Cost-Utility of Subcutaneous Methotrexate as a Second-Line Treatment for Moderate to Severe Rheumatoid Arthritis in the UK

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A Cooperation of

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Background

- Rheumatoid arthritis (RA) affects ~1% of the UK population and leads to disability, and reduced life expectancy [1,2]. It imposes £3.8–4.75 billion in annual costs (2000 values) and impairs quality of life (QoL).
- The National Institute for Health and Care Excellence (NICE) recommends stepwise treatment starting with conventional disease-modifying anti-rheumatic drugs (cDMARDs), typically methotrexate (MTX), followed by combination cDMARDs, then biologic or targeted therapy. Subcutaneous (SC) MTX offers higher, more consistent bioavailability, fewer gastrointestinal side effects, and faster absorption than oral MTX, at a higher acquisition cost [3,4].
- This study assessed if second-line SC MTX is a cost-effective treatment option versus the current UK standard of care.

Methods

- In a de novo hybrid decision tree–Markov model, developed following established standards [5], treatment sequencing as per NICE recommendations was assessed. Patients entered the decision tree to receive first-line treatment, with response evaluated after 3 months using ACR20 criteria. Responders continued first-line therapy; non-responders transitioned to second-line treatment (Figure 1).
- The Markov component (3-month cycle length) captured disease progression for up to four active treatments, with transitions driven by inefficacy- or toxicity-related discontinuation [6] (Table 1). Patients stayed in the model until death or entry into best supportive care (BSC), an absorbing state without further active therapy.
- Health Assessment Questionnaire (HAQ) scores impacted QoL, mortality, and hospitalization costs [7,8]. Mortality was HAQ-adjusted; QoL was mapped to EQ-5D [9,10]. Costs were drug acquisition and administration (Table 2), monitoring, adverse event (AE), and hospitalization costs. A 30-year horizon with 3.5% annual discounting was used, with a £20,000 willingness-to-pay threshold.
- SC MTX was positioned after oral MTX, before combination cDMARDs, to assess its potential to delay biologics. Baseline data: HAQ: 1.20, age 59.2 years, sex 64.2% female, weight 78.3 kg. ACR20: 64% (oral MTX), 78% (SC MTX) [8]. Transition probabilities and utilities were literature-based and costs updated to 2024 values. One-way, scenario and probabilistic (PSA) sensitivity analyses tested robustness.

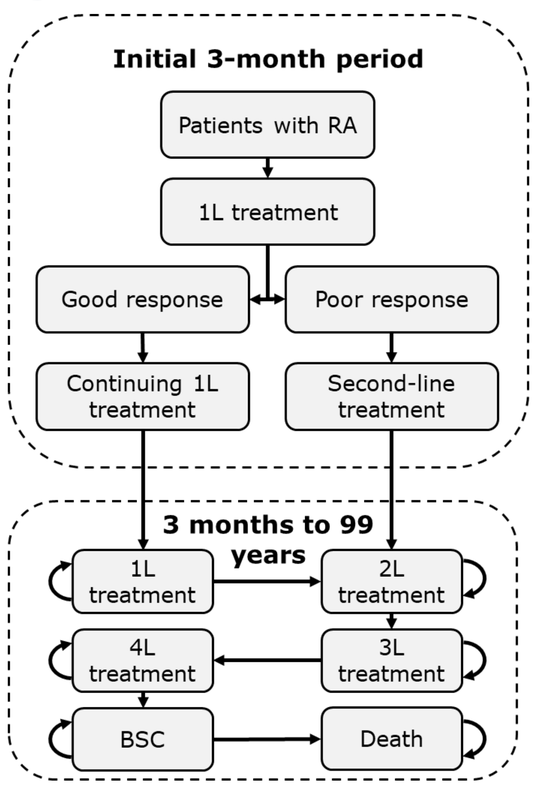
Table 1 State transition probabilities

Parameter	Value	Source
SC MTX to SC MTX	0.85	[6]
Oral MTX to oral MTX	0.69	[6]
Leflunomide to leflunomide	0.81	[11]
Infliximab to infliximab	0.97	[12]

Table 2 Treatment costs (per administration) [13]

Parameter	Costs(£)	Weekly frequency
SC MTX	15.56	1
Oral MTX	0.41	1
Leflunomide	0.10	7
Infliximab	739.27	0.5

Figure 1 Model schematic



Results

- Over 30 years, adding SC MTX as a second-line option was cost-saving and more effective than current standard of care, with £5,217 in savings and a 0.23 quality-adjusted life-year (QALY) gain projected. The net monetary benefit (NMB) was £9,789 (Table 3). Cost savings were mainly due to delayed/reduced biologic use (Table 4).
- One-way sensitivity analyses showed transition probabilities, baseline age, and HAQ to be key drivers of results. PSA results showed that SC MTX remained dominant, with average savings of £8,129 and a 0.29 QALY gain across all 10,000 simulations (Figure 2). Scenario analyses (Figure 3) consistently yielded positive NMB values, even when SC MTX was used as a first-line treatment.

Conclusions

- The treatment sequence including SC MTX was dominant, saving costs and increasing QALYs compared with the current standard of care (which includes only oral MTX). Findings were consistent across all scenario and sensitivity analyses, with SC MTX remaining dominant when also positioned as first-line treatment.
- Incorporating SC MTX into RA treatment could improve patient outcomes and reduce overall healthcare costs, representing a cost-effective, clinically beneficial strategy for the UK healthcare system.

