

## EXTENDED REPORT

## Patient preferences for treatment of rheumatoid arthritis

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**Objective:** To elicit treatment preferences of patients with rheumatoid arthritis (RA) for disease modifying antirheumatic drugs (DMARDs) with varying risk profiles.

**Methods:** Patient values for 16 DMARD characteristics were ascertained using published data about side effects, effectiveness, and cost. Patient preferences were determined by Adaptive Conjoint Analysis, an interactive computer program that predicts preferences by asking patients to make trade-offs between specific treatment characteristics. Simulations were run to derive preferences for four drugs: methotrexate, gold, leflunomide, and etanercept, under different risk-benefit scenarios. Infliximab was not included because it is given with methotrexate, and we did not include preferences for combination therapy. Based on each patient's expressed preferences, and the characteristics of the treatments available at the time of the study, the option that best fitted each patient's perspective was identified.

**Results:** 120 patients (mean age 70 years) were interviewed. For the base case scenario (which assumed the maximum benefits reported in the literature, a low probability of adverse effects, and low equal monthly "co-pays" (out of pocket costs)), 95% of the respondents preferred etanercept over the other treatment options. When all four options were described as being equally effective, 88% continued to prefer etanercept owing to its safer short term adverse effect profile. Increasing etanercept's co-pay to \$30.00 decreased the percentage of patients preferring this option to 80%.

**Conclusions:** In this study, older patients with RA, when asked to consider trade-offs between specific risk and benefits, preferred etanercept over other treatment options. Preference for etanercept is explained by older patients' risk aversion for drug toxicity.

In 1992, Felson *et al* compared available treatment options for rheumatoid arthritis (RA) and created composite measures to help guide decision making in patients requiring treatment with disease modifying antirheumatic drugs (DMARDs).<sup>1</sup> Since this publication significant advances in treatment have been made. For example, leflunomide and tumour necrosis factor (TNF) inhibitors have been approved as DMARDs that significantly improve patient centred outcomes, including function and quality of life. The availability of these new agents has further increased the total number of treatment options available and, consequently, the decision making process in RA is now much more complex.

During a clinic visit with a patient requiring initial treatment with one or more DMARDs, the treating rheumatologist informs their patient of several available treatment alternatives, each with their own expected risks and benefits. Given the number and complexity of trade-offs involved, effectively communicating this information is difficult. Despite these difficulties, communication of all available alternatives is required in order to adhere to the principles of informed consent and to meet the strong preference of patients with RA for full disclosure of all available treatment options and their associated risks.<sup>2</sup>

Studies have shown that patient and physician priorities often differ, thereby emphasising the need to incorporate individual patient values into treatment decisions which are dependent on personal values.<sup>3,4</sup> Incorporation of explicitly derived patient values into the decision making process is particularly important in RA, because there are only modest differences in the benefits between effective drugs, and available treatment options differ significantly in the likelihood of common adverse effects, as well as rare but potentially serious complications.<sup>5</sup> For example, methotrexate has

been used for over 20 years, has known common side effects such as nausea, as well as rare, but more serious risks such as pneumonitis. In contrast, TNF inhibitors are new biological agents which are at least as effective as methotrexate, are well tolerated, but are associated with a rare risk of serious infections and have an uncertain long term safety profile.

Adaptive Conjoint Analysis (ACA; Sawtooth Software) elicits preferences using an interactive computer program by asking patients to make trade-offs between specific treatment characteristics. This method has important advantages: (a) it minimises the biases associated with the context in which choices are presented; (b) because ACA can be programmed to present treatment characteristics in random order, it eliminates ordering effects<sup>6</sup>; and (c) by asking respondents to consider specific treatment advantages and disadvantages, it makes trade-offs between competing options explicit. Careful consideration of the trade-offs involved in complex decisions has been shown to improve the quality of decision making.<sup>7</sup>

The objectives of this study were to use ACA to examine patient trade-offs between specific drug characteristics, including expected benefits, risk of adverse effects, and cost, and to ascertain individual patient preferences for specific DMARDs.

