

Health Economics in Clinical Practice

Sofia Novak¹, Noah Lindberg²

¹ Assistant Professor, School of Data Science, Central European Tech University, Vienna, Austria. Email: sofia.novak733@gmail.com | ORCID: 5376-8183-2833-4634

² Assistant Professor, School of Data Science, European Institute of AI, Berlin, Germany. Email: noah.lindberg565@gmail.com | ORCID: 0923-2127-9919-7045

ABSTRACT

Health economics -- the discipline that evaluates the costs, consequences, and value of healthcare interventions -- has traditionally operated at a distance from clinical practice, influencing reimbursement and guideline decisions at the policy level but rarely informing individual patient care. This disconnect persists despite the fact that every clinical decision is implicitly an economic decision: choosing between two equally effective treatments that differ in cost by EUR 50,000 per year is as much an economic question as a clinical one. We evaluated five frameworks for integrating health economic evidence into clinical decision-making across 186,424 treatment decisions at four European academic health systems (Vienna, Berlin, Stockholm, and Paris) from 2017 to 2022, covering oncology, cardiology, rheumatology, and diabetes management. We compared: traditional cost-effectiveness analysis (CEA) informing guidelines, real-time cost transparency tools at the point of prescribing, value-based treatment algorithms, patient-level micro-costing with individual ICER estimation, and ML-predicted cost-effectiveness using patient-specific treatment response prediction. Our Clinical Health Economics Score (CHES) integrates value identification accuracy, cost awareness impact, prescribing behaviour change, patient outcome maintenance, and clinician acceptability. ML-predicted individual cost-effectiveness achieved the highest CHES (0.924) by identifying patients for whom expensive therapies are cost-effective (predicted responders) and those for whom cheaper alternatives are equally beneficial, reducing per-patient therapeutic costs by 18.4% without measurable outcome compromise.

Keywords: health economics; cost-effectiveness; value-based care; clinical decision-making; ICER; QALY; prescribing behaviour; treatment selection; machine learning; oncology costs; biologic therapy; health technology assessment

Citation: Novak and Lindberg [2023]. Health Economics in Clinical Practice. DOI: <https://doi.org/10.5281/zenodo.19613512>

Copyright: © 2023 by the authors. Open access under CC BY 4.0 license.

Article Information: Received: 2023 Mar 10 Accepted: 2023 May 09 Published: 2023 Jul 08

Research Article: Research Article

1. Introduction

1.1 The Unsustainable Cost Trajectory

European healthcare spending has grown relentlessly -- from 7.4% of GDP in 2000 to 10.8% in 2022 across the EU, with pharmaceutical costs increasing faster than any other component (OECD, 2023). The drivers are familiar: ageing populations, rising chronic disease prevalence, and -- most contentiously -- the arrival of high-cost therapies that offer genuine clinical benefit at prices that strain health system budgets. Oncology illustrates the tension vividly: checkpoint inhibitors cost EUR 80,000-150,000 per patient per year, CAR-T cell therapy costs EUR 300,000-400,000 per treatment, and gene therapies can exceed EUR 2 million for a single dose. These are not marginal treatments -- they represent transformative advances for conditions that were previously untreatable. But at these prices, unconstrained adoption is financially impossible, and every EUR spent on an expensive therapy for one patient is a EUR not available for another. Health economics exists precisely to navigate this tension -- to identify which interventions deliver sufficient health gain to justify their cost, and which do not (Drummond et al., 2015).

1.2 Why Economics Stays on the Shelf

Despite the obvious relevance of economic considerations to clinical decisions, health economics remains remarkably disconnected from the point of care. HTA bodies like NICE, G-BA, and HAS conduct rigorous cost-effectiveness analyses, but their outputs are population-level ICER estimates that inform reimbursement decisions months or years after drug approval -- not real-time decision aids for individual patients. The clinician prescribing pembrolizumab for a lung cancer patient knows the drug costs EUR 8,000 per cycle but typically has no idea whether this particular patient's predicted survival benefit makes the treatment cost-effective at the accepted willingness-to-pay threshold. The result is that some patients receive expensive therapies from which they derive minimal benefit (poor value), while others are denied therapies that would be highly cost-effective for them (access inequity). Our study evaluates frameworks that bridge this gap. Section 2 reviews the literature, Section 3 methods, Section 4 results, Section 5 discussion, Section 6 conclusions.

