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Correlation Between Ultra-Orphan Drug Costs, Cost-Effectiveness Metrics And Disease Prevalence

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Objective

Ultra-orphan drug prices frequently exceed conventional incremental cost-effectiveness ratio (ICER) thresholds. While previous research has identified links between treatment costs and rare disease epidemiology, limited evidence exists for ultra-rare, paediatric, severe diseases. In particular, the relationships between ICER, incremental Quality-Adjusted Life Years (QALYs), treatment costs, and disease prevalence remain insufficiently explored.

Methods

Ultra-orphan drugs used for paediatric patients with treatment duration >1 year and approved by Food and Drug Administration (FDA) and/or Medicines & Healthcare products Regulatory Agency (MHRA) with positive U.K. reimbursement for the U.K. specific analysis were considered.
Eligible therapies were identified by screening NICE *Highly Specialized Technologies (HST)* with positive recommendations, Institute for Clinical and Economic Review assessments, and peer-reviewed publications on paediatric ultra-rare disease approvals.
For U.S. analyses, Institute for Clinical and Economic Review or other U.S.-specific cost-effectiveness studies were prioritized; for the U.K., National Institute for Health and Care Excellence (NICE) and Scottish Medicines Consortium (SMC) appraisals were preferred. If unavailable, other European HTAs or independent assessments were used. HTA/independent agency models were prioritized over company-submitted models. Prices were inflation- and currency-adjusted, and the ICER matching the approved U.K./U.S. indication was selected when multiple subpopulation results were reported.
Annual list prices (based on a 40 kg paediatric patient) were extracted from NAVLIN (September 2025). All analyses used lifetime horizons.
Correlations were assessed between ICER, annual treatment cost, incremental cost, incremental QALY, and disease prevalence.

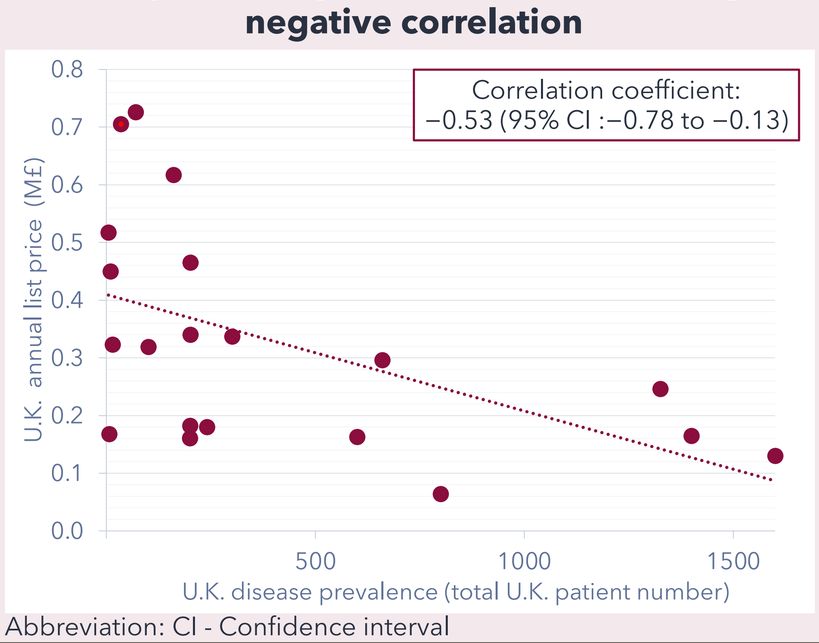
Results

Lower disease prevalence was generally associated with higher acceptable ICER thresholds and increased treatment costs, whereas greater incremental QALY gains corresponded with higher incremental costs. This pattern suggests that higher expenditures are considered more acceptable for rarer diseases and higher QALY gains. These findings reflect a higher willingness to pay for clinical benefit in the context of ultra-rare diseases and highlight the dual influence of disease rarity and therapeutic value in pricing and reimbursement decisions.

