JAMA Oncology | Review

Cost-Effectiveness of Adjuvant Immunotherapy in Cancer Treatments
A Systematic Review

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IMPORTANCE Adjuvant immunotherapy is increasingly integrated into cancer care to reduce recurrence and improve survival. However, its high cost raises critical concerns regarding affordability and economic value across diverse health system contexts.

OBJECTIVE To synthesize published economic evaluations of adjuvant immunotherapy and assess cost-effectiveness outcomes, quality-adjusted life-year (QALY)/life-year (LY) gains, and methodologic approaches.

EVIDENCE REVIEW A systematic search was conducted of PubMed, Scopus, Embase, and Web of Science for full economic evaluations published between January 1, 2015, and January 31, 2025. Eligible studies included cost-effectiveness or cost-utility analyses of adjuvant immunotherapy across any cancer type. Data were extracted on cancer type, treatment strategy (single vs combination therapy), treatment line, model structure, health utility instruments, funding sources, and cost-effectiveness outcomes. Methodologic quality was appraised using the Criteria for Health Economic Quality Evaluation 2023. Due to heterogeneity of health systems, findings were narratively synthesized.

FINDINGS The analysis included 69 studies covering a range of cancer types, most frequently non–small cell lung cancer and melanoma. Of these, 46 (67%) evaluated first-line therapy with single-agent checkpoint inhibitors. Higher QALY/LY gains were consistently reported among the adjuvant immunotherapy group (63 [91%]), particularly for non–small cell lung cancer, industry-funded studies, and combination regimens. More than half of the evaluations (40 [58%]) concluded that adjuvant immunotherapy was cost-effective, although results varied by cancer type, model assumptions, drug pricing, funding organizations, and country-specific thresholds. Markov modeling was the dominant analytic approach (46 [67%]) and EuroQol 5 Dimensions was the most commonly used health utility instrument (56 [81%]).

CONCLUSIONS AND RELEVANCE This systematic review found that adjuvant immunotherapy was frequently associated with meaningful QALY/LY improvements and was often considered cost-effective in high-risk or first-line settings. However, economic value remains context-specific, shaped by treatment strategy, drug costs, and modeling assumptions. These findings support the selective, value-based adoption of adjuvant immunotherapy and underscore the need for transparent, standardized economic evaluations to guide reimbursement and policy decisions.

JAMA Oncol. doi:10.1001/jamaoncol.2025.6080
Published online January 22, 2026.

Supplemental content

CME at jamacmelookup.com

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Cancer remains a leading cause of morbidity and mortality globally, accounting for nearly 15 million deaths in 2022 alone.[1,2] Advances in cancer therapeutics during the past decade have increasingly focused on immunotherapy, a treatment strategy that activates or enhances the body's immune response to recognize and destroy tumor cells. Among these, immune checkpoint inhibitors have shown promise across a broad range of malignant neoplasms, including non–small cell lung cancer (NSCLC), melanoma, renal cell carcinoma, and urothelial carcinoma.[3-5]

Checkpoint inhibitors, such as anti–programmed cell death 1 protein (PD-1; eg, nivolumab), anti–programmed cell death 1 ligand 1 (PD-L1; eg, atezolizumab), and anti–cytotoxic T-lymphocyte–associated protein 4 (eg, ipilimumab) work by preventing tumor-mediated immune evasion. Their clinical effectiveness has been demonstrated in both metastatic and earlier-stage disease settings. Increasingly, these agents are being incorporated as adjuvant therapies, treatments given after the primary intervention (usually surgery or chemoradiation) to reduce the risk of cancer recurrence and to improve long-term survival.[6]

Multiple phase 3 randomized clinical trials support adjuvant immunotherapy: CheckMate 816 trial[7] (neoadjuvant/adjuvant nivolumab) improved event-free survival and pathologic complete response in patients with resectable NSCLC; adjuvant pembrolizumab prolonged recurrence-free survival in resected stage III melanoma[8,9]; and the IMpower010 trial[10] showed atezolizumab reduced recurrence or death by 34% in PD-L1–positive stage II-IIIA NSCLC.

Despite these clinical benefits, immunotherapy agents come at a substantial financial cost. In many high-income countries, the cost of a full course of adjuvant checkpoint inhibitors can exceed $100 000 per patient.[11] This raises important questions for health care payers and policymakers: Are these therapies worth their cost, particularly when used in early-stage disease in which absolute gains may be smaller?