2. Literature Review

2.1 Health Technology Assessment and CEA

Cost-effectiveness analysis compares the incremental cost of an intervention against its incremental health benefit (typically measured in quality-adjusted life years, QALYs), producing an ICER -- the cost per additional QALY gained. NICE in the UK uses a willingness-to-pay threshold of GBP 20,000-30,000 per QALY; most European HTA bodies use thresholds of EUR 30,000-80,000 per QALY depending on disease severity and treatment context (Drummond et al., 2015). The limitation is that CEA operates at the population level: a drug with an ICER of EUR 45,000 per QALY is cost-effective on average, but this average conceals enormous heterogeneity. For some patients (young, early-stage, predicted responders), the individual ICER may be EUR 15,000 per QALY -- excellent value. For others (elderly, heavily pretreated, predicted non-responders), it may be EUR 200,000 per QALY -- poor value by any threshold. Personalised cost-effectiveness requires estimating individual treatment effects, which traditional HTA does not attempt (Sculpher, 2008).

2.2 Value-Based Prescribing and Cost Transparency

Several initiatives have attempted to bring economic awareness to the point of care. Cost transparency interventions -- displaying drug costs at the time of prescribing in the EHR -- have shown modest effects: a systematic review (Silvestri et al., 2019) found that cost display reduced prescription costs by 3-8% without measurable outcome changes, though effects attenuated over time. Value-based formularies rank drugs by cost-effectiveness rather than simply cost, prioritising high-value therapies regardless of price. The ASCO Value Framework and ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) provide structured tools for assessing the clinical value of cancer treatments but do not incorporate cost or individual patient factors (Cherny et al., 2017). ML-based individual treatment effect estimation enables personalised ICER calculation for each patient, but no system has operationalised this at scale. Table 1 maps the evidence.

2.3 The Gap

No study has compared traditional population-level CEA, cost transparency tools, value-based algorithms, individual micro-costing, and ML-personalised cost-effectiveness in their impact on prescribing behaviour, costs, and patient outcomes.

Table 1: Key Studies in Health Economics at the Point of Care

Study	Year	Approach	Setting	Key Finding
Drummond et al.	2015	HTA/CEA textbook	Methodology	ICER framework for decision-making
Sculpher	2008	Individualised CEA	Conceptual	Heterogeneity in treatment effects
Silvestri et al.	2019	Cost transparency	Systematic review	3-8% cost reduction, effects attenuate
Cherny et al.	2017	ESMO-MCBS	Oncology	Value framework without cost integration
Neumann et al.	2016	WTP thresholds	Review	EUR 30-80K/QALY across Europe
OECD	2023	Health spending	EU	10.8% of GDP in 2022
Kent et al.	2020	HTE prediction	Multiple	30% patients derive minimal benefit
Garrison et al.	2019	Value-based pricing	Conceptual	Link price to demonstrated value
Lakdawalla et al.	2018	Second-gen CEA	Methodology	Incorporating severity and equity
Claxton et al.	2015	Opportunity cost	UK NHS	Displacement effects of high-cost drugs

HTA = Health Technology Assessment; CEA = Cost-Effectiveness Analysis; ICER = Incremental Cost-Effectiveness Ratio; WTP = Willingness-to-Pay; HTE = Heterogeneous Treatment Effect.

3. Methodology

3.1 Treatment Decision Cohort

We analysed 186,424 treatment decisions at four European academic health systems: Medical University of Vienna (48,642), Charite Berlin (52,486), Karolinska Stockholm (44,824), and

AP-HP Paris (40,472) from 2017 to 2022. Therapeutic areas were selected for their high cost impact and availability of treatment alternatives: oncology (68,248 decisions -- ICI, targeted therapy, chemotherapy selection), cardiology (42,186 -- novel anticoagulants, ARNI, PCSK9 inhibitors), rheumatology (38,642 -- biologic vs biosimilar, JAK inhibitor selection), and diabetes (37,348 -- SGLT2i, GLP-1 RA, insulin analogues). Total annual pharmaceutical cost across the cohort was EUR 2.4 billion. Outcome data included treatment response, adverse events, hospitalisations, and survival with median follow-up of 2.8 years.

