AUSTRALIAN PATIENT PREFERENCES FOR TARGETED SYNTHETIC AND BIOLOGIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS: A Discrete Choice Experiment

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BACKGROUND/PURPOSE

- Factors such as quality of life and treatment convenience may influence patient treatment preferences.
- Patient preferences are important to consider as they can lead to improved patient adherence and outcomes.[1]

AIMS AND OBJECTIVES

To examine patient preferences for biologic or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs) in the treatment of (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA).

METHODS

- A prospective, Australia-wide web-based survey was set up to collect data from RA, PsA and AS patients, with data capture from August to September 2018.
- Patients were classed as b/tsDMARDs-experienced or b/tsDMARDs-naïve based on their treatment experience.
- Participants undertook a demographic survey followed by a Discrete Choice Experiment (DCE) to understand preferred treatment options. The DCE asked participants to trade-off between attributes relating to efficacy, disease progression, risk of mild-moderate side effects, risk of severe side-effects, frequency of administration, availability of real-world evidence ("tried and tested") management of related conditions and patient support programs.
- The DCE attributes and levels are outlined in Table 2, which was designed based on qualitative interviews with patients (n=15), previous research, literature review, clinical trial data and expert opinion. An example scenario is provided in Figure 1.
- Patients completed sixty DCE scenarios randomised into five blocks of twelve discrete choice tasks
- Patients were also asked to report their injection fear on a scale of 0 to 10 (higher scores indicating greater fear).
- Ethics approval was attained from Bellberry Limited and all participants underwent informed consent prior to participation.

Figure 1. Example DCE choice scenario

FEATURES	ORAL	INJECTION	INFUSION	None of these treatments
Clinical efficacy	50% improvement	50% improvement	50% improvement	
Slows the progress of the disease	SLOW Slows disease progression	SLOW Slows disease progression	SLOW Slows disease progression	
Mild-moderate side effects	50 out of 100 risk (50%)	15 out of 100 risk (15%)	10 out of 100 risk (10%)	
Severe side effects	1 to 5% risk	1 to 5% risk	1 to 5% risk	
Frequency of taking treatment	Once a week	Once every 4 weeks	Once every 6–8 weeks	
Tried and tested	1 3 5 7 7 years or more	1 3 5 7 7 years or more	1 3 5 7 7 years or more	
Management of related conditions	Treatment approved only in arthritis related conditions	Treatment approved to manage other auto-immune conditions	Treatment approved in other auto-immune conditions and some cancers	
Patient support program	Nurse support phone line and additional services around self-management	Self-injection program and nurse support phone line	No support service	
I would choose	☐	☐	☐	☐

DATA ANALYSIS

- A latent class model (LCM) was used to estimate the data
- The LCM accounts for differences in treatment preferences and can account for the influence of patient characteristics
- Statistical analyses were performed in Nlogit version 6 (Econometric Software, Inc) and p<0.05 criteria was used to determine statistical significance.

Results

206 patients (RA *n*=85, AS *n*=59, PsA *n*=62) were included in the analysis. Selected patient demographics and treatment experience are displayed in Table 1.

Table 1. Patient demographics and treatment experience

	RA *N*=85		AS *N*=59		PsA *N*=62		Total *N*=206	
Sex, *n* (%)								
Male	25	29.41%	16	27.12%	18	29.03%	59	28.64%
Female	59	69.41%	43	72.88%	44	70.97%	146	70.87%
Prefer not to answer	1	1.18%	0	0.00%	0	0.00%	1	0.49%
Age, *n* (%)								
18–40	17	20%	20	34%	17	27%	54	26%
41–60	32	38%	22	27%	33	53%	87	42%
61–80	36	42%	17	29%	12	19%	65	32%
Time since diagnosis, years, mean (*SD*)	8.3	(6.6)	8.8	(7.3)	8.8	(6.6)	8.6	(6.8)
b/tsDMARDs experience, *n* (%)								
Yes	24	28.24%	24	40.68%	19	30.65%	67	32.52%
No	61	71.76%	35	59.32%	43	69.35%	139	67.48%
Current medications, *n* (%)*								
NSAIDs	46	54.80%	31	52.50%	34	54.80%	111	54.10%
Steroids	19	22.60%	4	6.80%	10	16.10%	33	16.10%
Methotrexate	25	29.80%	5	8.50%	25	40.30%	55	26.80%
b/tsDMARDs	17	20.20%	21	35.60%	16	25.80%	54	26.30%
Hydroxychloroquine	17	20.20%	1	1.70%	3	4.80%	21	10.20%
Leflunomide	8	9.50%	0	0.00%	13	21.00%	21	10.20%
Sulfasalazine	9	10.70%	3	5.10%	5	8.10%	17	8.30%
Opioid pain medications	23	27.40%	20	33.90%	15	24.20%	58	28.30%
Other	0	0.00%	1	1.70%	0	0.00%	1	0.50%
Not currently taking medications	12	14.30%	12	20.30%	8	12.90%	32	15.60%