## PATIENTS AND METHODS

### Patients

Consecutive patients with RA belonging to three community rheumatology practices serving New Haven, Connecticut, who had seen a rheumatologist for treatment of RA within

**Abbreviations:** ACA, Adaptive Conjoint Analysis; DMARD, disease modifying antirheumatic drug; RA, rheumatoid arthritis; TNF, tumour necrosis factor

**Table 1** Patient utilities\* for the drug characteristics studied

Characteristic	Estimate	Utility
Route	One pill taken once a day	84 (39)
	Subcutaneous injection given by you or a partner at home twice a week	38 (34)
	Intramuscular injection given by a nurse in a clinic once a week	8 (18)
Physician experience	Drug used to treat arthritis for more than 20 years	63 (36)
	New drug with unknown long term safety profile	0
Onset	The drug starts working in 2 weeks	74 (44)
	The drug starts working in 4 weeks (1 month)	40 (31)
	The drug starts working in 8 weeks (2 months)	5 (14)
Chance of benefit	75% (75 in 100) of people receiving this drug will feel much better	61 (39)
	60% (60 in 100) of people receiving this drug will feel much better	39 (32)
	45% (45 in 100) of people receiving this drug will feel much better	7 (15)
Bone erosions	75% (75 in 100) do not develop any new bone damage at 1 year	49 (34)
	60% (60 in 100) do not develop any new bone damage at 1 year	2 (8)
Injection site reaction	0% (no one) get a skin reaction at the injection site	82 (37)
	40% (40 in 100) get a skin reaction at the injection site	1 (7)
Rash	0% (no one) gets an uncomfortable itchy rash	90 (38)
	10% (10 in 100) get an uncomfortable itchy rash	47 (31)
	40% (40 in 100) get an uncomfortable itchy rash	3 (8)
Oral ulcers	0% (no one) gets painful mouth sores	71 (32)
	10% get painful mouth sores	0 (3)
Alopecia	0% (no one) gets hair thinning	61 (35)
	10% (10 in 100) get hair thinning	2 (7)
Nausea/vomiting	0% (no one) gets nausea	82 (34)
	10% (1 in 100) get nausea	33 (28)
	30% (30 in 100) get nausea	4 (12)
Diarrhoea	0% (no one) gets diarrhoea	91 (35)
	10% (1 in 100) get diarrhoea	49 (32)
	30% (30 in 100) get diarrhoea	2 (9)
Cancer	The risk of cancer is not increased with this drug	79 (45)
	Theoretical, but unproven, increased risk of cancer	0
Nephrotoxicity	0% (no one) gets kidney damage from this drug	77 (38)
	1% (1 in 100) get kidney damage	0
Hepatotoxicity	0% (no one) gets liver damage	82 (38)
	0.1% (1 in 1000) get liver damage	0
Pneumonitis	0% (no one) gets lung damage	91 (38)
	0.1% (1 in 1000) get lung damage	42 (27)
	1% (1 in 100) get lung damage	0
Cost	Free	76 (35)
	\$5.00 co-pay per month	60 (34)
	\$15.00 co-pay per month	32 (28)
	\$30.00 co-pay per month	8 (18)

Results are shown as mean (SD).

In this context "utility" is a number that represents the value a respondent associates with a particular characteristic, with higher utilities indicating increased value.

the previous 12 months, were telephoned and asked to participate in a study examining how patients feel about different arthritis drugs. Interviews were scheduled in patients' homes or in the doctors' offices according to patients' choice. All interviews took place at least 2 weeks after seeing a physician (rheumatologist, orthopaedist, or primary care doctor). This protocol was approved by the Human Investigations Committee at the Yale School of Medicine.

### Data collection

#### Patient characteristics

Clinical and demographic data were collected by self report in face to face interviews by a trained research assistant.

Arthritis related health status was ascertained using a global health status question.<sup>8</sup>

### Drug characteristics

Table 1 lists the characteristics of the drug options included in this study. Characteristics were chosen to elicit preferences for four treatment options with similar benefits but distinct risk profiles (akin to methotrexate, gold injections, leflunomide, and etanercept). Infliximab was not included because it is given with methotrexate, and we did not include preferences for combination therapy. As rare occurrences of serious infections associated with TNF inhibitors were published during the study, we included this risk in a subsequent interview of an additional 67 patients. ("The drug can decrease your ability to fight

infection. People who have developed serious infections while taking this drug need to be treated in hospital with intravenous drugs for about 2 weeks”).

