

# Patient Preference for Self-Injection Devices in Rheumatoid Arthritis: A Discrete Choice Experiment in China

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**Objective:** Rheumatoid arthritis (RA) is increasingly treated with biologics, which is commonly administered by injection devices. The aim of this study is to evaluate patients' preferences for self-injection devices in RA, and to elicit their willingness to pay (WTP) for injector devices in China.

**Methods:** RA patients were recruited from Beijing, Shanghai, Guangzhou, Chengdu, Wuhan and Xi'an in China. A discrete choice experiment (DCE) was employed to elicit patient preferences. Patients were presented with 15 choice sets that consisted of seven attributes, which were developed based on literature review and further validated by physicians. The seven attributes were as follows: operation steps, injection pain, feedback indication, needle visibility, needle protection, size and out-of-pocket costs. A mixed logit model was used to analyze the relative importance of seven attributes and to calculate the WTP for a changed attribute level.

**Results:** Analyses included 114 adults with RA (mean age of 44.6 years old). When choosing the injection device, all attributes had significant influence. Among nonmonetary attributes, very slight injection pain was the most preferred for patients, followed by auto-injection method, thicker size, hidden needle, with needle protection and multiple feedback indication. Patients had a negative preference for increasing out-of-pocket costs. Patients were willing to pay CNY 45.26 for improving slight injection pain to very slight injection pain, CNY 13.26 for the auto-injection method, CNY 12.22 for the thicker size, CNY 10.06 for the hidden needle, CNY 9.82 for needle protection, and CNY 9.70 for multiple feedback indicators.

**Conclusion:** The results suggested that injection pain was the most important attribute for RA patients. Meanwhile, all other enhanced attributes of self-injection devices also significantly influence patients' selection on injection devices. Findings suggested that there is significant potential value in developing self-injection devices that could further help improve treatment adherence and promote patient-centered care in autoimmune diseases.

**Keywords:** self-injection devices, rheumatoid arthritis, patient preferences, discrete choice experiment

## Introduction

Rheumatoid arthritis (RA) is an autoimmune and inflammatory disease characterized by inflammatory arthritis and extra-articular involvement,<sup>1</sup> which could result in loss of function, progressive disability, and increased morbidity and mortality.<sup>2</sup> RA can occur at any age, with about 80% occurring between 35 and 50 years old.<sup>3,4</sup> Meanwhile, RA is more prevalent in females than males, and the ratio of females to males with RA is approximately 4:1.<sup>1,4,5</sup> Based on the data from the Chinese Registry of Rheumatoid Arthritis (CREDIT), there are more than 5 million RA patients in mainland China in 2020.<sup>4</sup> RA not only causes physical impairment and mental stress but also leads to a huge economic burden on patients.<sup>4</sup>

Patients diagnosed with RA should start treatment with disease-modifying antirheumatic drugs (DMARDs) as early as possible to improve patient outcomes.<sup>6,7</sup> As a newer class of treatment for RA, biologic DMARDs can decrease disease activity in a relatively short time by targeting specific steps in the inflammatory processes.<sup>8</sup> The use of biologics in RA management has become a global trend. In the United States, the proportion of RA patients treated with biologics has increased from 32.5% in 2001–2003 to 50.7% in 2010–2012.<sup>9</sup> The utilization of biologics in China might be lower than that in developed countries. Another study conducted by the CREDIT showed that the utilization rate of biologics in RA patients was 8.3% in 2017 in mainland China.<sup>10</sup> However, with more and more biologics listed in the national reimbursement drug list and biosimilars approved, an increasing proportion of patients was observed to treat RA with biologics in recent years.<sup>11</sup>

Many biologics are protein molecules and could be easily broken down by the digestive system, and therefore administration is usually via injection.<sup>12,13</sup> Compared with intravenous administration, subcutaneous administration has proven safe, effective, well-tolerated, generally preferred by both patients and healthcare providers.<sup>14,15</sup> To reduce the impact of administration on patients and healthcare givers, biologics are usually delivered via subcutaneous self-injection, which provides several user-friendly benefits for RA patients including reduced frequency of outpatient visits, reduced costs, reduced caregivers' burden, increased adherence rate, and increased flexibility.<sup>12,16,17</sup> For the current situation in China, the injection devices are sold together with the biologics as a whole package. Several self-injection devices are available on the market, including prefilled syringe (PFS) and auto-injection pen (AI), etc.<sup>12</sup> Biologics with different injection devices do not differ in prices. PFS is the most commonly used self-injection device but is associated with many challenges. Needle phobia, discomfort, fear and anxiety are often reported by patients using PFS to self-administrate biologics.<sup>12,17,18</sup> Therefore, optimizing features of injection devices to meet patient needs is necessary to improve disease management and increase treatment adherence. AI has become a new kind of injection device with many advantages such as hidden needle, ease of grip, increased comfort and portability.<sup>18,19</sup> However, it remains unclear which feature matters most for RA patients and how much patients are willing to pay for these enhanced features.