To answer this question and other related to it, economic evaluations are critically important. These evaluations assess both the costs and the health outcomes of competing treatment strategies, often using metrics such as incremental cost-effectiveness ratios (ICERs) and quality-adjusted life-years (QALYs). QALYs incorporate both the length and quality of life, offering a standardized way to compare the value of different interventions across diseases.[12]

Numerous economic evaluations of adjuvant immunotherapy have emerged in recent years. These studies vary widely in their methodologic approaches, including by type of decision-analytic model (eg, Markov vs partitioned survival), perspective (payer, health care system, or societal), and the health utility instruments used (eg, EuroQol 5 Dimensions [EQ-5D], European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 [EORTC QLQ-C30]). Moreover, cost-effectiveness results may differ by tumor type, line of treatment, drug combination strategy, and health system context. For example, while adjuvant nivolumab may be considered cost-effective in resected stage III melanoma in the US, it may not meet willingness-to-pay (WTP) thresholds in countries with constrained health budgets.[11,13,14]

Another important consideration is treatment-related toxic effects. While immunotherapies are often better tolerated than chemotherapy, they are not without risks. Immune-related adverse events (irAEs), such as pneumonitis, colitis, or endocrinopathies, can be serious and may require hospitalization or lifelong hormone replacement therapy.[15] These clinical consequences carry additional costs, both economic and quality of life–related, that must be considered in comprehensive value assessments.

Despite the growing volume of research, to our knowledge, there has been no broad synthesis that collates and analyses the global evidence on the economic value of adjuvant immunotherapy across cancer types, treatment strategies, and lines of care. Most existing reviews are limited to single cancers or single-drug comparisons. A comprehensive overview is urgently needed to inform clinical investment decisions, especially as health systems face increasing pressure to manage cancer care costs while ensuring equitable access to innovative therapies.

We conducted a systematic synthesis of 69 peer-reviewed economic evaluations of adjuvant immunotherapy published between 2015 and 2025. Our objectives were to summarize the cost-effectiveness decisions reported across diverse cancers and treatment strategies; compare outcomes based on drug regimens (single vs combination therapies); quantify reported QALYs/life-years (LYs) and health utility outcomes; and analyze modeling methods, sensitivity analyses, and value drivers across settings. This review outlines health gains and economic value, and identifies where future research, pricing reform, or prioritization are needed to support evidence-informed policymaking and sustainable use of immunotherapy in cancer treatment pathways.

Key Points

Question Is adjuvant immunotherapy cost-effective across cancer types?

Findings This systematic review including 69 economic evaluations (2015-2025) found that adjuvant checkpoint inhibitors, usually single-agent, were associated with higher quality-adjusted life-year/life-year gains and were determined to be cost-effective by 40 studies (58%), with the strongest signals in non–small cell lung cancer and melanoma, particularly in early-stage/high-risk populations, and for some combination regimens. Industry-funded studies more frequently reported cost-effective decisions and findings were sensitive to drug prices, model assumptions, and country-specific willingness-to-pay thresholds.

Meaning These findings suggest that adjuvant immunotherapy can offer good value for money in selected high-risk settings; decisions should be indication-specific, aligned with local health technology assessment thresholds, and supported by price negotiation or managed-entry agreements.

Methods

Study Design

This study followed the principles of a systematic synthesis of economic evaluations. The review was designed to identify, appraise, and summarize published evidence on the cost-effectiveness of adjuvant immunotherapy across various cancer types. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline was used as a reporting framework,[16] and the Criteria for Health Economic Quality Evaluation (CHEQUE)

tool[17] was consulted to ensure comprehensive reporting of economic evidence. The study was registered on PROSPERO (CRD420251127115).

Eligibility Criteria

Studies that met the following criteria were considered eligible:

1. Population: adult patients with any type of solid or hematological malignant neoplasm receiving adjuvant immunotherapy after primary treatment (ie, surgery, chemotherapy, or radiation therapy).
2. Intervention: adjuvant immunotherapy, including immune-checkpoint inhibitors (eg, nivolumab, pembrolizumab), administered as single agents or in combination regimens.
3. Comparator: standard of care, conventional chemotherapy, or alternative immunotherapies.
4. Outcomes: studies reporting at least 1 economic outcome, including ICER, cost per QALY gained, or cost per LY gained.
5. Study type: full economic evaluations (cost-effectiveness analysis [CEA], cost-utility analysis [CUA], cost-benefit analysis [CBA]) published in peer-reviewed journals between 2015 and 2025.
6. Language: English language publications.

We excluded studies that were reviews, conference abstracts, commentaries, methodologic papers without primary data, and studies focusing exclusively on metastatic or palliative settings without evaluating adjuvant use.

