

Economic Impact of Early Diagnosis and Treatment for Inborn Errors of Immunity with Focus on Common Variable Immunodeficiency (CVID) in Spain: A Cost-Effectiveness Perspective

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CONCLUSIONS

- Earlier diagnosis of IEI and **timely** initiation of IGRT is cost-effective and improves outcomes and is cost-effective compared with delayed diagnosis and treatment
- Timely detection reduces broader societal costs (e.g. productivity loss and premature **mortality**), supporting public health initiatives to improve awareness, access, and earlier diagnosis in Spain

BACKGROUND

- Inborn errors of immunity (IEIs) comprise > 550 rare genetic immune disorders affecting up to 1 in 1,200 people^{1,2}
- Common variable immunodeficiency (CVID), one of the most common IEIs, is characterized by impaired antibody production and a heterogeneous clinical presentation, which can result in recurrent infections and inflammatory complications³
- CVID diagnosis is often substantially delayed, increasing morbidity, mortality, and healthcare costs^{4,5}

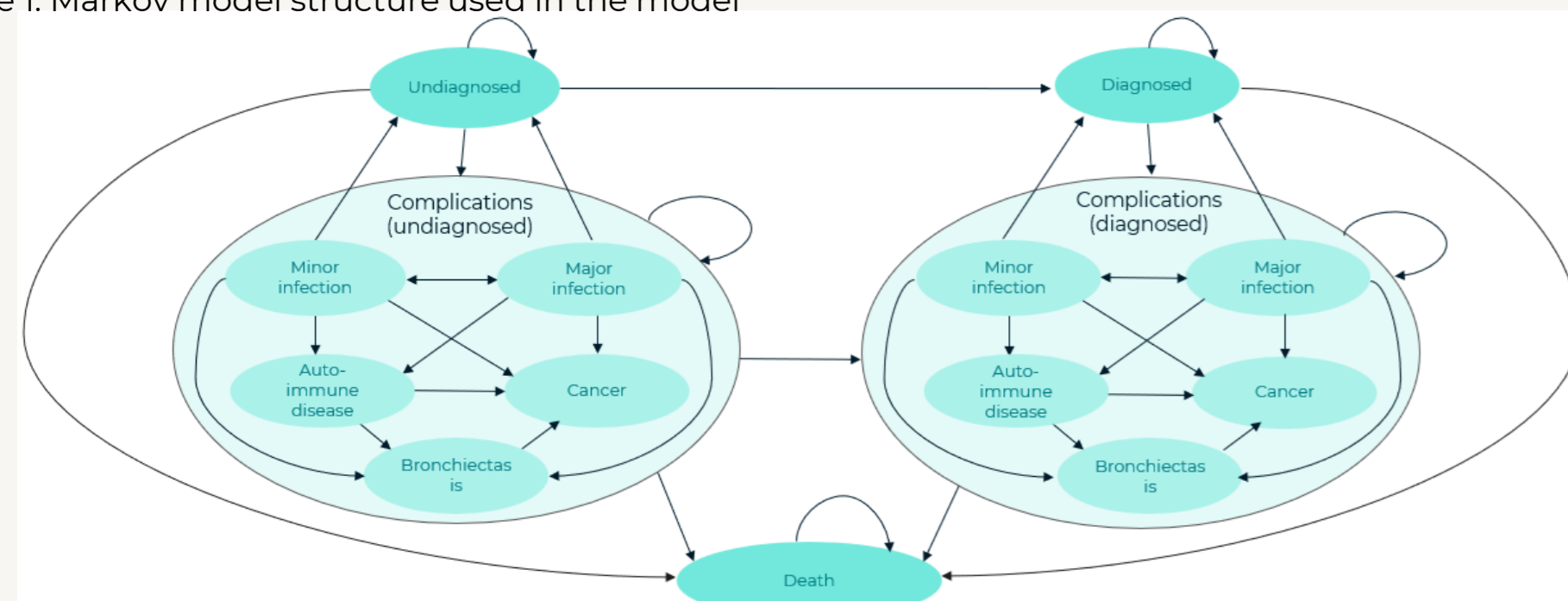
OBJECTIVE

To assess the cost-effectiveness and quality of life impact of early diagnosis and initiation of immunoglobulin replacement therapy (IGRT) vs. delayed diagnosis of CVID in Spain