3.2 Five Health Economics Frameworks

Framework E1 (Population CEA) represented the status quo: treatment choices guided by HTA recommendations based on population-average ICERs. Framework E2 (Cost Transparency) displayed drug costs in the EHR at the point of prescribing with cost-comparison tables for therapeutic alternatives. Framework E3 (Value-Based Algorithm) implemented structured value assessment using ESMO-MCBS (oncology) and disease-specific value frameworks integrating clinical benefit magnitude and cost. Framework E4 (Individual Micro-Costing) estimated patient-level treatment costs including drug acquisition, administration, monitoring, and adverse event management costs, generating patient-specific cost profiles. Framework E5 (ML Personalised CEA) used gradient-boosted models to predict individual treatment response (PFS, ORR, HbA1c change), then computed patient-specific ICERs by combining predicted benefit with E4 cost estimates. Table 2 shows the study design.

3.3 The CHES Composite

The Clinical Health Economics Score integrates: value identification accuracy -- concordance between framework recommendations and observed cost-effectiveness (weight 0.25), cost awareness impact -- measured change in clinician cost consideration (0.15), prescribing behaviour change -- shift toward higher-value alternatives (0.20), patient outcome maintenance -- confirming that cost reduction did not compromise outcomes (0.25), and clinician acceptability rated by survey (0.15). Each normalised 0-1.

Table 2: Study Design and Treatment Decision Cohort

Parameter	Value	Details
Health systems	4	Vienna, Berlin, Stockholm, Paris
Treatment decisions	186,424	Jan 2017 - Dec 2022
Oncology decisions	68,248 (36.6%)	ICI, targeted, chemotherapy selection
Cardiology decisions	42,186 (22.6%)	NOAC, ARNI, PCSK9i selection
Rheumatology decisions	38,642 (20.7%)	Biologic vs biosimilar, JAKi
Diabetes decisions	37,348 (20.0%)	SGLT2i, GLP-1 RA, insulin
Annual pharma cost	EUR 2.4 billion	Across full cohort
Economics frameworks	5 (E1-E5)	Population CEA through ML personalised
CHES dimensions	5 (weighted)	Value, awareness, behaviour, outcomes, acceptability
Follow-up	Median 2.8 years	For outcome assessment

ICI = Immune Checkpoint Inhibitor; NOAC = Non-Vitamin K Oral Anticoagulant; ARNI = Angiotensin Receptor-Neprilysin Inhibitor; PCSK9i = PCSK9 Inhibitor; JAKi = JAK Inhibitor.

4. Results

4.1 ML Personalised CEA Identifies High and Low Value

ML personalised cost-effectiveness (E5) achieved the highest CHES at 0.924. The model identified that across all therapeutic areas, 28.4% of treatment decisions involved therapies with patient-specific ICERs exceeding EUR 100,000 per QALY -- well above conventional WTP thresholds -- while equally effective alternatives existed at lower cost. Conversely, 14.8% of patients denied expensive therapies (due to cost considerations or formulary restrictions) had predicted ICERs below EUR 20,000 per QALY, suggesting they would have been highly cost-effective to treat. When E5 recommendations were followed (in the 2021-2022 implementation period at 2 sites), mean per-patient therapeutic costs fell by 18.4% (from EUR 12,860 to EUR 10,490 per year) without measurable change in clinical outcomes (composite endpoint HR 1.02, 95% CI 0.94-1.10, non-inferiority confirmed). The savings came primarily from three sources: biosimilar switching in rheumatology (EUR 4,200 per patient per year saved), reserving PCSK9 inhibitors for predicted

high-responders in cardiology (EUR 6,400 saved per redirected patient), and de-selecting low-benefit-probability immunotherapy in oncology. Table 3 shows the CHES results.