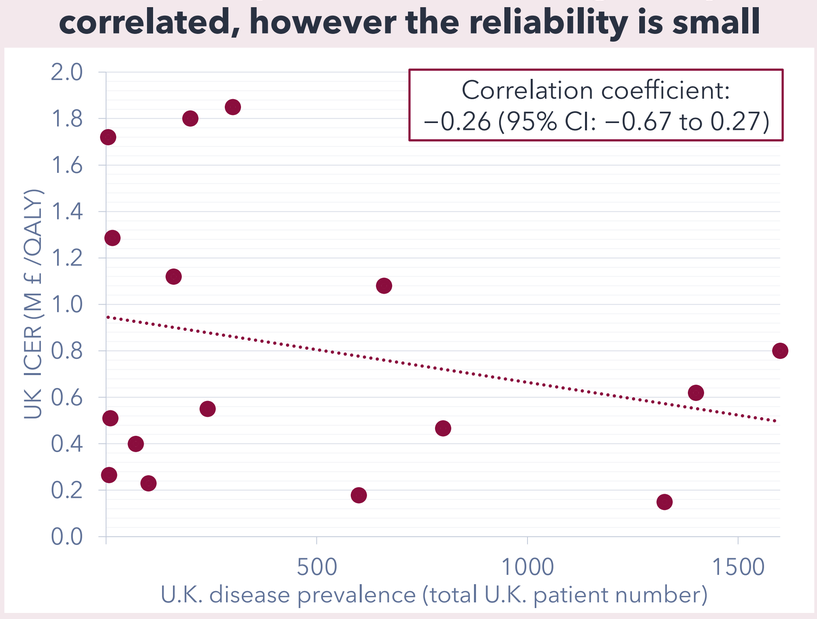
In the U.K., the correlation between ICER and prevalence is weak reflecting the stricter NICE thresholds.

21 reimbursed, paediatric, ultra orphan drugs were identified, of which 16 drugs have published ICERs.

List price and prevalence show a strong negative correlation



ICER and prevalence seem negatively correlated, however the reliability is small



Strong correlations were observed between list price and prevalence, incremental costs and ICER and incremental QALYs and incremental costs.

Correlation coefficient (95% CI)	U.K. annual list price	U.K. disease prevalence	ICER	Incremental QALY
U.K. annual list price	1			
U.K. disease prevalence	−0.53 (−0.78 to −0.13)	1		
ICER	0.19 (−0.38 to 0.66)	−0.26 (−0.7 to 0.31)	1	
Incremental QALY	0.15 (−0.41 to 0.63)	−0.19 (−0.66 to 0.38)	0.28 (−0.29 to 0.71)	1
Incremental cost	0.06 (−0.49 to 0.57)	−0.29 (−0.71 to 0.28)	0.78 (0.43 to 0.93)	0.74 (0.35 to 0.91)

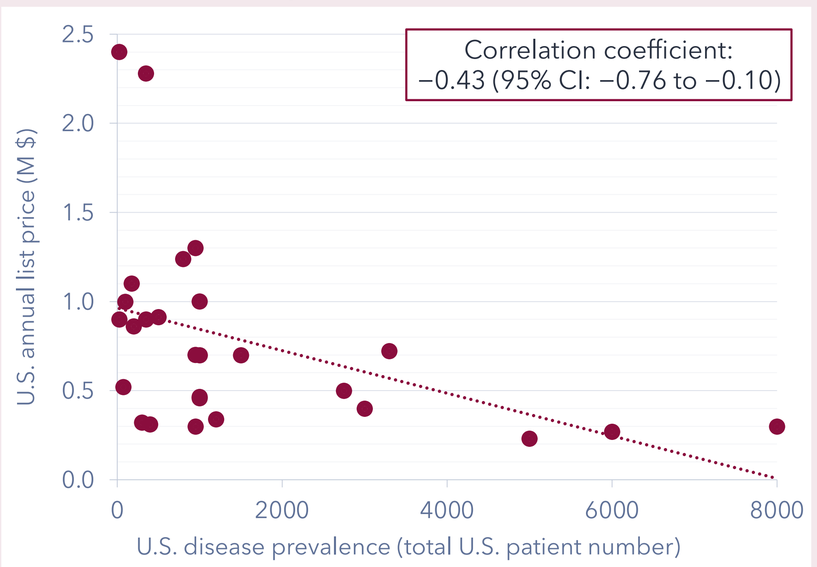
Negative correlation Positive correlation

