POSA319

Development of a Diminishing Marginal Disutility Model for Intravenous Iron Infusions Based on Data from a Time Trade-Off Study in China

Wu D[1], Zhang Y[2], Boegelund M[3], Pollock RF[4], Hu S[5]

[1] First Affiliated Hospital of Soochow University, Suzhou, China [2] Shanghai Institute of Technology, Shanghai, China [3] Incentive, Holte, Denmark [4] Covalence Research Ltd, London, UK, [5] School of Public Health, Fudan University, Shanghai, China

Background

Iron supplementation is the mainstay of treatment for iron deficiency (ID) and iron deficiency anemia (IDA). Oral iron supplementation is currently the standard therapy as it is easy to administer and available at low cost. Parenteral iron therapy is an alternative to oral therapy recommended if oral therapy is poorly tolerated (or adhered to) or if response to oral iron is insufficient, particularly in the case of severe ID.[1,2]

Administration frequency is one of many treatment-associated "process attributes", i.e., attributes pertaining to non-health-related aspects of receiving healthcare.[3,4] Other treatment process attributes include administration route, dose timing, and treatment location.

Process attributes that distinguish the various IV iron formulations, namely the number and duration of infusions required to correct iron deficits as well as the risk of long-term side effects, have not yet been investigated.

The aim of the present study was to examine how differences in process attributes would be valued in China. Health-state utilities derived from valuations for each state were then used to develop a diminishing marginal disutility (DMD) model to estimate disutility reductions associated with each additional iron infusion.

Methods

Study design

This vignette study was designed to elicit preferences regarding the frequency and duration of IV iron infusions as well as the associated risk, and to estimate health state utilities associated with specific combinations of infusion frequency and duration.

To ensure that vignettes were accurate and reflected patient experience, both the disease description and health state vignettes were developed based on the literature and summaries of product characteristics for IV iron formulations, in collaboration with a hematologist and a health economist based in China.

Table 1. Overview of health states and differences in process attributes

Health state ID	Number of infusions	Duration of an infusion (minutes)	Risk of serious long-term side effects associated with an infusion
1	1	30–60	No risk
2	2	30–60	No risk
3	5	30–60	No risk
4	7	30–60	No risk
5	1	15–30	No risk
6	2	15–30	No risk
7	2	15–30	1 out of 1,000 patients experiences serious long term side effects (softening of/fractured bones).

Disease description and health state vignettes

The survey began with a general disease description that presented the symptoms associated with anemia and IDA, followed by a description of treatment benefits and modalities, including the infusion procedure and possible needle insertion pain and infusion site reactions. The disease description also outlined the need to travel to the hospital for every infusion and the time needed for preparation, waiting, and post-infusion monitoring.

Health state (HS) 1 described treatment as one infusion lasting 30–60 minutes, with no risk of hypophosphatemic osteomalacia (Table 1). HS 2–7 differed from HS 1 in the number and duration of infusions, and the risk of serious long-term side effects.

Participants

Participants were recruited from a Chinese online panel provided by a market research analysis company (Kantar, London, UK). Participants were required to be at least 18 years old and were quota-sampled from the overall panel to represent 2020 age and sex distributions in China.

Statistical analysis

Utility values were calculated for each health state, with standard errors and 95% confidence intervals (CIs) obtained from non-parametric bootstrapping based on 10,000 iterations. Disutilities between states were calculated as the difference between utility values, after exclusion of outliers (2.5% at the bottom and top of the utility distribution, respectively). Analyses were performed using SAS® version 9.4 (SAS Institute Inc., Cary, NC, USA).

A DMD model was implemented based on the three estimated disutility values obtained for the first four health states (HS 2 vs 1, HS 3 vs 1, HS 4 vs 1). A power function of the form $U_d=\alpha\times x^{\beta}$ was estimated in a linear regression model with the log-transformed number of infusions and log-transformed disutilities as predictor and outcome, respectively.[5] Uncertainty was captured by power functions applied to the lower and upper CI limits of the estimated disutility values. The DMD model was implemented using R version 4.1.1 (R Core Team, Vienna, Austria).[6]

Results

The link to the survey was shared with 1,354 online panel members, of whom 1,270 (93.8%) started the survey. Of these 1,270 initial participants, 110 (8.7%) failed the TTO control question or did not trade with the premise of the TTO design, 63 (5.0%) did not complete all TTO tasks, and 6 (0.47%) did not provide information on age and gender, leaving 1,091 respondents (80.6% of contacted panel members and 85.9% of those who started the survey) for analysis.

