

# Patient Tradeoffs Between Frequency and Duration of Biologic Treatments for Rheumatoid Arthritis

Christine Poulos,<sup>1</sup> A Brett Hauber,<sup>1</sup> Juan Marcos González,<sup>1</sup> Sarika Ogale,<sup>2</sup> Adam Turpcu<sup>2</sup>

<sup>1</sup> RTI Health Solutions, Research Triangle Park, NC, United States;

<sup>2</sup> Genentech, Inc, San Francisco, CA United States

## BACKGROUND

- An estimated 1.3 million people in the United States (US) have rheumatoid arthritis (RA) (or almost 1% of the nation's adult population).<sup>1</sup>
- RA is a systemic inflammatory disease characterized by inflammation of the synovial lining of the joints.<sup>2</sup> Without treatment, RA leads to joint destruction, and profound morbidity and mortality.<sup>2</sup>
- The biologic disease-modifying antirheumatic drugs are very effective in treating RA.<sup>3</sup> The mode, frequency, and duration of administration of these treatments vary.
- Patient preferences for mode and frequency of administration are central to uptake and adherence to these medications.<sup>4</sup>
- Previous studies have found that the mode and frequency of administration matters to RA patients,<sup>5,7</sup> but none estimated patients' willingness to trade off between frequency and duration of treatment administration.

## OBJECTIVES

- Primary: to quantify the rate at which RA patients are willing to trade off the time required to administer treatment and treatment frequency.
- Secondary: to quantify the importance of these convenience attributes relative to efficacy and safety outcomes.

## STUDY DESIGN AND METHODS

### Sample

- Knowledge Networks (KN) administered an online survey to adults with self-reported physician-diagnosis of RA.
- RAPID3 (Routine Assessment of Patient Index Data, Version 3) was used to assess RA severity.
  - RAPID3 is a patient self-assessment of pain, function, and overall well-being, measured on a 30-point scale.
- Adults with moderate to severe RA (RAPID3 score  $\geq 6$ ) were recruited from two groups:
  - KN's online panel, a nationally representative panel of US households accessible for online surveys.
  - The RA Information, Service, and Education group (RISE) group, which patients, providers, and caregivers may join to learn more about RA treatment and management.

### Conjoint-Analysis Survey

- Conjoint analysis elicits patients' stated preferences for alternative treatments and treatment outcomes.
- Conjoint analysis postulates that the benefit or utility of a treatment is a weighted sum of the positive and negative features of the treatment. Weights reflect patients' perceived relative importance of each treatment feature.
- Choice-format questions elicit preferences between a series of pairs of hypothetical treatments.
- Each hypothetical treatment included six attributes: response rate, mode of administration, treatment time or duration, treatment frequency, and the risks of immediate mild and serious treatment reactions.

### Experimental Design

- Hypothetical treatment profiles were constructed using the information in Table 1.
- Profiles were presented in pairs. The sets of pairs were selected using an experimental design with known statistical properties that optimizes the statistical information generated with a given sample size.
  - 120 treatment pairs were divided into 12 sets of 10 treatment pairs.
  - Patients were randomly assigned to one of these sets.

Table 1. Treatment Attributes and Levels<sup>a</sup>

Treatment Attribute	Levels
Chance that the medicine will work well	<ul style="list-style-type: none"> <li>75 out of 100 patients (75%)</li> <li>60 out of 100 patients (60%)</li> <li>40 out of 100 patients (40%)</li> </ul>
The way you take the medicine (mode of administration)	<ul style="list-style-type: none"> <li>Injection at home</li> <li>Infusion at a doctor's office or clinic</li> </ul>
Time needed for infusion	<ul style="list-style-type: none"> <li>No time (injection at home)</li> <li>30 minutes</li> <li>1 hour</li> <li>2 hours</li> <li>4 hours</li> </ul>
How often you take injections or infusions	<ul style="list-style-type: none"> <li>Two treatments every week</li> <li>One treatment every 2 weeks</li> <li>One treatment every month</li> <li>Two treatments 2 weeks apart every 6 months</li> </ul>
Chance of an immediate mild treatment reaction	<ul style="list-style-type: none"> <li>1 out of 100 patients (1%)</li> <li>10 out of 100 patients (10%)</li> <li>25 out of 100 patients (25%)</li> </ul>
Chance of an immediate serious treatment reaction	<ul style="list-style-type: none"> <li>1 out of 100 patients (1%)</li> <li>10 out of 100 patients (10%)</li> <li>25 out of 100 patients (25%)</li> </ul>

<sup>a</sup> Respondents were told to assume that the cost of RA medicines and co-pays related to RA treatments were covered by health insurance.

Figure 1 presents an example choice task.