Discrete choice experiment (DCE) is a tool to study individual stated preferences, it can value the relative importance of various factors that may influence the choices and provide the willingness-to-pay (WTP) of these factors. DCEs are widely used to elicit patient preferences for the management of a variety of healthcare conditions in health technology assessment and patient preference studies. Study subjects will face a series of choice sets with two or more options consisting of multiple attributes and different levels of attributes that can affect the utility of the option.<sup>20,21</sup>

No previous studies were identified to report the preferences and WTP for biologic self-injection devices in China. The objective of this study is to understand and quantify patients' preferences and elicit their WTP for self-injection devices in RA. By collecting data on RA patients from multicenter settings in China and conducting a DCE analysis, it could help us better understand the acceptability of self-injection, optimize the development of injection devices, and provide quantitative reference for healthcare providers and decision-makers.

## Methods

### Study Population

A multicenter survey was designed to explore RA patients' preference in mainland China. Considering the accessibility of biologics with self-injection devices, this study focused on the first- and second-tier cities in China. To cover a wide geographical area, patients were recruited from tertiary hospitals in six cities, including Shanghai, Guangzhou, Chengdu, Beijing, Xi'an and Wuhan, to make sure at least one city was included to represent the eastern, southern, southwestern, northern, northwestern and central regions. Physicians from the rheumatology department of targeted hospitals were invited to assist in the patient recruitment. Physicians helped check whether patients met the recruitment criteria and then asked the willingness to participate in this survey for patients who met the criteria. For patients who met the recruitment criteria and were willing to participate in the study, physicians would forward their contact information to the interviewers to conduct the interview. The patient recruitment criteria were as follows: 1) patients were required to be over 18 years old with a clinical diagnosis of RA; 2) patients were receiving biologics for RA treatment; 3) patients had

the condition of self-injection out of hospitals (ie, had some motor function in their hands to perform the injection themselves, or had caregivers who can help with the injection).

The rule of thumb to determine the minimum sample size in DCEs proposed by Johnson and Orme suggested that the minimum sample size can be calculated using the equation  $N > (500 \times c) / (t \times a)$ , where  $c$  is the maximum number of attribute levels,  $t$  refers to the number of choice tasks per respondent and  $a$  is the number of alternatives within each task.<sup>22,23</sup> Therefore, the minimum sample size  $N$  for statistical analyses can be estimated as  $(500 \times 5) / (14 \times 2) = 89$ . Pearmain et al suggested that sample sizes over 100 are capable of providing a basis for analyses.<sup>24</sup> Taking into account the sample sizes used in earlier studies<sup>25</sup> and the fact that some patients may not be able to complete the survey, we targeted to recruit 120 patients in our study.

## DCE Questionnaire Development

As the first step of this study, we identified the attributes of self-injection devices and the levels of those attributes that might be important to RA patients. The attributes describing self-injection devices were developed based on the differences in existing injection devices and the review of published literature.<sup>19,26–30</sup> Potential attributes included ease of use, safety, indicators, needle visibility, practicality, out-of-pocket costs. The out-of-pocket cost indicated the cost of the injection device per injection. After in-depth interviews with clinical experts, key attributes with different levels were identified (Table 1).

The combination of seven selected attributes and levels resulted in 320 hypothetical scenarios (six attributes with two levels and one attribute with five levels). To reduce patients' cognitive burden, we used D-efficiency fractional factorial design to generate a manageable length of the questionnaire. It reduced the number of choice scenarios to a practical number of 14 representative combinations using SAS Statistics (version 9.4).

**Table 1** Summary of Attributes and Levels

Attributes	Levels
Operation steps	<ul style="list-style-type: none"> <li>Manual injection method: pull off the needle cap, determine the injection site and then manually push the syringe pusher continuously for injection</li> <li>Auto-injection method: pull off the needle cap, determine the injection site and unlock the needle by pressing the syringe on the skin, then the injection will be automatically conducted</li> </ul>
Injection pain	<ul style="list-style-type: none"> <li>Slight pain (VAS score: 1.67)</li> <li>Very slight pain (VAS score: 0.85)</li> </ul>
Feedback indication	<ul style="list-style-type: none"> <li>Visual indication only: the body of the injector is transparent, and the degree of syringe advancement can be seen to determine whether the injection is completed</li> <li>Visual, auditory and tactile indications <ul style="list-style-type: none"> <li>Visual indication: the body of the injector is transparent, and the degree of syringe advancement can be seen, and the visual indication window at the end of the injector will change color once the injection is completed</li> <li>Auditory indication: the injector will sound once the injection is completed</li> <li>Tactile indication: the tactile indication at the end of the injector will pop up after the injection is completed</li> </ul> </li> </ul>
Needle visibility	<ul style="list-style-type: none"> <li>Visible needle</li> <li>Hidden needle</li> </ul>
Needle protection	<ul style="list-style-type: none"> <li>Without needle protection device, unable to prevent needle stabbing injury</li> <li>With needle protection device, able to prevent needle stabbing injury</li> </ul>
Size	<ul style="list-style-type: none"> <li>The cap and body of the injector are thinner and not easy to hold</li> <li>The cap and body of the injector are thicker and easier to hold</li> </ul>
Out-of-pocket costs	<ul style="list-style-type: none"> <li>CNY 0</li> <li>CNY 25</li> <li>CNY 35</li> <li>CNY 50</li> <li>CNY 100</li> </ul>