Search Strategy and Study Selection

A comprehensive literature search was conducted in PubMed, Embase, Scopus, Web of Science, and the Cochrane Library for studies published in English from January 1, 2015, to January 30, 2025. The search strategy combined MeSH (Medical Subject Headings) and free-text terms related to adjuvant immunotherapy and economic evaluations (eTable 1 in Supplement 1). An example of the PubMed search strategy is: ("immunotherapy" OR "immune checkpoint inhibitors" OR "nivolumab" OR "pembrolizumab" OR "atezolizumab" OR "adjuvant") AND ("cost-effectiveness" OR "cost-utility" OR "cost-benefit" OR "economic evaluation" OR "QALY" OR "ICER") AND ("cancer" OR "carcinoma" OR "melanoma" OR "lung cancer"). Reference lists of included studies and relevant reviews were searched manually to identify additional eligible articles.

All records were imported into Mendeley to remove duplicates. Two reviewers (Y.C. and P.K.D.) independently screened titles and abstracts to identify potentially relevant studies. Full texts were then retrieved and assessed against the eligibility criteria. Disagreements were resolved through discussion or by consulting a third reviewer (R.A.M.). Details on all selected studies are available in the eFigure in Supplement 1.

Data Extraction

Data were extracted using a prepiloted form developed in Microsoft Excel. Extracted variables included: study characteristics, eg, year of publication, country/region, and cancer type; clinical characteristics, eg, immunotherapy type, combination strategy, treatment line (first-, second-, or later-line), and comparator; economic evaluation, type of analysis (CEA/CUA), perspective (payer/health care system/societal), time horizon, discount rates, and cost-effectiveness threshold; outcomes, eg, incremental QALYs, costs, and ICERs; modeling and/or utility measures, eg, economic model (Markov, partitioned survival, microsimulation, or discrete event simulation); health utility instruments (EQ-5D, EORTC QLQ-C30), and key sensitivity or scenario analyses; and decision cost-effectiveness at the authors' WTP threshold.

Data Synthesis

We performed a narrative synthesis and descriptive analysis, tabulated data by cancer type, drug strategy (single vs combination), treatment line, funding sources, and cost-effectiveness decision. We summarized patterns in QALY gains, utility measurement, and modeling approaches.

Given heterogeneity in clinical settings, health system perspectives, time horizons, and cost data, a formal meta-analysis of ICERs was not feasible. Instead, we grouped findings thematically (QALY improvement, drug-strategy, funding and cost-effectiveness trends) and reviewed methodologic trends, including the use of Markov modeling, probabilistic sensitivity analysis, and scenario analyses.

Quality Appraisal

We assessed study quality using the CHEQUE online tool.[17] The CHEQUE tool includes 48 attributes (24 methodologic and 24 reporting quality), each weighted from 1 to 9 by importance. Items were scored yes (full credit, × 1.0), somewhat (half credit, × 0.5), or (no credit, 0). Two reviewers (Y.C. and P.K.D.) independently appraised each study (perspective, comparator, model appropriateness, and uncertainty handling) and classified studies as high, moderate, or low quality.

Statistical Analysis

We summarized study characteristics and outcomes descriptively and compared the proportion of concluding cost-effectiveness across prespecified methodologic and reporting quality categories, and clinical and economic components. Associations between categorical variables were tested using Pearson χ^2 or Fisher exact tests. For contingency tables with small expected cell counts, we obtained Monte Carlo χ^2 *P* values (10 000 repetitions). Effect size was quantified with Cramér V (small or weak ≤0.20; moderate 0.20-0.60; strong >0.60). All tests were 2-sided with $\alpha = .05$. Analyses were conducted in Stata/SE, version 15.0 (StataCorp), with Microsoft Excel used for data management and figure preparation.

Results

Characteristics of Included Studies

A total of 69 studies evaluating the cost-effectiveness of adjuvant immunotherapy in cancer treatment modalities were included (details in eTable 2A in Supplement 1). The publication period covered from 2015 to 2025, with a marked increase in publications from 2019 to 2025 (59 studies [85%]). Most studies were conducted in high-income countries, with the US (26 [37%]) and China (20 [30%]) being the most frequent study settings. Only 5 studies (7%) involved multicounty evaluations. In terms of cancer types, NSCLC accounted for nearly half of all included studies (35 [51%]), followed by small cell lung cancer (5 [7%]), breast cancer (3 [4%]) and melanoma (4 [6%]); **Table 1**).