Abbreviations: b/tsDMARDs – biologic or targeted synthetic disease modifying antirheumatic drugs. NSAIDs – Non-steroidal anti-inflammatory drugs
*Multiple response item, percentages do not sum to 100%.

DCE Results

The best fitting model (table 2) was an LCM with two latent classes and b/tsDMARDs experience included in the model. Other demographic and treatment characteristics were not a significant predictor of class membership. The main findings demonstrate there was a preference for following attributes:

- Class 1 (0.599) valued clinical efficacy, stopping disease progression and the risk of mild-moderate side-effects across all modes of administration ($p<0.05$)
- Class 2 (0.401) valued both clinical and non-clinical attributes. They mostly valued efficacy, stopping disease progression and the risk of mild-moderate side-effects. They also valued injection frequency and patient support programs ($p<0.05$)
- Across both classes, patients with b/tsDMARDs experience were more likely to prefer injection treatments than patients who were b/tsDMARDs-naive ($p<0.05$).

Table 2. Parameter estimates

	CLASS 1		CLASS 2	
Class proportions	0.599		0.401	
Utility parameters	Parameter	T-Ratio	Parameter	T-Ratio
ORAL TREATMENT PARAMETERS				
Efficacy	0.039*	11.49	0.027*	6
Disease progression (reference category – does not slow disease progression)				
Slows disease progression	0	0	0	0
Stops disease progression	1.268*	14.09	0.673*	4.82
Risk of mild-moderate side effects	-0.022*	-5.32	-0.007	-1.03
Risk of severe side effects (reference category – <1% chance)				
1–5% chance	0	0	0	0
Frequency of administration (reference category – twice/once daily)				
Once a week	0	0	0	0
Availability of real-world evidence (tried and tested; reference category - treatment available for <3 years)				
Treatment available for 3–7 years	0	0	0	0
Treatment available for >7 years	0	0	0	0
Management of related conditions (reference category – approved in arthritis-related conditions only)				
Treatment approved to manage other auto-immune conditions	0	0	0	0
Patient support programs (reference category – no support)				
Nurse support line	0	0	0.379*	2.65
Nurse support line and additional services around self-management	0	0	-0.004	-0.03
b/tsDMARDs experience (reference category – b/tsDMARDs-naïve)				
b/tsDMARDs-experienced	0.768	1.37	-0.657*	-2.46
INJECTION TREATMENT PARAMETERS				
Efficacy	0.042*	12.91	0.037*	4.77
Disease progression (reference category – does not slow disease progression)				
Slows disease progression	0	0	0	0
Stops disease progression	1.287**	15.27	0.568*	3.39
Risk of mild-moderate side effects	-0.021*	-5.16	-0.018*	-2
Risk of severe side effects (reference category – <1% chance)				
1–5% chance	0	0	0	0
Frequency of administration (reference category – once a week/every 2 weeks)				
Once every 4 weeks	0	0	0.303*	1.93
Once every 12 weeks (PsA only)	0	0	0	0
Availability of real-world evidence (tried and tested; reference category – treatment available for <3 years)				
Treatment available for 3–7 years	0	0	0	0
Treatment available for >7 years	0	0	0	0
Management of related conditions (reference category – approved in arthritis-related conditions only)				
Treatment approved to manage other auto-immune conditions	0	0	0	0
Patient support programs (reference category – no support)				
Self-injection training and nurse support line	0	0	0.406*	2.25
Self-injection training, nurse support line and additional services around self-management	0	0	0.279	1.53
b/tsDMARDs experience (reference category – b/tsDMARDs-naïve)				
b/tsDMARDs-experienced	1.358*	2.43	0.813*	2.47
INFUSION TREATMENT PARAMETERS				
Efficacy	0.042*	12.91	0.037*	4.77
Disease progression (reference category – does not slow disease progression)				
Slows disease progression	0	0	0	0
Stops disease progression	1.287**	15.27	0.568*	3.39
Risk of mild-moderate side effects	-0.021*	-5.16	-0.018*	-2
Risk of severe side effects (reference category – <1% chance)				
1–5% chance	0	0	0	0
Frequency of administration (reference category for non-RA patients – once every 4 weeks; reference category for RA patients – once every 4/6-8 weeks)				
Once every 6–8 weeks (non-RA patients only)	0	0	0.303*	1.93
Once every 6 months (RA patients only)	0	0	0	0
Availability of real-world evidence (tried and tested; reference category – treatment available for <3 years)				
Treatment available for 3–7 years	0	0	0	0
Treatment available for >7 years	0	0	0	0
Management of related conditions (reference category – approved in arthritis-related conditions only)				
Treatment approved to manage other auto-immune conditions	0	0	0	0
Treatment approved to manage other auto-immune conditions and some cancers	0	0	0	0
Patient support programs (reference category – no support)				
Appointment reminder service and nurse support line	0	0	0.282	1.31
Appointment reminder service, nurse support line and additional services around self-management	0	0	0.384*	1.67
b/tsDMARDs experience (reference category – b/tsDMARDs-naïve)				
b/tsDMARDs-experienced	1.347*	2.4	0.284	1.06