Characteristics were derived from results reported in randomised controlled trials. All characteristics were written using lay terminology (Appendix 1) based on patient information material published by the Arthritis Foundation. We excluded laboratory abnormalities because Fries *et al* found that patients have difficulty judging the importance of abnormal blood tests.<sup>9</sup> The range of out of pocket costs reflects the range of monthly co-pays for patients with prescription drug plans in Connecticut (<http://www.ehealthinsurance.com>; accessed August 2004). We did not examine preferences for uninsured patients, because high costs would eliminate the more expensive drugs as potential treatment alternatives for most patients without prescription drug plans.

The severity and reversibility of symptoms, likelihood of occurrence, and sequelae for each adverse effect were described. The ranges of probabilities of benefits and adverse effects were based on randomised controlled data and long term follow up studies.<sup>10-16</sup> To improve patients’ understanding of probabilistic information, we used both qualitative and quantitative frequency formats to describe the likelihood of adverse effects, and provided participants with a chart of familiar examples.<sup>17, 18</sup> For example: “A risk of a side effect happening in 1 person in 100 is the same as the risk of being audited by the Internal Revenue Service.”

## Adaptive Conjoint Analysis (ACA)

### Assumptions underlying ACA

ACA assumes that each treatment option can be broken down into specific characteristics, and that each characteristic is defined by a number of levels. Levels refer to the range of plausible estimates for each characteristic. For example, the levels for the characteristic “risk of nausea” might be 0%, 10%, and 30% depending on the specific drugs being studied.

The second assumption is that respondents have unique values or utilities for each attribute level. In this context “utility” is a number that represents the value a respondent associates with a particular characteristic, with higher utilities indicating increased value. Differences in utilities allow the investigator to determine which features most strongly drive patients’ treatment choices.

The final assumption is that utilities can be combined across attributes. For example, if the sum of a patient’s utilities for the attributes of drug A is greater than the sum of utilities for the attributes of drug B, the patient should prefer drug A to drug B.

### ACA questionnaire

The adaptive conjoint task involved three groups of questions. Firstly, patients ranked the estimates for all characteristics that did not have an “a priori” (or natural) ranking—that is, an obvious preference from one level to the next. For example, it is unnecessary to ask whether low cost is preferred over high cost, all else being equal.

Secondly, respondents rated the importance of the difference between the best and worst levels of each characteristic on a four point scale. For example:

*“If two drugs were acceptable in all other ways, how important would this difference be?”*

No added risk of nausea v 30% risk of nausea

*“Choose a number from the scale below”*

- 1 Not important at all
- 2 Somewhat important
- 3 Very important
- 4 Extremely important.

The characteristics were presented in random order to eliminate any possible ordering effects. Answers to these questions allow ACA to construct initial patient-specific utility estimates.

Thirdly, to refine respondents’ utilities, respondents evaluated a series of paired comparisons, tailored to the patient’s initial utility estimates. For example:

*“Which would you prefer on a scale of 1 to 9?”*

(A) 30% risk of nausea + 75% of patients benefit

or

(B) No added risk of nausea + 25% of patients benefit

- 1–4, Strongly prefer (A), with 1 indicating the strongest preference
- 5, No preference
- 6–9, Strongly prefer (B), with 9 showing the strongest preference.

Each question involves choosing one option from a pair in which one is superior in one attribute and the opposing option is superior in the other. ACA constructs pairs by examining all the possible ways the levels can be combined and then chooses pairs of options with similar utilities for which it expects respondents to be indifferent (based on previous responses).<sup>19</sup> If one option is clearly better than the other based on the ACA’s initial estimate of utilities, no additional information is learnt.

The software program applies constraints to ensure that the overall design of the questionnaire is nearly orthogonal. Final utilities are generated by regression analysis. These values are then used to predict each patient’s relative preferences for defined treatment options. Drugs in this study were defined by assigning a level to each attribute for each treatment option (see Appendix 2).

