Predicting Italian EQ-5D-3L Health State Utilities from UK Values: Validation of a Nonlinear Utility Adjustment Model Using Real-World Evidence

Abdul Jabbar Omar Alsaleh[1], Elisheva Lew[2], Jérôme Msihid[3], Lorenzo Pradelli[4], Massimiliano Povero[4], Charlie Nicholls[5]

[1]Sanofi, Milan, Italy; [2]Sanofi, Paris, France; [3]Sanofi, Gentilly, France; [4]AdRes HE&OR, Torino, Italy; [5]Sanofi, Reading, United Kingdom

Poster No. PCR189

OBJECTIVE

To develop a model that translates EuroQoL 5-dimensional 3-level (EQ-5D-3L) utilities based on the United Kingdom (UK) value set into equivalent values, reflecting Italian (IT) societal preferences, leveraging a previously established nonlinear modelling approach.

CONCLUSIONS

- **This validation confirms that the nonlinear mapping model reliably translates UK EQ-5D-3L mean utilities into IT-equivalent values with high accuracy.**
- **By providing a simple and practical tool for utility transfer, the model facilitates economic evaluations in contexts where only mean utilities are available, while ensuring alignment with Italian societal preferences.**
- **Despite individual-level patient data (IPD) being the gold standard for utility adjustment between countries, utility mapping approaches can support more robust health technology assessment (HTA) by improving the cultural and methodological validity of health utility inputs as a supporting tool in the absence of IPD.**

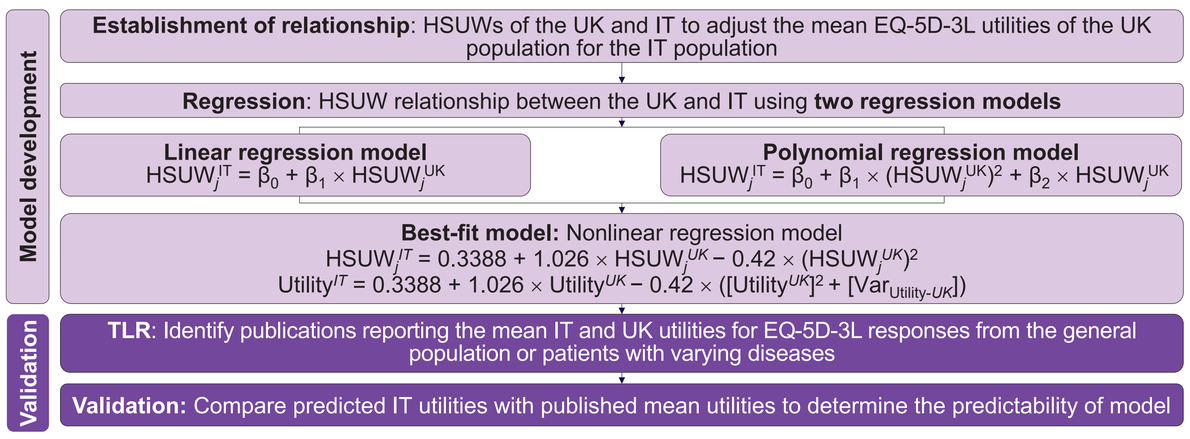
BACKGROUND

- The transferability of health state utility weights (HSUWs) across countries remains a key methodological challenge in HTAs.
- The utilities derived from the EQ-5D-3L instrument reflect country-specific societal preferences, and direct application of utilities from one country to another can misrepresent local preferences, leading to biased cost-effectiveness evaluations.[1,2]
- The National Institute for health and Care Excellence (NICE) recommends adjusting utilities before transferring them across countries to account for population differences in health state valuations.[3]
- Although the gold-standard approach for cross-country adaptation involves re-estimating utilities using country-specific tariffs applied to IPD, such data are often unavailable in published studies or secondary analyses.
- Furthermore, methods have not been established for recalibrating published utilities to reflect another country's societal preferences.
- Previously, a nonlinear model was developed to statistically translate the mean EQ-5D-3L utilities derived using the UK value set into equivalents, consistent with the IT tariff.[4]

METHODS

- The model was developed by incorporating the published IT and UK EQ-5D-3L HSUWs (N = 243) into linear and nonlinear regression analyses to establish the relationship between the weights of the two countries, with IT HSUWs as the dependent variable and UK HSUWs as the regressor.[4]
- An optimal model was selected based on coefficient of variation (R^2) values and visual analysis.
- For model validation, a targeted literature review (TLR) was conducted through electronic searches in PubMed, EMBASE, and Google Scholar up to April 2025.
- The search strategy identified studies reporting mean utilities derived from both IT and UK EQ-5D-3L scores, with no other restrictions on Participants, Intervention, Comparator, Outcomes and Study design (PICOS) framework to maximise the inclusion of relevant publications.
- Only English language publications were included, and studies reporting single-tariff utilities, non-EQ-5D-3L instruments, or missing mean values were excluded.
- The extracted data, including geographical location, sample size, study design, and mean utilities, were used for model validation.
- The model's predictive accuracy was assessed by comparing the predicted IT utilities against published values. Detailed methodology is illustrated in **Figure 1**.