	CLASS 1		CLASS 2	
Class proportions	0.599		0.401	
Utility parameters	Parameter	T-Ratio	Parameter	T-Ratio
TREATMENTS MODE CONSTANTS				
RA treatment constants (reference category – RA oral)				
RA no treatment constant	-1.454*	-3.11	0.284	1.06
RA injection constant	-0.002	-0.01	-1.79**	-3.21
RA infusion constant	-0.148	-0.51	-2.334*	-3.71
AS treatment constants (reference category – AS oral)				
AS no treatment constant	-2.328*	-3.86	3.563*	8.13
AS injection constant	-0.335	-1.13	-0.983	-1.34
AS infusion constant	-0.682**	-2.31	-0.419	-0.58
PsA treatment constants (reference category – PsA oral)				
PsA no treatment constant	-0.527*	-1.65	0.046	0.12
PsA injection constant	-0.14	-0.48	-2.169*	-3.23
PsA infusion constant	-0.203	-0.69	-3.272*	-4.59

*$p<0.05$, **$p<0.01$.
Restricted log likelihood: -6142.689; Log likelihood: -2235.316; Rho-squared: 0.411; Number of respondents: 206; Number of observations: 2472.

Relative Attribute Importance

The graphs below show the relative importance (calculated from the parameter estimates in Table 2) of the attributes by both class and mode of administration, where longer bars represent greater attribute importance. Attribute importance is presented separately for RA patients given different treatment dosing regimens.