**Abbreviations:** VAS, visual analog scale; CNY, Chinese Yuan.

The final questionnaire mainly included three parts. The first part was the screening questions, which was designed to check if the patient met the recruitment criteria. The second part aimed to collect demographic characteristics (eg, gender, education level, and household income) and patients' treatment experience (eg, time since diagnosis, past and current treatment). The third part included explanation of attributes and levels, qualitative importance ranking of seven attributes and DCE questions (see Figure 1 for a DCE survey example). At the end of the questionnaire, we asked patients about WTP for the AI (with all enhanced attributes) relative to the PFS by an open-ended question.

We conducted pilot interviews with two patients to test the acceptability, comprehensibility and validity of the survey instrument. Meanwhile, to ensure the quality of the data, a consistency test was included in the DCE questions. The fifteenth choice set was duplicated as the third choice set. Patients were considered to have failed the consistency test if they did not choose the same alternative, and their results were excluded from the analysis.

## Data Collection

The survey was conducted between August 15, 2021 and November 31, 2021. Data were collected through one-on-one face-to-face interviews using the native language of the interviewees (in Chinese). Before the survey, interviewers would give all patients detailed introduction of the study purpose and the main contents of questionnaire. All patients must be clear that they were faced with selections of a series of virtual products, with no right or wrong between alternatives, and

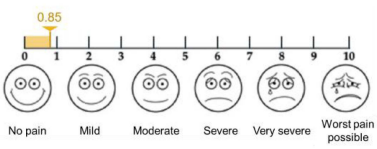
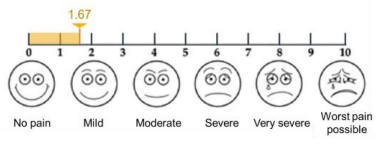






	Injector A	Injector B
<b>Operation steps</b>	<b>Manual injection method:</b> pull off the needle cap, determine the injection site and then manually push the syringe pusher continuously for injection	<b>Auto-injection method:</b> pull off the needle cap, determine the injection site and unlock the needle by pressing the syringe on the skin, then the injection will be automatically conducted
<b>Injection pain</b>	 <p>Very slight pain</p>	 <p>Slight pain</p>
<b>Feedback indication</b>	 <p>Visual, auditory and tactile indications</p>	 <p>Visual indication only</p>
<b>Needle visibility</b>	 <p>Needle visible</p>	 <p>Needle hidden</p>
<b>Needle protection</b>	Without needle protection device, unable to prevent needle stabbing injury	With needle protection device, can prevent needle stabbing injury
<b>Size</b>	 <p>The cap and body of the injector are thicker and easier to hold</p>	 <p>The cap and body of the injector are thinner and not easy to hold</p>
<b>Out-of-pocket costs</b>	CNY 0	CNY 50
<b>I prefer</b>	<input type="checkbox"/>	<input type="checkbox"/>

Figure 1 DCE survey example.

they could choose a preferred product according to their own preference. All interviewers were required not to interfere with the selection of interviewed patients.

All patients were informed to have right to refuse to participate and signed an informed consent form. The study received ethic approval from the Fudan University School of Public Health Institutional Review Board (IRB#2021-08-0914, August 12, 2021–December 31, 2021).

After finishing the patient survey, we also did a telephone revisit to verify if all patients met the inclusion criteria and the authenticity of the questionnaire results.

## Data Analyses

Before conducting data analyses, we assessed the reliability of the data by checking if any patients had inconsistent answers in the third and fifteenth choice sets, or if they had always selected the same option (eg, always injector A), as indicators of non-understanding or performing the task without due attention. These unqualified data were excluded from the analysis.

Descriptive analyses were conducted to summarize the socio-demographic characteristics of the included patients. Continuous variables were summarized using mean and standard deviation (SD). Categorical variables were summarized using frequencies and percentages.