Figure 1: Flowchart depicting the steps for estimating the mean EQ-5D-3L utility values for IT from the UK values

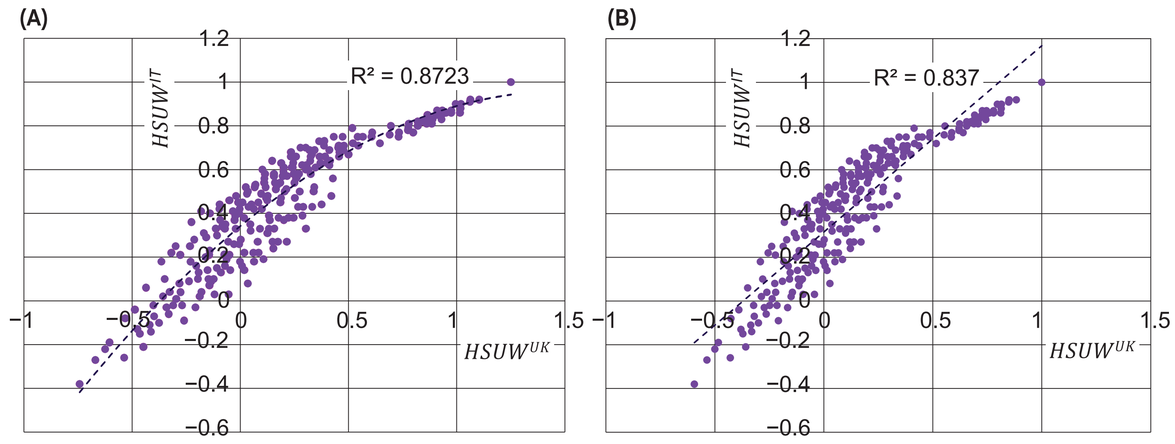


EQ-5D-3L, EuroQoL 5-dimensional 3-level; HSUW, health state utility weight; IT, Italy; j, health states from 1 to 243; n, sample size; TLR, targeted literature review; UK, United Kingdom; β_0, slope; β_1, intercept; β_2, coefficient of quadratic term

RESULTS

- Nonlinear model was deemed the best-fit model based on both visual inspection and R^2 values compared to the linear model (R^2 = 0.8723 vs 0.837) (**Figure 2**).
- The final model was expressed as:
  - $HSUW_j^{IT} = 0.3388 + 1.026 \times HSUW_j^{UK} - 0.42 \times (HSUW_j^{UK})^2$, ($j$ = 1−243 health states, IT = Italy, UK = United Kingdom)
- This relationship was then extended to mean utilities for application in published studies.
  - $Utility^{IT} = 0.3388 + 1.026 \times Utility^{UK} - 0.42 \times ([Utility^{UK}]^2 + [Var_{Utility\text{-}UK}])$.

Figure 2: Nonlinear (A) and linear (B) regression models



HSUW, health state utility weight; IT, Italy; R^2, coefficient of determination; UK, United Kingdom

- Two studies meeting the inclusion criteria were identified using TLR (**Table 1**):
  - Mozzi *et al*., (2016) evaluated health-related quality of life among patients with Crohn's disease (N = 500)
  - Joelson *et al*., (2021) assessed pre- and post-operative outcomes in patients with spinal stenosis or disc herniation (N = 27,328).