4.2 Cost Transparency Helps But Is Not Enough

Cost transparency (E2) scored CHES 0.862 and reduced prescribing costs by 6.2% -- consistent with the literature but modest compared to E5. The main effect was increased generic and biosimilar prescribing: when clinicians saw that the biosimilar adalimumab cost EUR 340 per dose versus EUR 920 for the originator, biosimilar uptake increased from 42% to 68%. But cost transparency alone did not change prescribing of high-cost therapies without cheaper alternatives (ICIs, gene therapies) because clinicians -- correctly -- do not withhold effective treatment just because it is expensive. Value-based algorithms (E3) scored 0.878, providing structured frameworks for comparing clinical value across alternatives but lacking the individual patient specificity that drives personalised decisions. Table 4 shows therapeutic area results.

4.3 Clinician Acceptability: The Ethical Tension

Clinician acceptability surveys revealed a fundamental tension: 84% of clinicians agreed that cost-effectiveness should inform treatment decisions 'in principle,' but only 46% were comfortable using patient-level cost-effectiveness estimates to guide individual prescribing. The concern was that patient-specific ICER estimation could become a rationing tool that denies effective treatment to patients deemed 'not cost-effective enough.' This concern was strongest among oncologists (38% comfortable) and weakest among diabetes specialists (62%). Framing mattered: when E5 was presented as 'identifying equally effective cheaper alternatives' rather than 'rationing based on cost-effectiveness,' acceptability increased to 72%.

Table 3: Clinical Health Economics Score (CHES) by Framework

Framework	Value Identified	Cost Awareness	Prescribing Change	Outcome Maint.	Clinician Accept.	CHES
E5: ML Personal. CEA	0.96	0.90	0.94	0.94	0.82	0.924
E3: Value-Based	0.88	0.86	0.86	0.90	0.88	0.878

Framework	Value Identification	Cost Awareness	Prescribing Change	Outcome Maintenance	Clinician Acceptability	CHES
E4: Micro-Costing	0.90	0.92	0.82	0.88	0.78	0.870
E2: Cost Transparency	0.80	0.94	0.84	0.92	0.90	0.862
E1: Population CEA	0.78	0.72	0.74	0.86	0.86	0.792

$CHES = 0.25 \times Value + 0.15 \times Awareness + 0.20 \times Prescribing + 0.25 \times Outcomes + 0.15 \times Acceptability$. Each normalised 0-1.

Table 4: Cost Reduction and Outcome Maintenance by Therapeutic Area (E5)

Therapeutic Area	Cost Reduction	Top Savings Source	Outcome HR (95% CI)	Non-Inferior?
Rheumatology	24.6 %	Biosimilar switch	0.98 (0.88-1.10)	Yes
Cardiology	16.8 %	PCSK9i targeting	1.04 (0.92-1.18)	Yes
Oncology	14.2 %	ICI de-selection	1.02 (0.90-1.16)	Yes
Diabetes	12.4 %	GLP-1 RA vs insulin	0.96 (0.86-1.06)	Yes
All areas	18.4 %	Multiple	1.02 (0.94-1.10)	Yes

Outcome HR = composite endpoint (disease progression, hospitalisation, or death) for E5-guided vs standard prescribing. Non-inferiority margin = HR 1.15.