Table 1. Characteristics of Included Cost-Effectiveness Analyses (N = 69 Studies)

Characteristic	Cost-effectiveness analyses, No. (%)
Year of publication	
2015-2018	10 (14.49)
2019-2022	31 (44.93)
2023-2025	28 (40.58)
Study settings/origins	
Single-country study	
Australia	2 (2.90)
Canada	2 (2.90)
China	20 (28.99)
France	3 (4.35)
Italy	1 (1.45)
Singapore	2 (2.90)
Spain	2 (2.90)
Switzerland	2 (2.90)
United Kingdom	3 (4.35)
US	26 (37.67)
Vietnam	1 (1.45)
Multicounty study	
Canada and Sweden	1 (1.45)
China and US	2 (2.90)
United Kingdom and US	1 (1.45)
Australia, Canada, United Kingdom, and US	1 (1.45)
Tumor type	
Bladder cancer	1 (1.45)
Breast cancer	3 (4.35)
Cervical cancer	1 (1.45)
Colorectal cancer	1 (1.45)
Diffuse large B-cell lymphoma	3 (4.35)
Endometrial cancer	2 (2.90)
Esophageal and gastroesophageal	1 (1.45)
Esophageal squamous cell carcinoma	2 (2.90)
Hepatocellular carcinoma	1 (2.90)
Lymphoblastic leukemia	1 (1.45)
Melanoma	4 (5.80)
Multiple myeloma	1 (1.45)
Nasopharyngeal carcinoma	3 (4.35)
NSCLC	35 (50.72)
SCLC	5 (7.25)
Renal cell carcinoma	4 (5.80)
Urothelial carcinoma	1 (1.45)
Drug combination status in the adjuvant immunotherapies (intervention)	
Single drug (1 drug)	55 (79.71)
Combined (≥2 drugs)	14 (20.29)
Drug combination status/strategy in the comparator group (control group)	
Single drug (immunotherapy drug)	14 (20.29)
Combined drug (≥2 immunotherapy drugs)	11 (15.94)
Standard chemotherapy	36 (52.17)
Standard of care	8 (11.59)
Type of treatment mode(s)	
First-line	46 (66.67)
Second-line	15 (21.74)
First- and second-line	2 (2.90)
Third-line and later	1 (1.45)
Not reported (no data)	5 (7.25)

Abbreviations: NSCLC, non–small cell lung cancer; SCLC, small cell lung cancer.

Drug Strategies and Treatment Lines

In the intervention groups, most studies evaluated single-agent adjuvant immunotherapy (55 of 69 [80%]), while combination immunotherapies (≥2 agents) were assessed in 20% (14) of studies (Table 1). In contrast, the comparator groups most frequently involved standard chemotherapy (36 [52%]), followed by single-agent immunotherapy (14 [20%]), combined immunotherapy (11 [16%]) and standard of care (8 [12%]). By treatment setting, the majority of interventions were applied as first-line adjuvant therapy (46 [67%]), with fewer studies assessing second-line (15 [22%]) or later-line (1 study [1%]) treatment. The most frequently evaluated immunotherapy agents were pembrolizumab (21 [18%]) and nivolumab (16 [14%]). In the comparator groups, standard chemotherapy was used in 39 (48%) studies, followed by agents such as docetaxel and best supportive care (eTable 3 in Supplement 1).

Economic Outcomes and Economic Approaches

Most studies assessed 2 economic outcomes (QALYs/LYs gained) (43 [62%]), while the remainder used a single outcome (25 [38%]; **Table 2**). The most reported outcome was QALYs alone (36%), followed by a combination of QALYs and LYs (62%; details in eTable 2C in Supplement 1). Health utility values were primarily derived using the EQ-5D-3L instrument (33 [48%]), followed by the EQ-5D-5L (23 [33%]), EORTC QLQ-C30 (5 [7%]), standard gamble (3 [4%]), and time trade-off (3 [4%]). Only 1 study reported using the cancer-specific QLQ-C29 instrument (eMethods in Supplement 1). Economic modeling was dominated by Markov models (46 [67%]), followed by partitioned survival models (19 [28%]), with limited use of microsimulation (3 [4%]), and 1 discrete event simulation (details in eTable 2B in Supplement 1). The most common model structure comprised 3 health states (progression-free disease, progressed disease, death) in 53 studies (78%), while 5 state variants were used in 4 studies (6%). Time horizons varied: 17 studies (approximately 25%) adopted a lifetime horizon, 18 (26%) used 6- to 10-year horizons, and 6 (9%) used 1-year to 5-year time horizons. Most evaluations applied either a health care system (32 [46%]) or payer perspective (26 [38%]), with fewer studies adopting a societal (3 [4.4%] or combined perspective (6 [9%]). Sensitivity analyses were widespread, with 98% (68 studies) conducting probabilistic sensitivity analysis and 93% (64 studies) performing 1-way sensitivity analysis. Scenario or subgroup analyses were performed in 62% (42 studies; details in eTable 2D in Supplement 1).