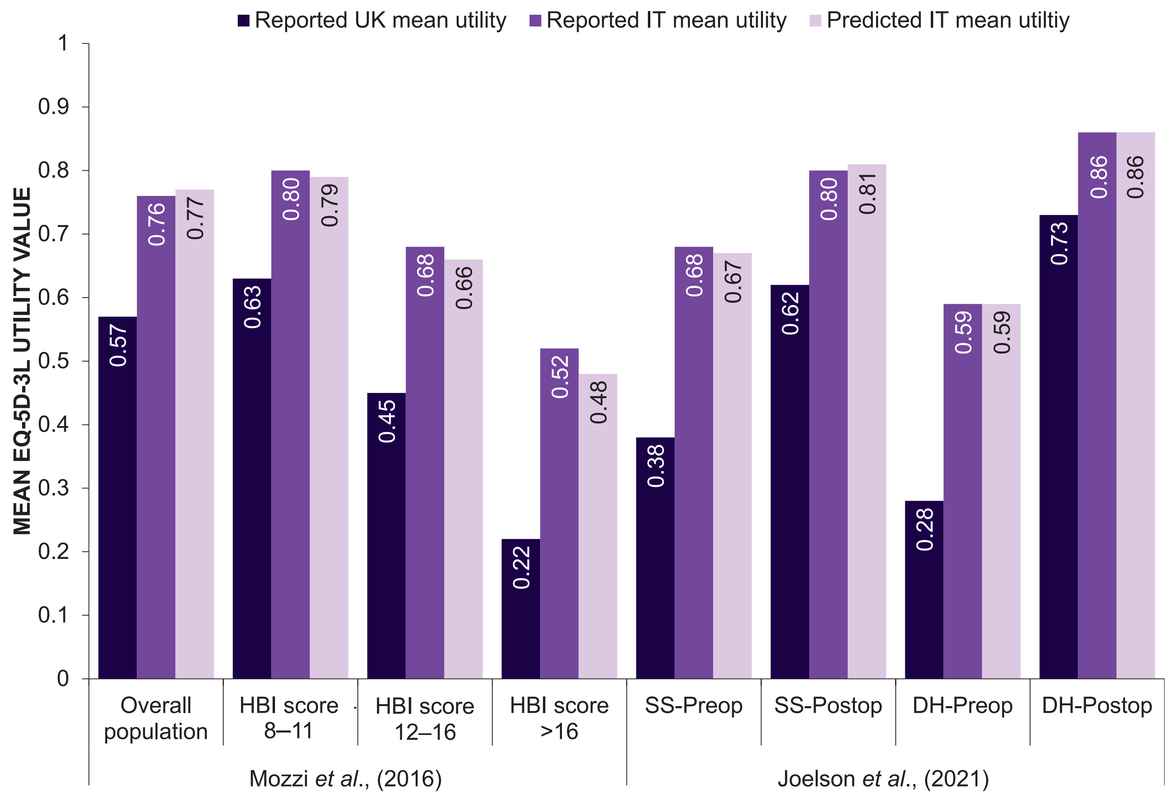
Table 1: Characteristics of the included studies

Author (year)	Location; Study design	*N*; Sample population	Mean age (SD); gender (F/M)	Disease condition
Mozzi *et al*., (2016)[5]	IT; Survey	500 HBI 8–11: (n = 389) HBI 12–16: (n = 84) HBI>16: (n = 27)	41.2 (13.8); 249/251	CD
Joelson *et al*., (2021)[6]	Multinational; Longitudinal register study	27,328 SS: (n = 16,791) DH: (n = 10,537)	NA 63.3 (0.1); 8,005/8,786 47.1 (0.1); 4,818/5,719	SS and DH

CD, Crohn's disease; DH, disc herniation; F, female; HBI, Harvey Bradshaw Index; IT, Italy; M, male; *N*, total population; *n*, sample population; NA, not available; SD, standard deviation, SS, spinal stenosis

- Across both studies, the IT utilities were consistently higher than the UK utilities, underscoring systematic differences in valuation between the two countries.
- The predicted IT utilities were closely aligned with the published IT utilities (differences <0.005 for EQ-5D-3L utility values), indicating predictive accuracy of the method (**Figure 3**).
- A slight underestimation of IT utility values was observed, likely attributable to sample size, which did not represent a significant concern for the validation.

Figure 3: Comparative illustration of reported UK and IT mean utilities versus predicted IT mean utilities



DH, disc herniation; EQ-5D-3L, EuroQoL 5-Dimensions 3-Level; HBI, Harvey Bradshaw Index; IT, Italy; Postop, postoperative; Preop, preoperative; SS, spinal stenosis; UK, United Kingdom

LIMITATIONS

- Validation was based on only two disease areas (Crohn's disease and spinal disorders), which may limit the generalisability of the model across broader populations.
- The model was developed specifically for EQ-5D-3L UK and IT value sets; its applicability to other countries or newer EQ-5D-5L tariffs remains untested.

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ACKNOWLEDGEMENT

Medical writing support was provided by Keerthana Diyya and Mau Sinha of Sanofi.

CONFLICTS OF INTEREST

AJOA, EL, JM, and **CN** are employees of Sanofi and may hold stocks and/or stock options in the company. **LP** and **MP** are employees, and **LP** is the co-owner of AdRes HE&OR.

FUNDING

The study was funded by Sanofi.

Poster presented at ISPOR Europe 2025, November 09–12, Glasgow, Scotland