Abbreviation: CI - Confidence interval

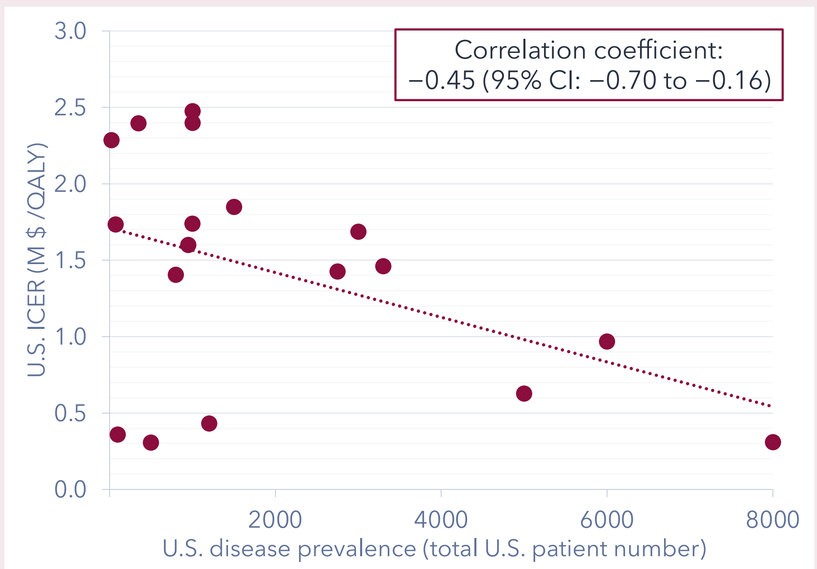
In the U.S., a strong correlation exists between ICER and prevalence reflecting the dominance of market-based pricing.

27 paediatric, ultra orphan drugs were identified, of which 18 drugs have published ICERs.

List price and prevalence show a strong negative correlation



ICER and prevalence show a strong negative correlation



Strong correlations were observed between list price and disease prevalence, ICER and prevalence, incremental costs and ICER, and incremental QALYs and incremental costs.

Correlation coefficient (95% CI)	U.S. annual list price	U.S. disease prevalence	ICER	Incremental QALY
U.S. annual list price	1			
U.S. disease prevalence	-0.43 (−0.76 to −0.10)	1		
ICER	0.47 (0.16 to 0.78)	-0.45 (−0.84 to −0.06)	1	
Incremental QALY	0 (−0.37 to 0.37)	-0.27 (−0.70 to 0.16)	0.37 (−0.04 to 0.78)	1
Incremental cost	0.23 (−0.12 to 0.58)	-0.35 (−0.78 to 0.08)	0.64 (0.29 to 0.99)	0.92 (0.74 to 1.00)

Negative correlation Positive correlation

Abbreviation: CI - Confidence interval

Conclusions

Pricing of ultra-orphan drugs is influenced by both the rarity of the disease and the magnitude of the anticipated clinical benefit. Lower disease prevalence generally supports higher pricing, while greater QALY gains can justify higher ICERs. However, health system-specific rules–such as ICER thresholds can moderate the strength of this relationship. Understanding these dynamics is essential for making informed reimbursement decisions and developing sustainable, value-based pricing strategies for ultra-rare diseases.

LatticePoint has been working with clients for decades in a range of therapeutic areas. Our clients trust our world-class team of market access leader's experience in the sciences, industry, venture capital and negotiations assess your product in the marketplace.

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