Incremental Health Outcomes and Cost-Effectiveness Decisions

Among 63 studies reporting QALY/LY outcomes (**Table 3**), single-drug regimens reported higher (positive) incremental QALYs/LYs in 43 of 48 studies (90%), lower (negative) in 5 (10%). Combination regimens (≥2 drugs) were associated with higher values in 20 of 21 studies (95%), with only 1 study reporting a lower value. By treatment setting, first-line adjuvant immunotherapy was associated with higher (positive) values in 43 of 46 studies (94%); second-line setting in 13 of 15 (87%). By cancer type, NSCLC reported higher values in 30 of 35 (86%), with comparable patterns across melanoma and other cancers (Table 3 and additional details are available in eTable 2C in Supplement 1).

Across all 69 studies, 58% (40 studies) concluded the intervention was cost-effective, while 42% (29 studies) found it not cost-effective by WTP thresholds (**Table 4**; details in eTable 2D in Supplement 1). When stratified by drug strategy: single-agent immunotherapy was deemed cost-effective in 27 of 48 studies (56%) and not cost-effective in 21 of 48 studies (44%). Combination immunotherapies were considered cost-effective in 13 of 21 studies (62%) vs not cost-effective in 8 of 21 studies (38%). When stratified by line of treatment: first-line adjuvant immunotherapy yielded cost-effective results in 25 of 46 studies (54%). Second-line settings showed similar proportions (8 of 15 studies [53%]). Data were limited for third-line and beyond (1 study reported cost-effective outcome), and in 5 studies, line of treatment was not specified.

By disease subcategory (lung [NSCLC+SCLC] vs others; NSCLC vs others; melanoma vs others), proportions were broadly similar and χ^2 tests showed no statistically significant association (Cramér V ≤0.20; Table 4). In addition, among the 69 included studies, 29% (20 studies) were industry-funded, 41% (28 studies) were nonindustry funded (ie, academic, public, government), and 30% (21 studies) did not report funding (Table 2). Cost-effectiveness conclusions were more frequently positive among industry-funded studies (17 of 20 studies [85%]) than nonindustry funded studies (13 of 28 studies [46%]), an association that was statistically significant (Cramér V = 0.35; Table 4), while incremental QALYs/LYs gains were similar across industry-funding groups (Table 3).

Methodologic and Reporting Quality

eTable 4 in Supplement 2 shows the distribution of the methodologic and reporting quality scores for the 69 CEAs. Most studies achieved moderate to high quality (>95%), indicating broad adherence to economic standards (eTable 4 in Supplement 2). A small number were low quality, typically due to limited model transparency, insufficient sensitivity analysis or incomplete reporting of key inputs and assumptions (**Figure**). Comparing conclusions by quality category (eTable 4 in Supplement 2): on the methodologic scale, higher-quality studies were more likely to report cost-effective results than were lower- to moderate-quality studies (27 of 39 [69%] vs 13 of 30 studies [43%]; Pearson χ^2 = 4.67; Cramér V = 0.26). On the reporting scale, the difference was smaller and not significant (32 of 50 studies [64%] vs 9 of 19 [47%]; Pearson χ^2 = 1.58; *P* = .21; Cramér V = 0.15; Figure). Overall, higher methodologic quality was associated with increased cost-effective conclusions, while reporting quality did not.

Discussion

This review synthesized the current landscape of economic evaluations assessing adjuvant immunotherapy across a range of cancer types. Our findings suggest that adjuvant immunotherapies are frequently associated with QALY gains and are often judged as cost-effective, particularly across treatment settings and regimens. These results highlight the growing body of evidence supporting the use of immune checkpoint inhibitors as part of adjuvant cancer care, aligning with recent data[8-10,18] demonstrating improved recurrence-free survival and durable immune response in early-stage disease.