Figure 1. Example Choice Question

Medicine A	Medicine Feature	Medicine B
<p>40 out of 100 (40%)</p>	Chance that the medicine will work well	<p>75 out of 100 (75%)</p>
<p>Infusion at a doctor's office or clinic</p>	The way that you take the medicine	<p>Injection at home</p>
<p>2 hours</p>	Time needed for each infusion (if not injection)	<p>One treatment every 2 weeks (26 treatments per year)</p>
<p>Two treatments every 6 months (2 weeks apart) (4 treatments per year)</p>	How often you take injections or infusions	<p>One treatment every 2 weeks (26 treatments per year)</p>
<p>1 out of 100 (1%)</p>	Chance of immediate mild treatment reaction	<p>25 out of 100 (25%)</p>
<p>25 out of 100 (25%)</p>	Chance of immediate serious treatment reaction	<p>1 out of 100 (1%)</p>
Medicine A	Which medicine would you choose if these were the only two medicines available?	Medicine B

## Statistical Methods

- Statistical analysis of the pattern of choices revealed the relative importance weights.
- We estimated a random-parameters logit choice model of respondent choice.
- The dependent variable was the probability of choosing a treatment profile, and the independent variables included all treatment features in Table 1.
- Parameter estimates measure relative importance weights, which were used to calculate the relative importance of treatment attributes and the marginal rate of substitution between treatment time and frequency.
- Random-parameters logit also controls for heterogeneity in preferences and the panel nature of data.

## RESULTS

### Sample

- 901 adults completed the online survey.
- Respondents with moderate to severe RA (RAPID3 score  $\geq 6$ ) were recruited from two groups:
  - 396 adults were recruited from KN's online panel.
  - 505 adults were recruited from the RISE group.
- Sample characteristics are summarized in Table 2.