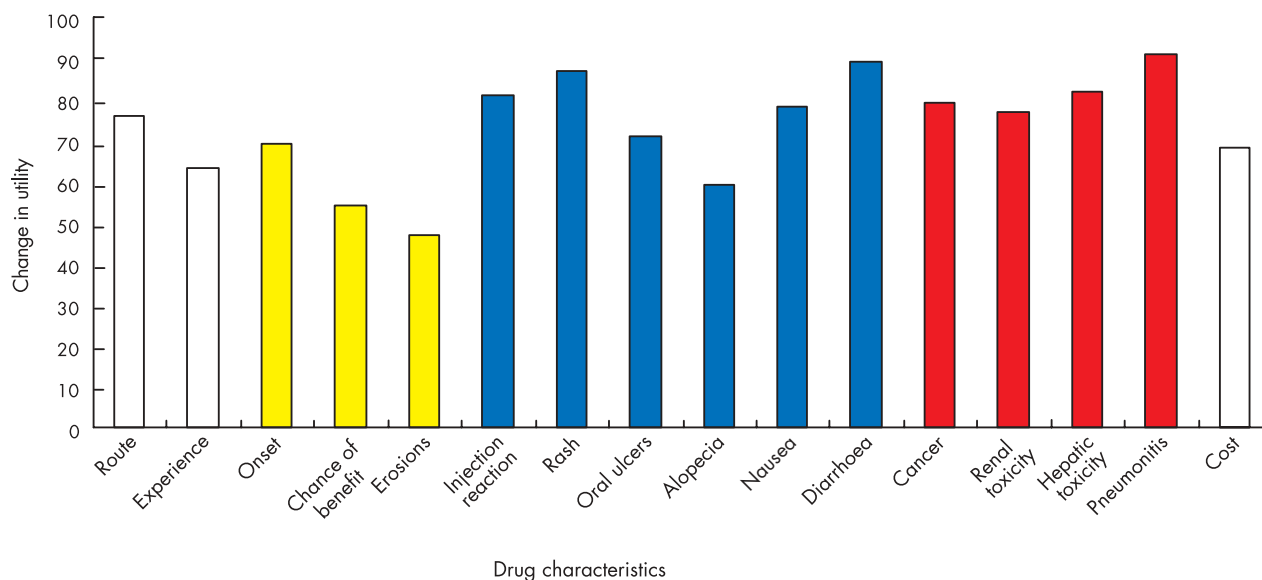
## Analyses

Preference data derived from ACA (version 4.0, Sawtooth Software, Inc, Sequim, WA) were imported into SAS computer files (SAS Software, version 6.12, SAS Institute, Inc, Cary, North Carolina).

We first described the mean (SD) utility for each characteristic. ACA assigns a value close to zero for the least preferred level of each characteristic. Pertinent information is found in the relative differences between the utilities, with differences in utilities reflecting the relative values respondents associate with changes in specific characteristics. We examined the association of patient values with age and health status using Spearman rank correlation and Wilcoxon rank sum test, respectively.

We then performed simulations, analogous to sensitivity analyses in decision models, to assess the impact of varying specific drug characteristics on treatment preference. ACA allows the researcher to derive preferences for a range of options (both real and hypothetical) by specifying a level for each attribute, thereby allowing the investigator to assign varying or identical risks and/or benefits to each treatment option. For each simulation, the file of the respondent’s utilities is read, and a computation is made of each respondent’s relative utility for each option included in the simulation.

We described treatment preferences for the “base case” scenario, where levels were assigned to four options (used to represent drugs commonly chosen either in the United States, Canada, or Europe for patients with moderate to severe RA) based on estimates from published reports. In the base-case scenario (see Appendix 2), options were described using the maximum benefits reported in the literature, a low probability of adverse effects, and low equal monthly co-pays. We used the first choice model (which assumes that each



**Figure 1** y axis: change in utility reflects how much patients valued elimination of the risk of specific adverse effects or maximal gains in improvement. x axis: range of benefits and risk of adverse effects associated with the DMARDs studied. Yellow: drug characteristics describing benefits; blue: drug characteristics describing common reversible adverse effects; red: drug characteristics describing less common, but potentially more serious, adverse effects.

respondent chooses the product having the highest utility) to predict the percentage of patients choosing each option. We subsequently ran simulations, by making adjustments in the “base case” to examine how changing specific characteristics influenced the percentage of patients choosing each option.