CLASS 1 59.90% CLASS 2 40.10%

Figure 2A: Attribute importance by mode of administration for RA patients

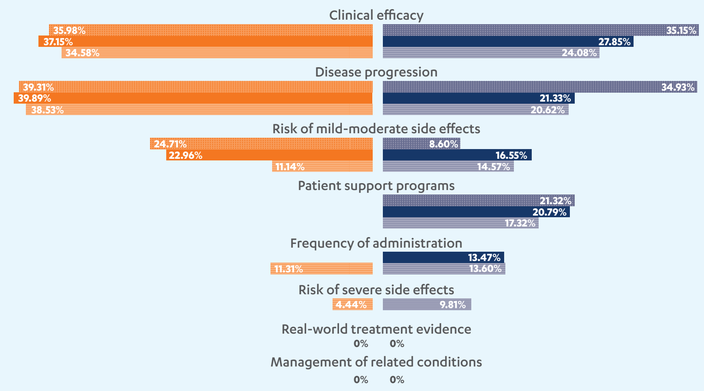
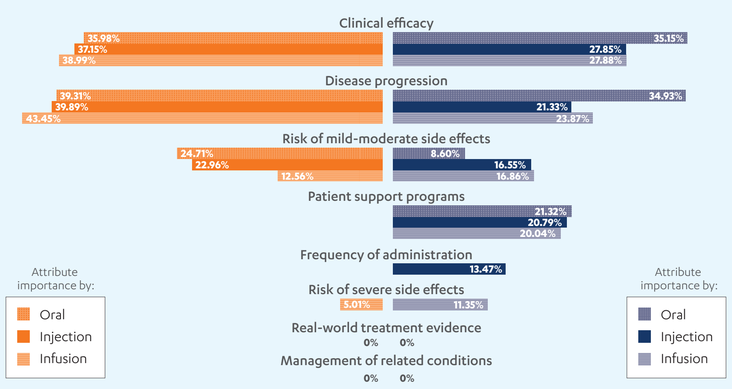
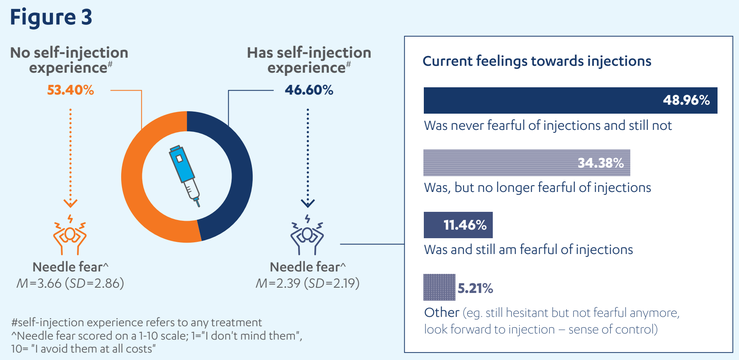


Figure 2B: Attribute importance by mode of administration for AS and PsA patients



Treatment Experience and Injection Fear

Figure 3



DISCUSSION

- Patients across both latent classes value clinical efficacy, stopping disease progression and the risk of mild to moderate side effects.
- Patients in class 2 also value non-clinical attributes including the inclusion of self-injection training and the availability of a nurse support line as part of a patient support program.
- To our knowledge, this is the first arthritis preference study in Australia. It is also the first study that comprehensively examined attributes beyond clinical trial data within a local context (e.g., patient support programs) that may influence patients' preference for treatments. The findings highlight the value patients attribute to services and support that complements the care they receive from rheumatologists.
- Patients' experience with b/tsDMARDs also influenced their preferences for mode of administration. Across both latent classes, compared to b/tsDMARDs-naïve patients, b/tsDMARDs-experienced patients were more likely to prefer injection treatments.
- As b/tsDMARDs are commonly administered as injection-based treatments, this may suggest that experience with injection treatments influences people's perceptions and preferences of different modes of administration. This is consistent with self-injection experience and needle fear findings in the literature.[2]
- Limitations: Convenience sampling was used. Other than for the type of arthritis (RA, AS, PsA), quotas were not used to ensure representativeness of the sample to Australian patients.

CONCLUSIONS

- This study demonstrates that patients value treatment attributes differently. While a subgroup of patients only value clinical attributes, another subgroup of patients value both clinical and non-clinical attributes.
- Previous experience with b/tsDMARDs may also influence patients' treatment preferences.
- Findings have important implications for shared decision making in Australia where patients have access to different b/tsDMARDs which are clinically similar but differ in the non-clinical treatment attributes (such as treatment frequency and patient support groups).

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Reference: 1. Say, E. and Thomson, R. (2003). The importance of patient preferences in treatment decisions – challenges for doctors, *The BMJ*, 327:542-5. 2. Harrison M, Marra C, Shojania K, Bansback N. Societal preferences for rheumatoid arthritis treatments: evidence from a discrete choice experiment. *Rheumatology (Oxford).* 2015;54(10):1816-25. doi:10.1093/rheumatology/kev113.

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