METHODS

- A cohort Markov model with a Spanish payer perspective was adapted from van Wilder et al.,⁶ with a societal perspective assessed in a scenario analysis
- Model inputs (transition probabilities, mortality, costs, and health utilities) were sourced from the literature and validated by a clinical expert. Patients with delayed diagnosis were modelled to have a higher probability of complications compared to patients with early diagnosis
- IGRT was modeled as standard treatment for diagnosed patients in a complication health state
- The model used a lifetime horizon with 28-day cycles, applying a 3% annual discount rate to costs and health outcomes
- Cost-effectiveness was evaluated using Spain's €30,000/quality-adjusted life year (QALY) willingness-to-pay (WTP) threshold

Figure 1: Markov model structure used in the model



RESULTS

Results for early vs. delayed diagnosis

- **Early diagnosis was cost-effective** vs. delayed diagnosis at a WTP threshold of €30,000
- Due to **productivity loss averted in the early diagnosis** arm, the incremental costs were lower with the societal perspective, leading to an ICER of €14,643
- Results were robust to parameter uncertainty, with the probabilistic sensitivity analysis showing that early diagnosis was 71% cost-effective at a €30,000 WTP threshold

Table 1: Results for early vs. delayed diagnosis using the payer and societal perspective

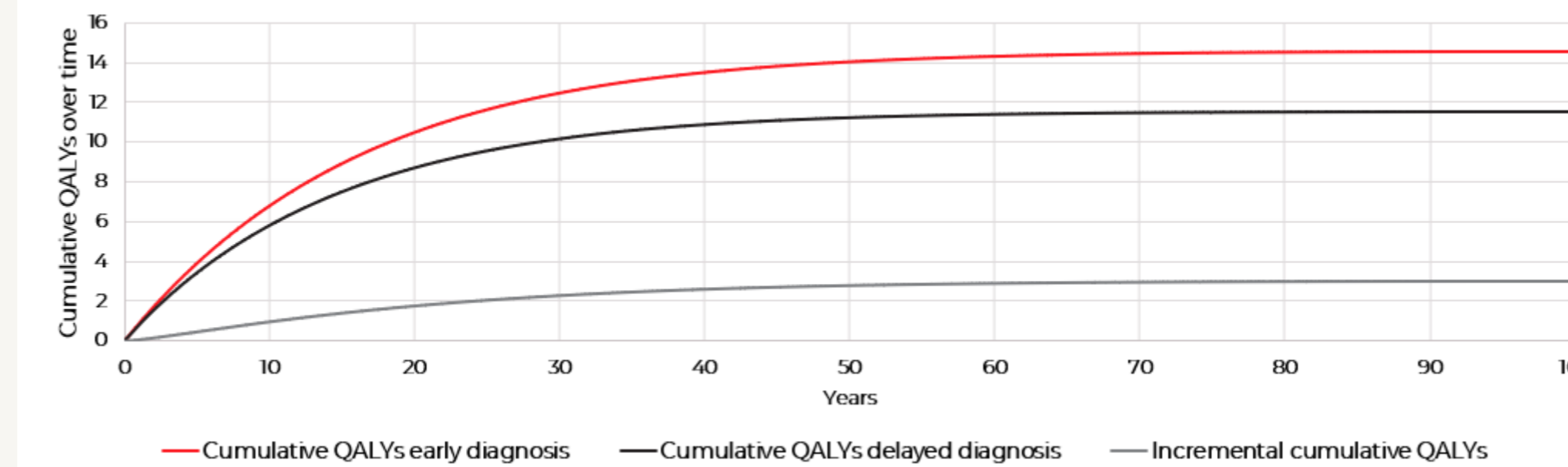
	Total costs	Total LYs	Total QALYs	Incremental costs	Incremental LYs	Incremental QALYs	ICER
Payer perspective							
Delayed diagnosis	€299,732	13.492	11.571	-	-	-	
Early diagnosis	€378,855	16.513	14.568	€79,123	3.021	2.997	€26,402
Societal perspective							
Delayed diagnosis	€563,374	13.492	11.571	-	-	-	
Early diagnosis	€607,614	16.513	14.568	€44,240	3.021	2.997	€14,643

Key: ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year.
 Note: Costs and outcomes are discounted at 3%.