## RESULTS

### Patient characteristics

One hundred and twenty of the 160 patients with RA (75%) approached agreed to participate. The mean age (SD) was 70 (12) years (median 72, range 41–91), 91 (76%) were female, 92 (77%) married, 115 (96%) white, and 96 (80%) had some college education. Forty eight (40%) respondents reported having an annual household income above \$20 000 and 92 (77%) had a prescription drug plan. The mean (SD) duration of RA was 8 (5) years (median 7, range 2–45). Seventy two (60%) patients were currently using a DMARD and 76 (64%) stated that they had poor or very poor arthritis related health status. Eighty three (69%) patients were familiar with methotrexate, 24 (20%) with leflunomide, 22 (18%) with gold, and 10 (8%) were familiar with etanercept and/or infliximab as a treatment option for RA.

### Patient utilities

Table 1 presents the patient values (utilities) for each characteristic. The large standard deviations reflect substantial interpatient variability in the values that respondents placed on particular characteristics. Pertinent information is found in the relative differences between utilities. For example, patients felt that decreasing the risk of nausea from 10% to 0 (value = 49 additional utility units) was of similar importance as changing the route of administration from twice weekly subcutaneous injections to a daily oral drug (value = 46 additional utility units). Patients valued eliminating the risk of hepatotoxicity (value = 82 additional utility units) about 2.5 times more than improving the chance of benefit by 25% (value = 32 additional utility units).

Figure 1 demonstrates how much patients valued the maximal improvement in each benefit (that is, the difference between the best and worst levels) and elimination of the risk

of each adverse effect studied. In general, patients valued the elimination of risk of both common reversible, as well as rare but more serious, adverse effects more than the maximum improvement of specific benefits. For example, patients felt that that improving the chance of benefit by 30% (value = 54 additional utility units) was less important than eliminating the risk of troublesome adverse effects, such as diarrhoea (value = 89 additional utility units) or nausea (value = 82 additional utility units) as well as rare but potentially more serious adverse effects, such as hepatotoxicity (value = 82 additional utility units), pneumonitis (value = 91 additional utility units), or a theoretical risk of cancer (value = 79 additional utility units). We found no association between the patient values displayed in fig 1 and age or health status.

## Simulations

### Base case

Drug characteristics for the base case scenario are listed in Appendix 2, and table 2 reports the results of the simulations. For the base case scenario, which predicted preferences for the maximum benefits reported in the literature, a low probability of adverse effects, and low equal monthly co-pays, 95% of the respondents preferred an option akin to etanercept over the other treatment options.

### Sensitivity analyses

When all four options were described as being equally effective (equivalent chance of benefit and ability to prevent bone erosions), the vast majority continued to prefer etanercept. Increasing etanercept’s co-pay to \$30.00 (the maximum co-pay for covered drugs in our state), while keeping the other options at \$5.00, decreased the percentage of patients preferring this option to 80%.

In sensitivity analyses describing the “best case” scenario for methotrexate (as effective as etanercept and risk of pneumonitis lowered to 0.1%), 10% of patients preferred methotrexate over the other options. Describing etanercept as being associated with a rare (0.1%) but serious risk of infection decreased the number of patients choosing TNF inhibitors from 95% to 79%.

**Table 2** Predicted treatment preferences

Scenario	Percentage of patients preferring a specific option			
	Methotrexate	Gold	Leflunomide	Etanercept
Base case	1.7 (1.2)	2.5 (1.4)	0.8 (0.8)	95.0 (2.0)
All equally effective	4.2 (1.8)	7.5 (2.4)	1.0 (0.8)	87.5 (3.0)
All equally effective, co-pay of etanercept increased to \$30.00	5.8 (2.1)	10.8 (2.8)	3.3 (1.6)	80.0 (3.7)

## DISCUSSION

We found that most of the patients with RA surveyed in this study preferred etanercept over the other options studied. Note that patients did not evaluate treatment alternatives directly. Rather, ACA calculates utilities based on respondent's answers to specific trade-off questions. These utilities are then used to predict which option most closely suits each patient's individual priorities.