The predominance of favorable cost-effectiveness outcomes indicates that adjuvant immunotherapy may offer value for money under appropriate clinical and economic conditions. These conclu-

Table 2. Distribution of Methods, Outcomes, and Economic Decisions in Adjuvant Immunotherapies for Cancer Treatment, 2015 to 2025

Economic components	Cost-effectiveness analyses, No. (%)
No. of economic outcomes	
1	29 (42.03)
2	40 (57.97)
Type of economic outcomes	
Composite outcome (QALYs)	25 (36.23)
Natural outcome (LYs)	1 (1.45)
Both composite and natural outcomes (QALYs and LYs)	43 (62.32)
QoL instrument	
EORTC QLQ-C29	1 (1.45)
EORTC QLQ-C30	5 (7.25)
EQ-5D-3L	33 (47.83)
EQ-5D-5L	23 (33.33)
Standard gamble	3 (4.35)
Time trade-off	3 (4.35)
Not applicable	1 (1.45)
Economic models	
Markov	46 (66.67)
Partitioned survival	19 (27.54)
Microsimulation	3 (4.35)
Discrete event simulation	1 (1.45)
No. of health states used in models	
3	53 (76.81)
4	7 (10.14)
5	4 (5.80)
6	5 (7.25)
Type of economic evaluations	
Cost-effectiveness analysis	63 (91.31)
Cost-utility analysis	3 (4.35)
Cost-effectiveness and cost-utility analyses	3 (4.35)
Time horizons used in models, y	
1-5	6 (8.70)
6-10	18 (26.09)
11-15	3 (4.35)
16-20	14 (20.29)
21-25	1 (1.45)
26-52	6 (8.70)
Lifetime horizon	17 (24.64)
Not reported (no data)	4 (5.80)
Perspective of economic evaluations	
Health insurance	2 (2.90)
Health care system	32 (46.38)
Health care system and societal	6 (8.70)
Payer perspective	26 (37.68)
Societal perspective	3 (4.35)
Included sensitivity and scenario analyses	
1-Way sensitivity analysis	64 (92.75)
Probabilistic sensitivity analysis	67 (98.53)
1-Way and probabilistic sensitivity analysis	64 (92.75)
Scenario/subgroup analysis	43 (62.31)
Cost-effectiveness decision	
Cost-effective	40 (57.97)
Not cost-effective	29 (42.03)
Funding sources	
Industry funded	20 (28.99)
Not industry (academic/government funding)	28 (40.58)
No funding/not reported (no data)[a]	21 (30.43)

Abbreviations: EORTC QLQ-C29 and -C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 29 and Core 30; EQ-5D-3L and -5L, EuroQol 5 Dimensions 3 levels and 5 levels; LYs, life-years; QALYs, quality-adjusted life-years; QoL, quality of life.

[a] Five studies did not report funding sources.

Table 3. Number of Studies With Positive vs Negative Incremental Quality-Adjusted Life-Years (QALYs) and Life-Years (LYs) by Clinical and Economic Components

Clinical components	Incremental QALYs/LYs in intervention vs control groups, No. of CEAs	
	Positive[a]	Negative[b]
Drug combination status in the adjuvant immunotherapy (intervention)		
Single drug (1 drug)	43	5
Combined (≥2 drugs)	20	1
Type of treatment mode(s) in the adjuvant immunotherapy (intervention)		
First-line	43	3
Second-line	13	2
First- and second-line	1	1
Third-line and later	1	0
Not reported (no data)	5	0
Cancer type		
Bladder cancer	1	0
Breast cancer	3	0
Cervical cancer	1	0
Colorectal cancer	1	0
Diffuse large B-cell lymphoma	3	
Endometrial cancer	2	0
Esophageal and gastroesophageal	1	0
Esophageal squamous cell carcinoma	1	1
Hepatocellular carcinoma	1	0
Lymphoblastic leukemia	1	0
Melanoma	4	0
Multiple myeloma	1	0
Nasopharyngeal carcinoma	3	0
NSCLC	30	5
SCLC	5	0
Renal cell carcinoma	4	0
Urothelial carcinoma	1	0
Funding sources		
Industry funded	19	1
Not industry (academic/government funding)	27	1
No funding/not reported (no data)	17	4
Total No. of CEAs	63	6

Abbreviations:
CEA, cost-effectiveness analysis; NSCLC, non–small cell lung cancer; SCLC, small cell lung cancer.

[a] Positive = study reports incremental QALYs (ΔQALY) or LYs (ΔLY) >0 for the intervention vs control (comparator).

[b] Negative = ΔQALY or ΔLY <0.

sions are reinforced by widespread QALY improvements, suggesting that immunotherapies can enhance both survival and patient quality of life. However, these findings should be interpreted cautiously, as cost-effectiveness decisions were highly sensitive to national WTP thresholds, treatment comparators, pricing structures, and model assumptions.[12,19,20] In countries with lower thresholds or more restrictive funding frameworks, the same intervention may not be considered cost-effective.