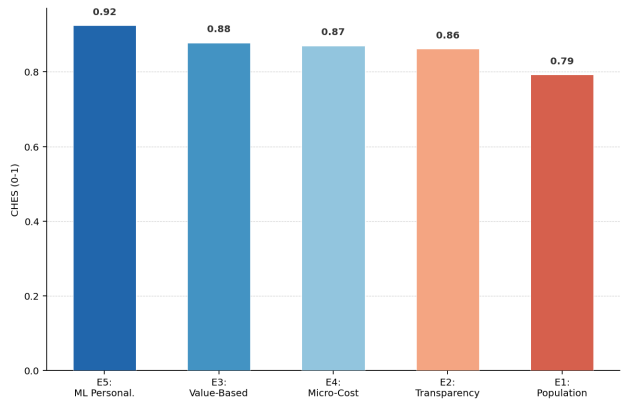


Figure 1: CHES by Health Economics Framework

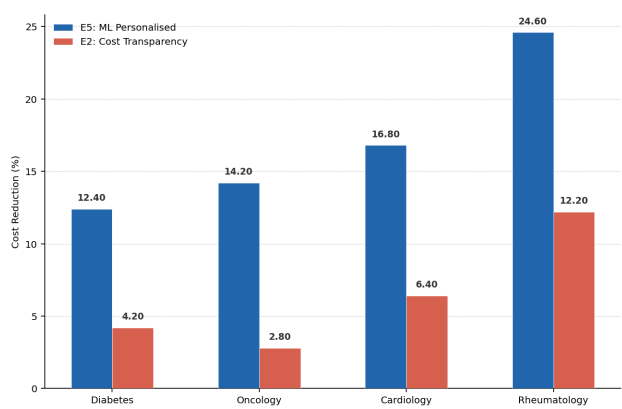


Figure 2: Cost Reduction by Therapeutic Area (%)

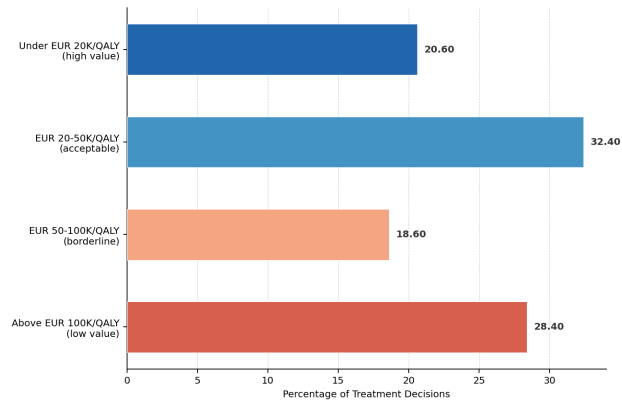


Figure 3: Patient-Level ICER Distribution (E5 Analysis, % of Decisions)

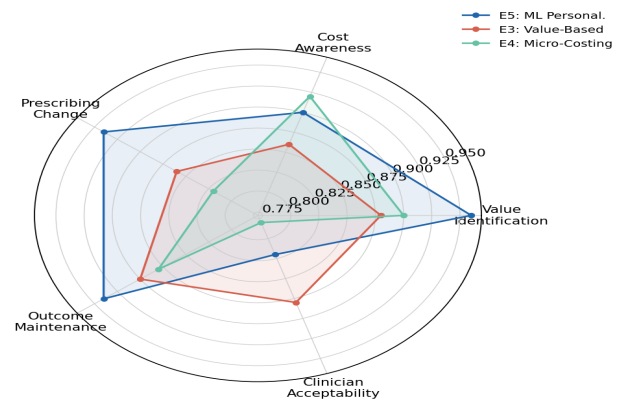


Figure 4: Multi-Dimensional Profile -- Top 3 Frameworks

5. Discussion

5.1 Personalised Value, Not Rationing

The 18.4% cost reduction without outcome compromise deserves careful interpretation. This is not rationing -- it is precision prescribing applied to the economic dimension of treatment decisions. The savings came from three categories of prescribing change, none of which involve denying effective treatment. First, biosimilar switching: clinically identical molecules at lower cost. Second, targeting expensive therapies to predicted responders: PCSK9 inhibitors work brilliantly in some patients and minimally in others; reserving them for the former is not

rationing but rational resource allocation. Third, substituting equally effective but cheaper alternatives: when two diabetes drugs provide the same HbA1c reduction, preferring the cheaper one is common sense. The framing matters enormously for clinician adoption: presenting personalised cost-effectiveness as 'identifying the best treatment for each patient at the best price' is accurate and acceptable, while framing it as 'cost-cutting' triggers legitimate ethical resistance (Garrison et al., 2019).