Cumulative QALYs accrued throughout the time horizon in each arm

- Over a lifetime horizon (99 years), the early diagnosis arm (red) **accrued significantly more QALYs than the delayed diagnosis arm** (black)
- By the end of the time horizon, the early diagnosis cohort accumulated roughly 15 QALYs, compared with around 12 QALYs for the delayed diagnosis cohort
- The rapidly widening gap between the early and delayed diagnosis in the first 30–40 years indicates that **early intervention delivers its greatest benefit during the initial stages**

Figure 2: Cumulative QALYs accrued throughout the time horizon

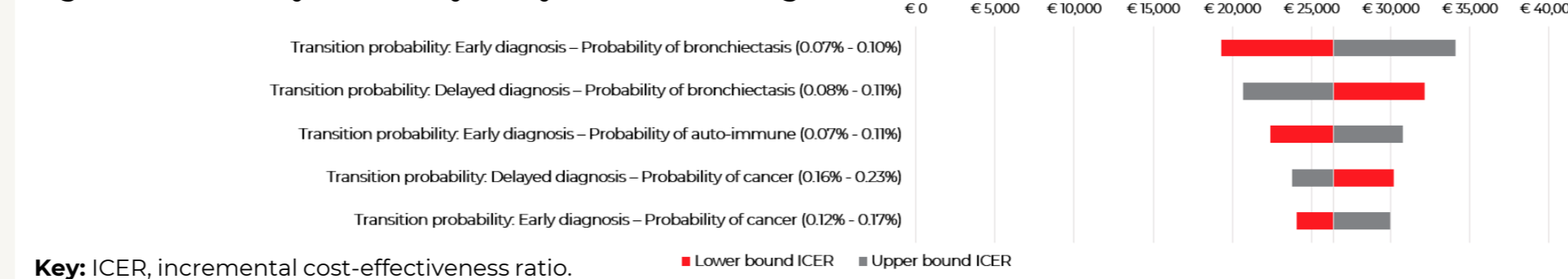


Key: QALY, quality-adjusted life year.
 Note: QALYs are discounted at 3%.

One-way sensitivity analysis (top 5 most impactful parameters)

- Transition probabilities associated with more severe complications were the biggest drivers of the model results
- **Lower transition probabilities in the early diagnosis arm and higher probabilities in the delayed diagnosis arm made the intervention more cost-effective**

Figure 4: One-way sensitivity analysis tornado diagram



Key: ICER, incremental cost-effectiveness ratio. ■ Lower bound ICER ■ Upper bound ICER

Total QALYs disaggregated by health states in each arm

- Patients in the early diagnosis arm **lived longer and remained asymptomatic for longer**, as reflected by an incremental gain of 2,348 QALYs in the asymptomatic health state. This corresponds to around 60% of the total incremental QALYs
- Patients diagnosed and treated earlier who developed autoimmune or bronchiectasis complications were expected to **have longer survival than comparable patients with delayed diagnosis**