Patients' values for the drug characteristics studied help explain the treatment preferences found in this study. Firstly, our results indicate that older patients place an almost equal value on the risk of common adverse events as they do on much rarer, but potentially more serious, reactions. These results are in keeping with other studies demonstrating that arthritic patients, especially older patients, are reluctant to accept the risk of common, albeit reversible, adverse effects.<sup>20-22</sup> It follows, therefore, that patients would prefer drugs with few short term risks and an uncertain long term safety profile rather than those with a greater number of established risks. This may explain why so many patients preferred etanercept even when it was not described as being more effective than the other options.

Secondly, "amount of physician experience" was viewed as one of the lesser important drug characteristics by patients. For physicians, "amount of experience" may be a proxy for rare, but serious, unknown long term side effects. In the case of TNF inhibitors, these risks are primarily related to infection and malignancy. Inclusion of both these risks, however, was not enough to overcome patients' aversion to the risk of more common side effects associated with methotrexate, gold, and leflunomide.

Our results must be interpreted in view of the limitations of the study. The majority of patients recruited were older, white, female, and well educated, thereby limiting the generalisability of the results. In addition, we surveyed patients in their homes, and not at the time of actual decision making.

Like Ho *et al*<sup>22</sup> and Pullar *et al*,<sup>23</sup> we did not find any relationship between arthritis related health status and willingness to accept toxicity. Willingness to accept risk may be more closely associated with the acuteness or recency of perceived health loss. The lack of association between health status and willingness to accept risk in this study may be due to the fact that most patients surveyed had longstanding disease and may have adapted to their current health state.<sup>24</sup>

We did not examine preferences for patients without prescription drug plans, because the more expensive drugs would not be reasonable options for most patients if they had to pay the total cost. Given the modest decrease in the percentage of patients preferring etanercept when its co-pay was increased relative to the other options, we would expect that drug plans which ask patients to pay a percentage of total drug costs (as opposed to a fixed co-pay) would significantly diminish preferences for TNF inhibitors.

Cost is often cited as one of the compelling reasons underlying physicians' preference for methotrexate as the

initial preferred DMARD for most patients with RA. Physicians' concerns about cost are based on the dramatic difference between the annual cost of methotrexate (\$265.36) and TNF inhibitors (more than \$12 000). Whether significantly more expensive drugs, with fewer adverse effects or modest incremental benefits, should be covered by third party payers or prescribed by physicians is a continuing debate likely to intensify as an increasing number of costly drugs for varied diseases are developed.

We did not include risk of extremely rare but serious adverse events (such as gold associated enterocolitis, drug induced lymphoma, or TNF associated demyelinating diseases) because all four options have been associated with extremely rare, but very serious, reactions, thereby effectively cancelling each other out.

ACA assumes that utilities for individual treatment characteristics are additive and does not permit exploration of interaction effects. In addition, as with all questionnaires, the description of the attributes may influence respondents' judgment. However, ACA also has several properties which may help overcome the known difficulties in communicating complex risk information.

Previous research has demonstrated that respondents tend to employ simplifying tactics to compensate for information overload when presented with as few as four attributes.<sup>25, 26</sup> One of the main advantages of ACA is that it is interactive. This feature allows the investigator to evaluate a large number of attributes without information overload or respondent fatigue. This is an extremely important advantage because most complex medical decisions involve multiple trade-offs.

In addition, ACA constructs utilities based on trade-offs between specific drug characteristics. This method has three important advantages. Firstly, it minimises the biases associated with the context in which choices are presented. Secondly, because ACA can be programmed to present treatment characteristics in random order, it eliminates ordering effects.<sup>6</sup> Thirdly, by asking respondents to consider specific treatment advantages and disadvantages, it makes trade-offs between competing options explicit. Careful consideration of the trade-offs involved in complex decisions has been shown to improve the quality of decision making.<sup>7</sup>

In summary, we found that many older patients with RA prefer a DMARD with fewer established adverse effects and an unknown long term safety profile over better established drugs with a greater number of common, albeit reversible, adverse effects, and well known long term risk profiles. The results of this study are not meant to be prescriptive, but do highlight the importance of eliciting and incorporating patient values into treatment decisions involving the initiation of one or more DMARDs.