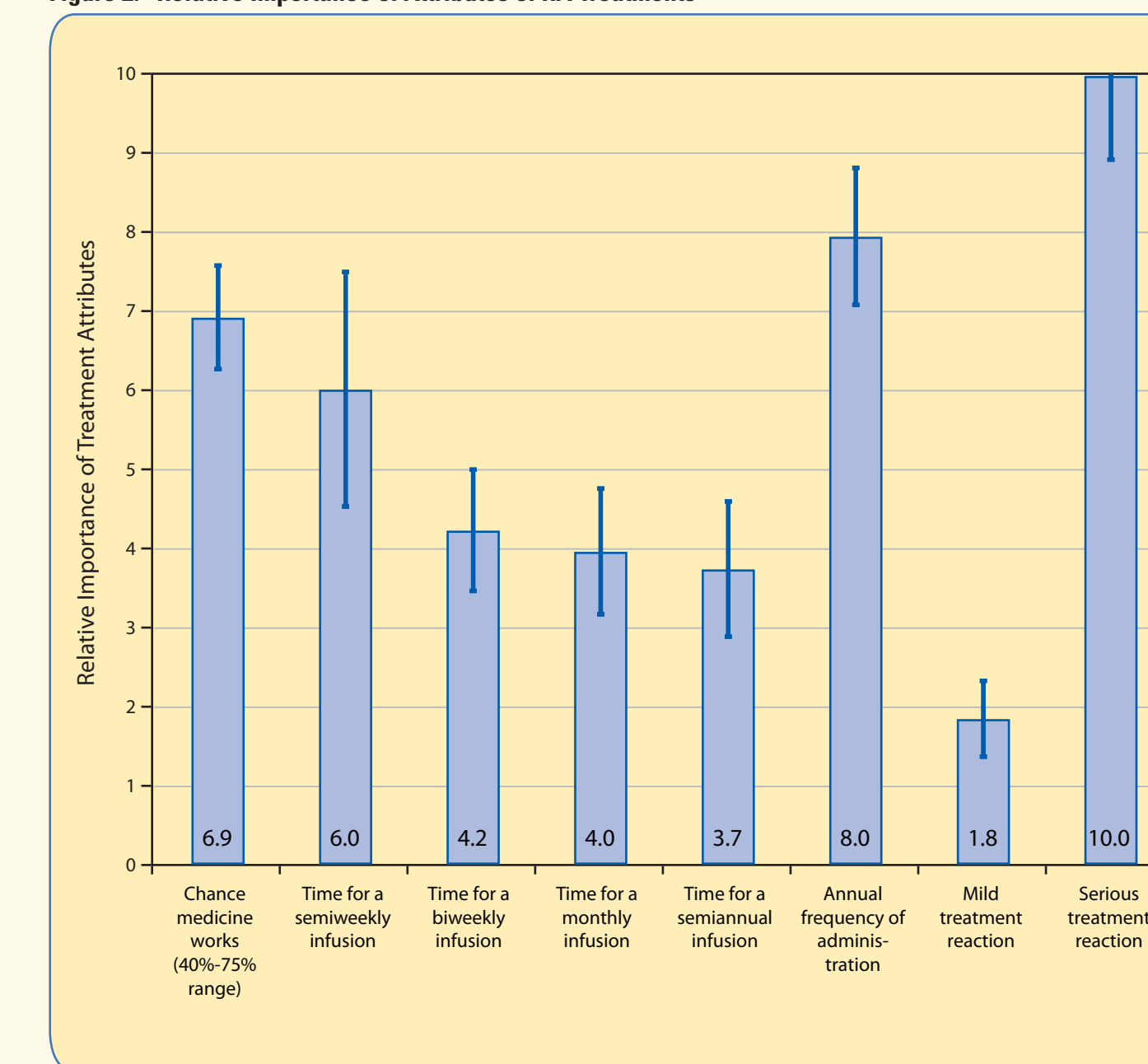
Table 2. Sample Characteristics

Characteristic	n (%)
<b>Age group, years</b>	
18-24	13 (1.4)
25-34	30 (3.3)
35-44	89 (9.9)
45-54	226 (25.1)
55-64	332 (36.8)
65+	211 (23.4)
<b>Sex</b>	
Male	226 (25.1)
Female	674 (74.9)
<b>Race/ethnicity</b>	
White, non-Hispanic	707 (78.5)
Black, non-Hispanic	87 (9.7)
Other, non-Hispanic	25 (2.8)
Hispanic	46 (5.1)
Two or more races, non-Hispanic	36 (4.0)
<b>Education level</b>	
Less than high school	48 (5.3)
High school	195 (21.7)
Some college	400 (44.5)
Bachelor's degree or higher	256 (28.5)
<b>Metropolitan area</b>	
Nonmetropolitan	263 (29.3)
Metropolitan	634 (70.7)
<b>Employment status</b>	
Working—as a paid employee	278 (31.0)
Working—self-employed	43 (4.8)
Not working—on temporary layoff from a job	5 (0.6)
Not working—looking for work	41 (4.6)
Not working—retired	216 (24.1)
Not working—disabled	277 (30.8)
Not working—other	38 (4.2)
<b>Household income level</b>	
Less than \$25,000	247 (28.3)
\$25,000-\$49,999	246 (28.2)
\$50,000-\$74,999	151 (17.3)
\$75,000-\$99,999	100 (11.5)
\$100,000 and higher	129 (14.8)

## Conjoint Analysis

- The chance of an immediate serious treatment reaction was the most important treatment attribute (Figure 2).
- The next most important treatment attributes were the annual frequency of administration and the treatment response rate.
- The importance of treatment time decreased as the frequency of treatment increased.
- The least important attribute was the chance of an immediate mild treatment reaction.

Figure 2. Relative Importance of Attributes of RA Treatments<sup>a,b</sup>



<sup>a</sup> Brackets indicate 95% confidence intervals.

<sup>b</sup> All attributes entered the model as linear variables, except the chance the medicine works and the annual frequency of administration, both of which entered the model as logarithmic variables.

## Marginal Rates of Substitution

- Figure 3 presents a set of indifference (or constant-utility) curves. Each indifference curve represents a set of combinations of duration and frequency that respondents prefer equally (i.e., combinations among which they are indifferent).
- Indifference curves that are lower or further to the left in Figure 3 represent combinations of frequency and duration that are preferred to combinations on indifference curves that are higher or further to the right.
- For example, suppose one starts at X1 (duration of 4 hours and a frequency of 2 times per year) and moves to Y (increasing frequency to 4 times per year). Y is worse, and therefore, on a higher indifference curve than X. By decreasing duration to 2.5 hours, we move from Y to X2. The loss experienced by increasing frequency (moving from X1 to Y) is exactly offset by the gain experienced by decreasing duration (moving from Y to X2), and patients prefer X1 and X2 equally.
- Select points on the curves presented in Figure 3 and the marginal rate of substitution between different points are presented in Table 3.

