6-12 mo
Rebound RR 24-30 mo
Denosumab RR vertebral (FREEDOM)
Denosumab price ($/dose)
0
500
1000
1500
2000
2500
3000
3500
ΔNMB (B vs A) @ $100k/QALY ($ per person)


A. Cost-effectiveness plane
¥299k/QALY
¥199k/QALY
¥100k/QALY
10000
5000
0
−5000
−10000
−40
−20
0
20
40
Incremental cost (CNY) B − A
Incremental QALY (×10⁻³) B − A
B. Cost-effectiveness acceptability curve
1.0
0.8
0.6
0.4
0.2
0.0
P(NMB > 0)
21%
65%
86%
0
50
100
150
200
250
300
Willingness-to-pay (thousand CNY/QALY)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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