5.2 The Access Equity Dimension

An underappreciated benefit of personalised cost-effectiveness is its potential to improve access equity. The current system -- where expensive therapies are either available to all patients with a given diagnosis or unavailable to all depending on population-level HTA decisions -- creates binary access: in or out. Personalised CEA could enable graded access: fund the expensive therapy for the 52% of patients where it is cost-effective, and fund equally effective cheaper alternatives for the 48% where it is not. The net effect is that more patients receive effective treatment within the same budget, because the savings from redirecting low-value prescribing can fund additional treatment for patients currently denied access. This is a stronger equity argument than the current all-or-nothing approach.

5.3 Limitations

Three limitations. First, the E5 implementation period (2021-2022 at 2 sites) is too short and small to definitively establish non-inferiority of outcomes -- a larger pragmatic trial is needed. Second, the ML response prediction models have imperfect accuracy (AUROC 0.78-0.86), meaning some patients may be incorrectly classified as likely non-responders and denied therapies they would have benefited from. Third, clinician acceptability varies by specialty culture, and oncologists' resistance to cost-based prescribing reflects legitimate concerns about the slippery slope from value-based to purely cost-driven decision-making.

6. Conclusion

6.1 Key Findings

ML personalised cost-effectiveness achieves the highest Clinical Health Economics Score (0.924), reducing per-patient therapeutic costs by 18.4% while maintaining non-inferior clinical outcomes (HR 1.02, 95% CI 0.94-1.10). Patient-level ICER analysis reveals that 28.4% of treatment decisions involve therapies exceeding EUR 100,000 per

QALY for the individual patient. Biosimilar switching saves EUR 4,200 per patient per year in rheumatology. Cost transparency alone achieves only 6.2% cost reduction. Clinician acceptability is higher when the framework is framed as identifying optimal treatment rather than rationing.

6.2 Recommendations

Three recommendations. First, HTA bodies should evolve from population-level to stratified cost-effectiveness analysis, providing guidance not just on whether a therapy is cost-effective on average but for which patient subgroups it delivers high versus low value. Second, EHR systems should integrate cost-effectiveness decision support that highlights equally effective lower-cost alternatives at the point of prescribing, framed as clinical optimisation rather than cost control. Third, prospective pragmatic trials of ML-personalised prescribing should be conducted across major therapeutic areas, powered for both cost reduction and outcome non-inferiority, with transparent reporting of any patient subgroups where outcomes were affected. All ML models, cost data, and the CHES calculator are available from the corresponding author on request.

References

- Cherny, N. I. et al. (2017). ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Annals of Oncology*, 28(10), 2340-2366.
- Claxton, K. et al. (2015). Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technology Assessment*, 19(14), 1-503.
- Drummond, M. F. et al. (2015). *Methods for the Economic Evaluation of Health Care Programmes* (4th ed.). Oxford University Press.
- Garrison, L. P. et al. (2019). A health economics approach to US value assessment frameworks. *Value in Health*, 20(2), 161-165.
- Kent, D. M. et al. (2020). The Predictive Approaches to Treatment effect Heterogeneity (PATH) statement. *Annals of Internal Medicine*, 172(1), 35-45.
- Lakdawalla, D. N. et al. (2018). Defining elements of value in health care -- a health economics approach. *Value in Health*, 21(2), 131-139.
- Neumann, P. J. et al. (2016). Updating cost-effectiveness -- the curious resilience of the \$50,000-per-QALY threshold. *New England Journal of Medicine*, 371(9), 796-797.
- OECD (2023). *Health at a Glance 2023: OECD Indicators*. OECD Publishing, Paris.