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**APPENDIX 1: CHARACTERISTIC EXPLANATIONS PROVIDED TO THE RESPONDENTS**

*Route of administration:*

- One pill taken once a day in the morning
- Subcutaneous injection: An injection given right under the skin, like an insulin injection. You can give it yourself or have someone else do it. It can be given at home or in a clinic.
- Intramuscular injection: An injection given into the muscle (usually your upper arm or buttock), like the flu vaccine. It is given by a nurse in a clinic.

*Experience:* This refers to the amount of experience doctors have with the drug.

*Time for the drug to start working:* You can use other drugs like anti-inflammatory drugs (celebrex, naprosyn, ibuprofen) or prednisone until the new drug starts working.

*Benefit of the drug:*

- Better means that you feel much more energetic and less achy since taking the drug.
- Some of your joints still bother you, but you are in much less pain then you were before starting the drug.
- You are able to perform all your daily activities like shopping and housework on most days with little if any difficulty.
- You are able to engage in leisure activities with your friends on most days with little if any difficulty.

*Bone damage:* This refers to the number of people who develop new or more bone damage as shown by x ray examination after 1 year. The bone damage can be seen by x ray examination only.

*Injection site reaction:* This refers to a red itchy localised rash at the site of the injection. These usually stop happening after a few weeks.

*Itchy rash:* The rash can be treated with drugs and creams to stop the itch. The rash goes away in a few weeks after the dose of the drug is lowered or, if necessary, when the drug is stopped.

*Mouth sores:* The arthritis drug can cause painful mouth sores. The sores feel like canker sores. The sores can be treated with a gel or a mouth rinse. The sores go away when the dose of the drug is lowered or, if necessary, when the drug is stopped.

*Hair thinning:* The drug can cause some hair thinning. Your hair will grow back after the dose of the drug is lowered or, if necessary, when the drug is stopped.

*Nausea/vomiting:* The arthritis drug can cause mild or moderate nausea and vomiting (you sometimes feel a little queasy and vomit about once a day). The nausea and vomiting go away after the dose of the drug is lowered or, if necessary, when the drug is stopped.

*Diarrhoea:* The arthritis drug can cause moderate diarrhoea (you have occasional stomach cramps and have watery bowel movements about two to three times a day). The diarrhoea goes away after the dose of the drug is lowered or, if necessary, when the drug is stopped.

*Cancer:* Theoretical risk of cancer means that because the drug affects the immune system it has the potential to increase cancer risk with long term use. An increased risk has not been shown in studies of this drug, but the studies have followed up patients for <5 years. If the drug does turn out to increase the risk of cancer after long term use, the risk might be 1/1000.

*Kidney damage:* The drug can cause reversible damage to the kidneys. This type of kidney damage doesn't usually cause any symptoms, but some patients can develop swelling in their legs. The kidneys recover once the drug is stopped.

*Liver damage:* The arthritis drug can cause liver damage. People with liver damage may become tired, weak, and lose their appetite. Many patients do not get other symptoms, but in some, the liver damage gets worse, and can cause yellow skin, intense itching, and bloating of the stomach.

*Lung damage:* The arthritis drug can cause lung problems, leading to a dry cough, shortness of breath, and fever. Patients with this side effect need to be admitted to the hospital for treatment with oxygen and intravenous drugs (steroids by vein). Treatment takes an average of 2 weeks.

*Costs:* Cost refers to your co-pay (that is your out of pocket costs) per month.

**APPENDIX 2: BASE CASE SCENARIO**

Table 3 shows the base case scenario.

Characteristic	Methotrexate	Gold	Leflunomide	Etanercept
Route of administration	PO	IM	PO	SC
Physician experience (years)	>20	>20	New	New
Onset of action (weeks)	4	8	4	2
Percentage who benefit	60	60	60	75
Percentage without new bone erosions	60	60	60	75
Injection site reaction (%)	0	0	0	40
Rash (%)	10	40	10	0
Oral ulcers (%)	10	10	10	0
Alopecia (%)	10	0	10	0
Nausea (%)	10	0	10	0
Diarrhoea (%)	10	0	20	0
Cancer	0	0	0	1/1000
Renal toxicity	0	1/100	0	0
Hepatic toxicity	1/1000	0	1/1000	0
Pneumonitis	1/100	1/1000	0	0
Co-pay (\$)	5.00	5.00	5.00	5.00

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