Looking ahead, the cost-utility of adjuvant PD-1 or PD-L1 therapies will likely evolve with the entry of generics or biosimilars (eg, nivolumab, pembrolizumab).[21] Because drug acquisition costs commonly dominate incremental costs, even modest price erosion via competition, tendering, or reimbursement renegotiation could lower ICERs[22] and move borderline evaluations below WTP thresholds. The magnitude of change will vary by setting (confidential discounts, indication-specific pricing, procurement models)[23] and may be offset by utilization shifts (eligibility, duration) and nondrug costs (administration, monitoring, immune-related adverse events). Therefore, the findings of this synthesis should be viewed as a snapshot under current prices, underscoring the need for periodic reappraisal[24,25] and, when appropriate, threshold-price analyses or price-based agreements to identify discount levels required for cost-effectiveness.

Our review extends the current evidence base beyond tumor-specific evaluations. Previous economic reviews have largely focused on individual cancers such as NSCLC, with mixed conclusions regarding cost-effectiveness due to high drug prices and variable clinical benefit across subgroups.[26-30] In our review sample, the proportion of studies reporting cost-effectiveness was similar across treatment lines (first-line, 54% vs second-line, 53%) and only modestly higher for combination than single-agent immunotherapy (62% vs 56%). These differences are small and should not be overinterpreted, given heterogeneity in models, inputs, and reporting.[31,32]

Table 4. Distribution of Cost-Effectiveness Decisions by Clinical and Economic Components, 2015 to 2025

Clinical and economic components	Cost-effectiveness decision, No. of CEAs	
	Cost-effective	Not cost-effective
Drug combination status in the adjuvant immunotherapy (intervention)		
Single drug (1 drug)	27	21
Combined (≥2 drugs)	13	8
χ^2 Test of independence	0.19	0
P value	.66	0
Cramér V value[b]	0.05 (negligible association)	0
Type of treatment mode(s) in the adjuvant immunotherapy (intervention)		
First-line	25	21
Second-line	8	7
First- and second-line	1	1
Third-line and later	1	0
First-line	5	0
Fisher exact χ^2 test of independence	4.78	0
Asymptotic *P* value	.31	0
Monte Carlo χ^2 *P* value[a]	.31	0
Cramér V value[b]	0.26 (small association)	0
Cancer type (disease)		
Bladder cancer	1	0
Breast cancer	3	0
Cervical cancer	0	1
Colorectal cancer	0	1
Diffuse large B-cell lymphoma	3	0
Endometrial cancer	0	2
Esophageal and gastroesophageal	1	0
Esophageal squamous cell carcinoma	1	1
Hepatocellular carcinoma	0	1
Lymphoblastic leukemia	1	0
Melanoma	3	1
Multiple myeloma	1	0
Nasopharyngeal carcinoma	3	0
NSCLC	19	16
SCLC	1	4
Renal cell carcinoma	2	2
Urothelial carcinoma	1	0
Disease subcategory		
Lung vs other cancers		
Lung (NSCLC + SCLC)	20	20
All other cancers	20	9
χ^2 Test of independence	2.48	0
P value	.11	0
Cramér V value[b]	0.19	0
NSCLC vs all other cancers		
NSCLC	19	16
Other cancers	21	13
χ^2 Test of independence	0.39	0
P value	.52	0
Cramér V value[b]	0.08	0
Melanoma vs all other cancers		
Melanoma	3	1
All other cancers	37	28
Fisher exact χ^2 test of independence	0.51	0
P value	.63	0
Cramér V value[b]	0.09	0

(continued)

Table 4. Distribution of Cost-Effectiveness Decisions by Clinical and Economic Components, 2015 to 2025 (continued)

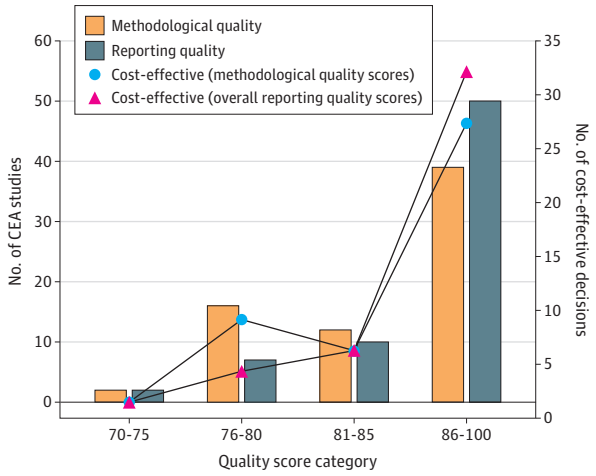
Clinical and economic components	Cost-effectiveness decision, No. of CEAs	
	Cost-effective	Not cost-effective
Funding sources		
Industry funded	17	3
Not industry (academic/government)	13	15
No funding/not reported (no data)	10	11
Fisher exact χ^2 test of independence	8.45	0
P value	.01	0
Cramér V value[b]	0.35	0
Total No. of CEAs	40	29

Abbreviation: CEA, cost-effectiveness analysis; NSCLC, non–small cell lung cancer; SCLC, small cell lung cancer.