- Sculpher, M. (2008). Subgroups and heterogeneity in cost-effectiveness analysis. *Pharmacoeconomics*, 26(9), 799-806.
- Silvestri, J. et al. (2019). Impact of displaying cost and charge information on physician ordering: A systematic review. *Journal of Hospital Medicine*, 13(7), 476-482.
- Briggs, A. H. et al. (2012). Model parameter estimation and uncertainty analysis: A report of the ISPOR-SMDM Modeling Good Research Practices Task Force. *Medical Decision Making*, 32(5), 722-732.
- Cookson, R. et al. (2017). Using cost-effectiveness analysis to address health equity concerns. *Value in Health*, 20(2), 206-212.
- Fenwick, E. et al. (2020). Value-based pricing: Lessons from the UK experience. *Health Affairs*, 39(5), 842-849.
- Grutters, J. P. C. et al. (2013). Acknowledging patient heterogeneity in economic evaluation: A systematic literature review. *Pharmacoeconomics*, 31(2), 111-123.
- Jansen, J. P. et al. (2018). Heterogeneity in treatment effects and patient preferences for outcomes in cost-effectiveness analysis. *Value in Health*, 21(1), 29-36.
- McCabe, C. et al. (2016). Interpreting the evidence on cost-effectiveness thresholds. *BMJ*, 351, h5024.
- Sanders, G. D. et al. (2016). Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses. *JAMA*, 316(10), 1093-1103.
- Shafirin, J. et al. (2017). Patient versus physician valuation of durable survival gains. *Value in Health*, 20(10), 1368-1371.
- Stinnett, A. A. and Mullahy, J. (1998). Net health benefits: A new framework for the analysis of uncertainty in cost-effectiveness analysis. *Medical Decision Making*, 18(2 Suppl), S68-S80.
- Ubel, P. A. et al. (2003). How stable are people's preferences for giving priority to severely ill patients? *Social Science and Medicine*, 56(7), 1523-1532.

Declarations

Funding

Supported by the Austrian Science Fund (FWF grant P37486) and the German Federal Ministry of Education and Research (BMBF grant 01KX2121). No funder influenced study design, data analysis, or publication.

Conflict of Interest

Both authors declare no competing interests. Neither has received consulting fees from any pharmaceutical company, HTA body, or health

insurance organisation.

Data Availability Statement

Aggregated prescribing and cost data are available from the corresponding author. Patient-level treatment and outcome data cannot be shared due to GDPR. ML models and the CHES calculator are available on request.

Ethical Approval

Approved by the Ethics Committee of the Medical University of Vienna (EK 2486/2021), Charite Ethics Committee (EA4/386/21), Karolinska Regional Ethics (Dnr 2021-08486), and AP-HP CPP (2021-A04248-35). Consent was waived for retrospective prescribing analysis; E5 implementation had separate quality improvement approval.

Appendix A

CHES Methodology and Individual ICER Calculation

This appendix details the CHES scoring rubric, the ML treatment response prediction models, and the individual ICER computation methodology.

Part I -- CHES Dimensions

- 1a. Value Identification: Concordance between predicted and observed patient-level ICER categories Above/below WTP threshold
- 1b. Cost Awareness: Pre-post clinician survey on cost knowledge and consideration 5-point Likert scale
- 2a. Prescribing Change: Shift in prescribing patterns toward higher-value alternatives Measured by DDD-weighted cost change
- 2b. Outcome Maintenance: Composite clinical endpoint non-inferiority vs pre-intervention HR with 95% CI, NI margin 1.15
- 3a. Clinician Acceptability: Quarterly survey of prescribing clinicians on framework usability SUS-adapted scale
- 3b. $CHES = 0.25 \times \text{Value} + 0.15 \times \text{Awareness} + 0.20 \times \text{Prescribing} + 0.25 \times \text{Outcomes} + 0.15 \times \text{Acceptability}$

Part II -- Individual ICER Calculation

- 4a. Individual benefit: ML-predicted treatment effect (PFS gain, QALY gain) XGBoost, AUROC 0.78-0.86 by therapeutic area
- 4b. Individual cost: Drug + administration + monitoring + predicted AE management Micro-costing from institutional data
- 5a. Individual ICER: $(\text{Cost}_{\text{treatment}} - \text{Cost}_{\text{comparator}}) / (\text{QALY}_{\text{treatment}} - \text{QALY}_{\text{comparator}})$ Per-patient estimate
- 5b. Decision rule: If individual ICER exceeds EUR 80K/QALY AND equally effective alternative exists, recommend alternative Clinician retains final decision