Table 3 Base case cost-effectiveness by sequence

Output	Intervention	Comparator	Δ
Life years	20.95	20.87	0.08
QALYs	7.09	6.86	0.23
Costs (£)	116,807	122,024	−5,217
NBM (£)			9,789
ICER	Intervention sequence less costly, more effective		

Table 4 Breakdown of cost outputs by treatment sequence

Category	Intervention	Comparator	Δ
Treatment			
Oral MTX	43	43	0
SC MTX	1,456	NA	1,456
Leflunomide	108	115	−8
Infliximab	76,173	82,403	−6,230
Total	77,779	82,561	−4,781
Monitoring			
Oral MTX	1,382	1,382	0
SC MTX	1,888	NA	1,888
Leflunomide	1,693	1,718	−25
Infliximab	3,963	4,060	−98
BSC	13,635	15,084	−1,448
Total	22,561	22,244	317
Hospitalisation			
Oral MTX	75	75	0
SC MTX	231	NA	231
Leflunomide	189	192	−3
Infliximab	754	776	−22
BSC	9,200	10,190	−990
Total	10,449	11,232	−784
Death	5,862	5,982	−30
AEs	156	95	61
Total	**116,808**	**122,025**	**−5,217**

Figure 2 Results from PSA

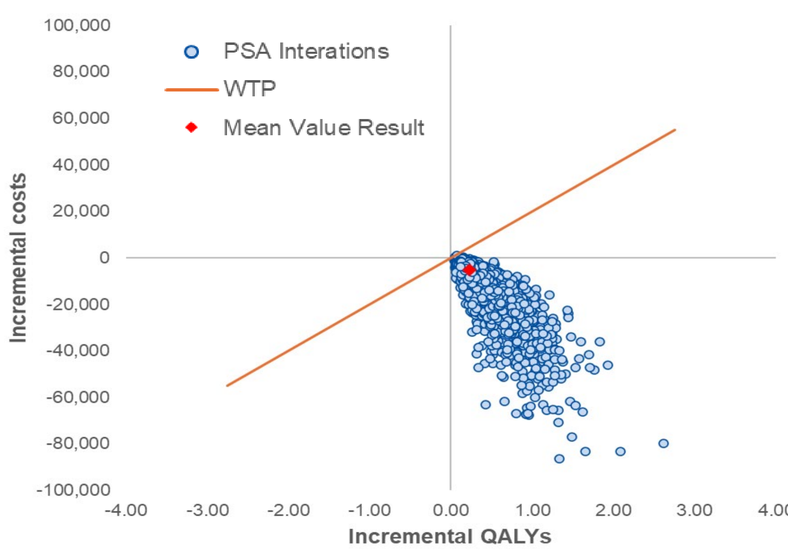
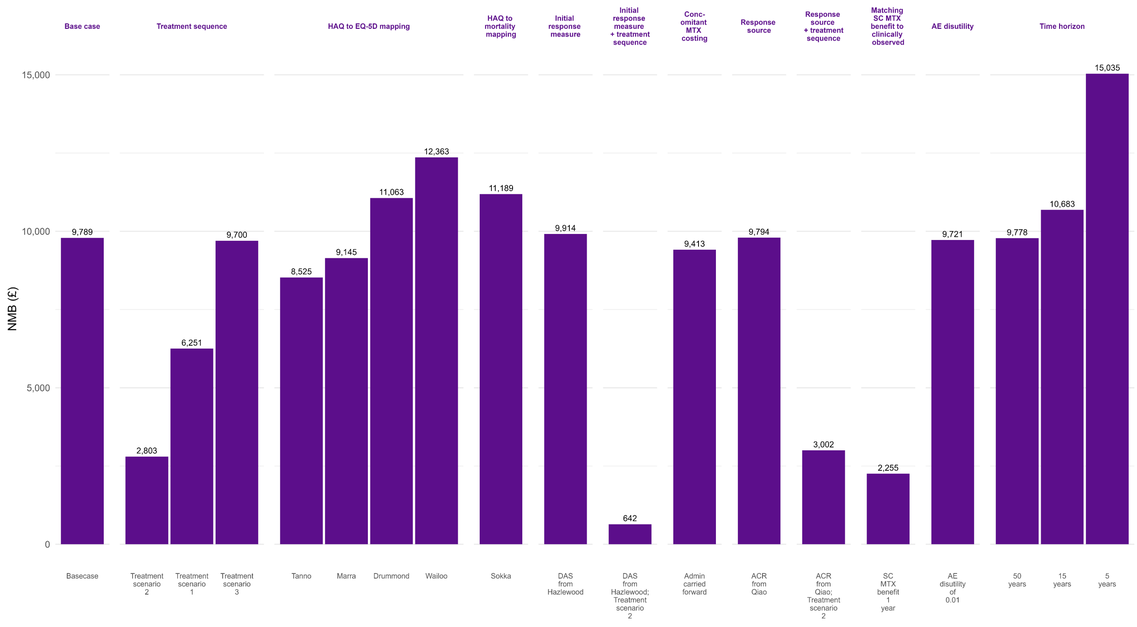


Figure 3 Results from scenario analyses



References

[1] Aletaha, JAMA. 2018;320:1360–72. [2] Pugner, Semin Arthritis Rheum. 2000;29:305–20. [3] NICE, 2018. Report No.: NG100. [4] Tanaka, Mod Rheumatol. 2023;33:633–9. [5] Husereau, Value Health. 2022;25:10–31. [6] Hazlewood, Ann Rheum Dis. 2016;75:1003–8. [7] Arnett, Arthritis Rheum. 1988;31:315–24. [8] Fries, Arthritis Rheum. 1980;23:137–45. [9] NICE, 2010. Report No.: TA195. [10] Malottki, Health Technol Assess. 2011;15: 1–278. [11] van Roon, Br J Clin Pharmacol. 2004;57:790–7. [12] Soliman, Ann Rheum Dis. 2011;70:583–9. [13] Joint Formulary Committee. British National Formulary [Internet]. 2025.