[a] Monte Carlo χ^2 *P* value was generated through 10 000 simulations (appropriate due to small expected counts); Monte Carlo χ^2 was applied when row cell count × column cell count was <2 or any cell had an expected count <1.

[b] Cramér V benchmarks value (small/weak association if V value ≤0.20; moderate association if 0.20 <V value ≤0.60; strong association if V value >0.60).

Figure. Distribution of Quality Score Category With Cost-Effective Decision Among 69 Cost-Effectiveness Analyses



Using the quality bands, we grouped studies as lower or moderate quality (≤85) vs higher quality (86-100) and compared the proportion concluding the intervention was cost-effective. The probability value (*P* value) was generated using Pearson χ^2 (2 × 2) test; test 1 ($\chi^2 1$ = 4.67; Cramér V = 0.26, small or moderate association) and test 2 ($\chi^2 1$ = 1.58; Cramér V = 0.15, small association). Methodological quality, test 1: 27 of 39 studies (69.2%) rated as higher quality vs 13 of 30 (43.3%) rated as lower or moderate quality and concluded cost-effective; *P* = .03. Reporting quality, test 2: 27 of 39 studies (69.2%) rated as higher quality vs 13 of 30 (43.3%) rated as lower or moderate quality and concluded to be cost-effective (*P* = .21).

Limitations

The methodologic heterogeneity observed across studies warrants attention. While most evaluations used Markov or partitioned survival models, substantial variation existed in time horizons, discounting, extrapolation of survival data and health utility measurement. These inconsistencies can affect the comparability and robustness of findings. Moreover, although nearly all studies included sensitivity analyses, only a minority adopted a societal perspective, considered long-term adverse effects, or incorporated patient preferences.[33,34] As a result, many studies may underestimate long-term costs and overstate treatment value, especially in clinical settings.

Geographic distribution was another limitation, with most studies conducted in high-income countries. This limits generalizability to low- and middle-income settings, where affordability and access remain key barriers. Given the high price sensitivity observed across included studies, future updates should re-evaluate ICERs given that PD-1/PD-L1 prices change with generic/biosimilar entry. Recent initiatives have highlighted the importance of expanding economic evaluations to these contexts, particularly as global cancer incidence continues to shift toward lower-resource regions.[35,36] Moreover, few evaluations incorporated adaptive pricing schemes, confidential rebates, or managed entry agreements, factors that increasingly influence clinical reimbursement decisions. Given the observational, study-level synthesis and unmeasured design heterogeneity, the association between sponsorship and favorable cost-effectiveness conclusions should be interpreted cautiously because it may reflect funding-related bias and selective-reporting or publication bias rather than causation.

Conclusions

From a policy standpoint, the findings of this systematic review support the use of structured, context-specific health technology assessment frameworks to evaluate adjuvant immunotherapies. For health systems under financial constraints, prioritizing subgroups with the highest absolute benefit may be a viable approach to ensure sustainable access. Countries such as Australia, Canada, and the United Kingdom have begun to apply value-based pricing or conditional funding mechanisms to immunotherapies, and such models may need to expand as the treatment landscape evolves.

Clinically, this review reinforces the importance of careful patient selection, particularly for therapies with substantial up-front costs. Biomarker-guided strategies, risk stratification, and shared decision-making may help align clinical outcomes with economic value. In parallel, ongoing efforts to collect clinical data on outcomes, costs, and health-related quality of life will be essential to update and validate economic models over time.

Adjuvant immunotherapy appears to offer meaningful health gains and is often cost-effective across a range of cancer types and treatment strategies. However, its economic value is context-dependent and influenced by methodologic, clinical, and policy-

specific factors. Future research should prioritize transparent and standardized economic methods, address evidence gaps in under-represented settings, and inform equitable and cost-conscious integration of immunotherapy into cancer care.

ARTICLE INFORMATION

Accepted for Publication: November 10, 2025.

Published Online: January 22, 2026. doi:10.1001/jamaoncol.2025.6080

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Author Contributions: Dr Mahumud had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Mahumud, Dahal.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Mahumud, Chen, Dahal.
Obtained funding: Mahumud.
Administrative, technical, or material support: Mahumud, Shahjalal, Dahal, Alam.
Supervision: Mahumud, Alam.
Other: Shahjalal, Dahal.

Conflict of Interest Disclosures: None reported.

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