Comparing pairs of health states, after removal of extreme outliers, showed a preference for fewer and shorter treatments and lower risk in most, but not all, comparisons (Figure 1). Relative to one infusion of 30–60 minutes with no hypophosphatemic osteomalacia risk, seven such infusions were associated with a utility decrement of 0.039 (95% CI: 0.030 to 0.048), while five such infusions were associated with a utility decrement of 0.022 (95% CI: 0.016 to 0.029) and two infusions with a utility decrement of 0.017 (95% CI: 0.010 to 0.025).

The power model of disutilities associated with infusions with a duration of 30–60 minutes and no risk of hypophosphatemic osteomalacia had the functional form $U_d = 0.016 \times x^{0.39}$ (Figure 2).

Figure 1. Disutilities in direct comparisons of health states

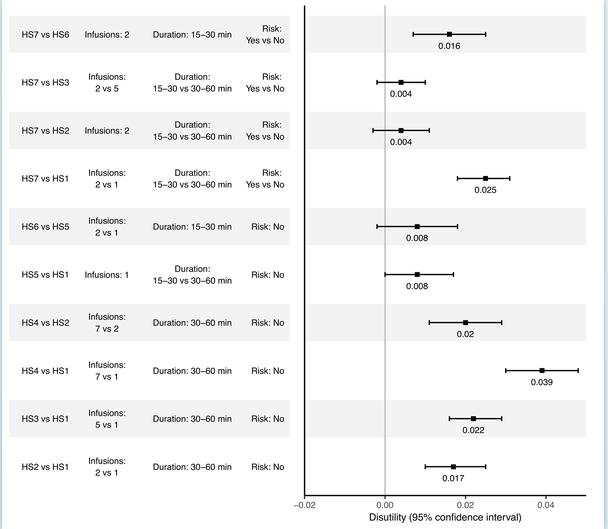
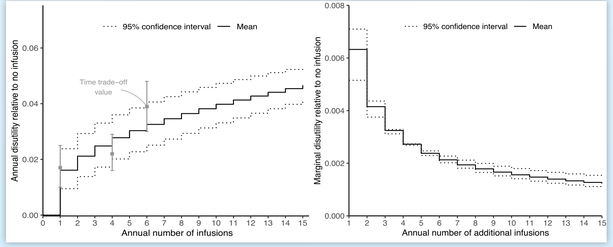


Figure 2. Annual disutility by annual number of infusions (left) and marginal disutility by number of additional infusions (right)



Discussion

This is the first study to assess how attributes and risk of IV iron infusions affect health state utilities associated with IV iron treatment. Results from vignette-based TTO tasks performed by Chinese study participants showed that certain treatment attributes, e.g., fewer and shorter infusions, and treatment options not associated with risk of hypophosphatemic osteomalacia, were associated with higher utility values than more frequent treatment options, treatments requiring longer infusions, and treatments associated with hypophosphatemic osteomalacia risk.

The differences in utilities attributable to treatment process attributes are small, but process attributes represent a treatment dimension in addition to efficacy and safety that is relevant to patients and should be considered in health economic analyses.

The analysis of disutilities associated with 30–60 minutes infusions without hypophosphatemic osteomalacia risk indicated that disutilities increased but at a diminishing rate as the number of infusions increased. This finding suggested that, similar to the "first being worst" phenomenon previously observed for hypoglycemic events, the first IV iron infusion seems to be "worst" while additional infusions have a more limited albeit still detrimental effect on health state utilities.

The findings are subject to certain limitations, including those common to all vignette-based TTO studies: preferences are expressed for (and utilities are therefore derived from) vignettes and their content, not for actual health states as experienced by patients.

Conclusions

The present study reports the first set of health state utilities associated with IV iron infusions in China. These utilities, obtained from a large sample of Chinese respondents in an online survey using the time trade-off methodology, can inform future health economic evaluations, treatment choices, and reimbursement decisions by patients, clinicians, and healthcare payers, particularly in the Chinese setting.

References

1. Camaschella C. (2015). Iron-deficiency anemia. N Engl J Med, 372(19), 1832–1843.
2. Numan S and Kaluza K. (2020). Current Medical Research and Opinion, 36(11), 1769–1782.
3. Higgins A *et al.* (2014). Value in Health, 17(8), 877–887.
4. Brennan VK and Dixon S. (2013). PharmacoEconomics, 31(8), 677–691.
5. Smith G. (2015). Essential statistics, regression, and econometrics (2nd ed., 339–367). Academic Press.
6. R Core Team. (2021). https://www.R-project.org/
7. Lauridsen J. *et al.* (2014). Quality of Life Research, 23(9), 2645–2650.

Poster presented at Virtual ISPOR Europe 2021.
30 November – 3 December, 2021.