Table 2: Disaggregated QALYs by arm for each health state

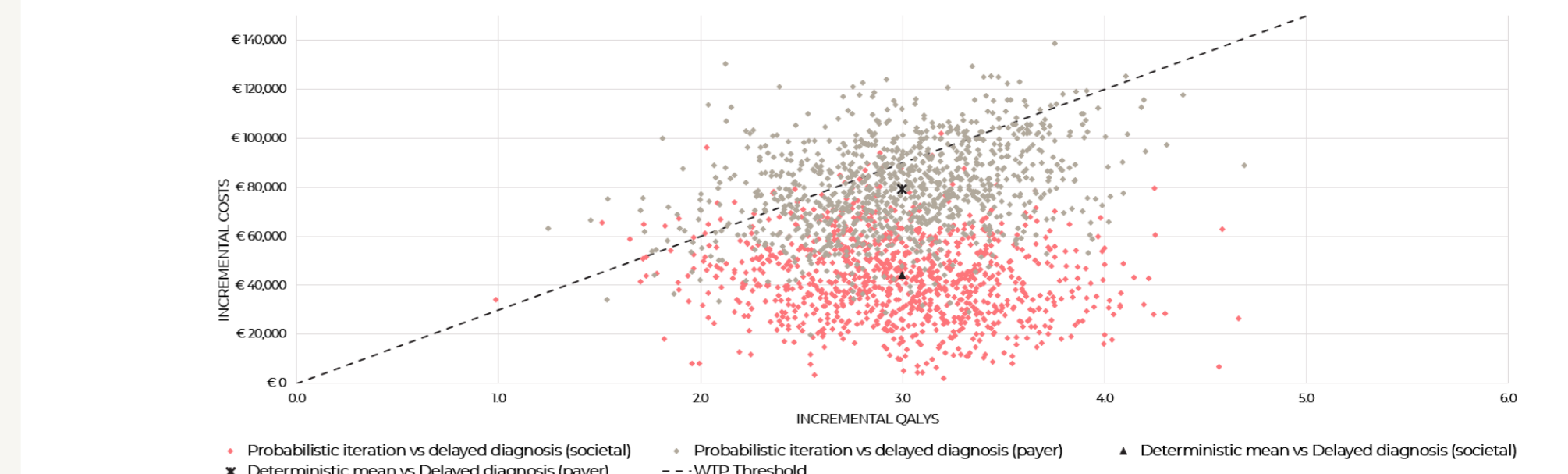
Health state	Early diagnosis (QALYs)	Delayed diagnosis (QALYs)	Increment
Asymptomatic	10.696	8.348	2.348
Minor infection	0.290	0.366	-0.077
Major infection	0.053	0.189	-0.136
Auto-immune disease	0.849	0.299	0.550
Bronchiectasis	1.640	1.266	0.374
Cancer	1.040	1.102	-0.062
Total	14.568	11.571	2.997

Key: QALY, quality-adjusted life year.
 Note: QALYs are discounted at 3%.

Cost-effectiveness plane for early vs. delayed diagnosis

- Probabilistic ICERs from **both the payer and societal perspective fell below the €30,000 WTP threshold** (dashed line)
- 71% of iterations for the payer perspective fell below the WTP line, indicating that early diagnosis is highly likely to be cost-effective at a WTP of €30,000
- Adopting a societal perspective increased the probability of cost-effectiveness to 98% at a WTP of €30,000

Figure 3: Cost-effectiveness plane using payer and societal perspectives

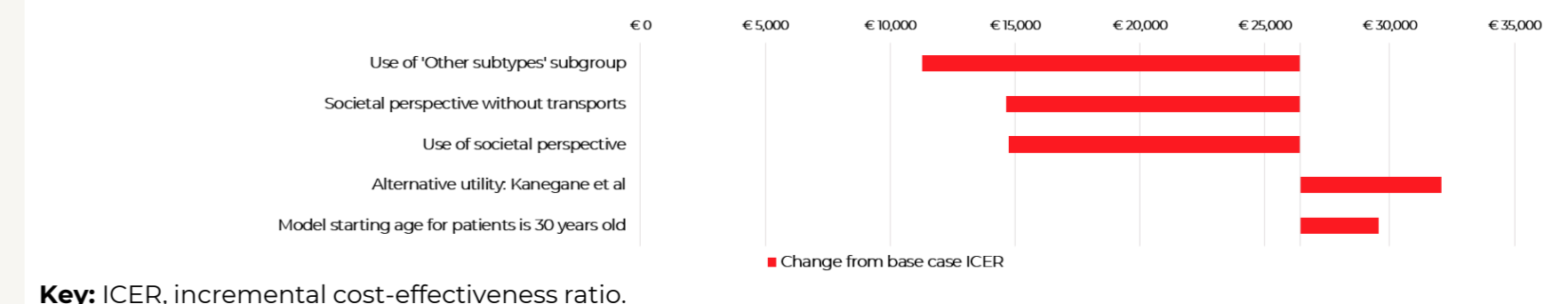


Key: QALY, quality-adjusted life year; WTP, willingness-to-pay.

Scenario analysis (5 most impactful scenarios)

- Considering an alternative subgroup (other IEI subtypes) presented the biggest reduction in ICER
- Adopting a later baseline age (30 years) reduced cost effectiveness (although the ICER remained under €30k), suggesting that **screening remains a cost-effective use of resources into adulthood**

Figure 5: Scenario analysis – tornado diagram



Key: ICER, incremental cost-effectiveness ratio.