Figure 3. Indifference Curves Between Duration of Treatment (Hours) and Annual Frequency of Treatments

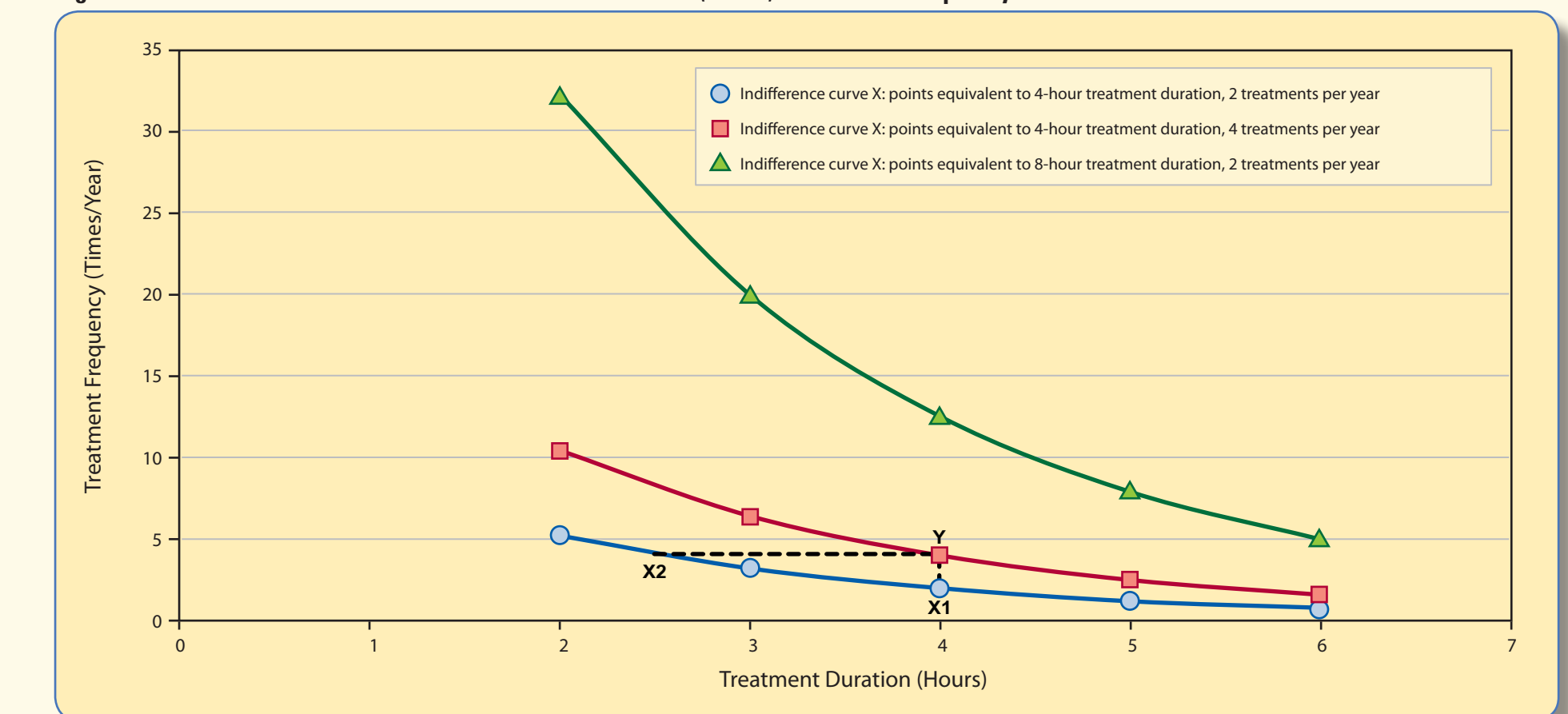


Table 3. Selected Points on Indifference Curves and Marginal Rate of Substitution Between Duration and Frequency<sup>a</sup>

Scenarios	Column A From		Column B To		=	Column C From		Column D To	
	Duration	Frequency	Duration	Frequency		Duration	Frequency	Duration	Frequency
Scenario 1	4	4	2	4	=	4	4	4	1.6
Scenario 2	2	6	0.0	6	=	2	6	2	2.3

<sup>a</sup> This table reports selected changes in the frequency or duration of RA treatments that result in equivalent changes in utility. For example, changing the duration of an infusion administered 4 times per year from 4 hours to 2 hours (Columns A and B, Scenario 1) is equivalent to changing the frequency of a 4-hour infusion from 4 times per year to 1.6 times per year (Columns C and D, Scenario 1). Further, both of these changes are equivalent to changing the frequency of a 2-hour infusion from 6 times per year to 2.3 times per year (Columns C and D, Scenario 2).

## CONCLUSION

In addition to concerns over safety and efficacy, convenience attributes of RA treatment, such as treatment time required and frequency of administration, are important to patients and could play an important role in the choice of treatment.

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## DISCLOSURE

This study was funded by Genentech.

## CONTACT INFORMATION

**Christine Poulos, PhD**  
Senior Economist  
RTI Health Solutions  
200 Park Offices Drive  
Research Triangle Park, NC 27709  
Phone: +1.919.541.7130  
Fax: +1.919.541.7222  
E-mail: cpoulos@rti.org  
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