Regarding the DCE data, the attribute of out-of-pocket costs was coded for linearity, and other attributes were all coded as dummy variables. Mixed logit model was used to estimate the relative preferences of the attributes as it can take unobserved preference heterogeneity among patients into consideration by estimating a distribution for each preference parameter. The coefficients from the mixed logit model can be interpreted as relative preference weights. Each preference weight indicated the relative strength of preference for the attribute level compared with the reference level, and a higher preference weight corresponded to a more preferred level of an attribute. Then, the relative importance score was calculated based on preference weights:

$$\text{Relative importance score} = \frac{\text{Difference in preference weights between the most and least preferred level}}{\text{Sum of differences across all attributes}} \times 100$$

The larger the score of an attribute, the greater the impact perceived with a change on the attribute's level.

The results from the model were also used to calculate the marginal WTP for each attribute level, where patients' valuation for obtaining an enhanced feature of the injector. Then, we calculated the value of specific combinations of enhanced attributes in a self-injection device (ie, AI) compared to the standard PFS by the compensating variation (CV).<sup>31</sup> Finally, we simulated the selection probability changes of AI and PFS under different addition out-of-pocket costs of AI. The selection probability was calculated based on the estimated coefficients and actual combinations of nonmonetary attributes of two self-injection device. All analyses were analyzed using STATA statistical software (version 15 SE).

## Results

### Patient Characteristics

A total of 120 patients met the inclusion criteria and completed the survey. As six of them failed the consistency check within the DCE section, data from 114 patients were included in the final analysis. Among the 114 patients, the majority were female (74.6%). The mean age of the patients was 44.6 years old, which is consistent with the mean age at symptom onset reported in previous studies (42.2–46.2 years).<sup>32,33</sup> The RA disease duration was less than 4 years for nearly two-thirds of patients. The most frequently used biologics was Recombinant Human TNF-  $\alpha$  Receptor II: IgG Fc Fusion Protein, followed by adalimumab. Less than 10% of the patients were using AI for injection. More demographics and baseline characteristics of the included patients are summarized in Table 2.

### Importance Rating

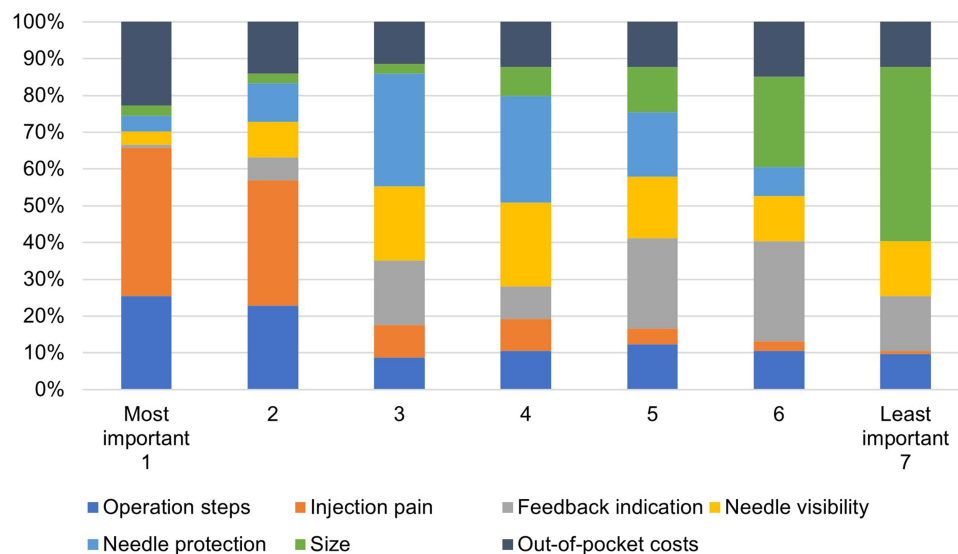
Before conducting the DCE exercises, patients were asked to rank attributes directly from the most to the least important. Based on the importance rating results, in summary, patients attached the greatest importance to injection pain, followed

**Table 2** Demographics and Baseline Characteristics of the Analyzed Patients

Characteristics	n = 114
<b>Cities</b>	
Beijing	28 (24.6)
Shanghai	30 (26.3)
Guangzhou	27 (23.7)
Chengdu	10 (8.8)
Xi'an	10 (8.8)
Wuhan	9 (7.9)
<b>Gender</b>	
Female	85 (74.6)
Male	29 (25.4)
<b>Age, years, mean (SD)</b>	44.6 (10.6)
<b>Highest level of education completed</b>	
Primary school and below	4 (3.5)
Junior secondary school/ Senior secondary school	23 (20.2)
Junior college and above	87 (76.3)
<b>Employment status</b>	
Employed, full-time	87 (76.3)
Employed, part-time	1 (0.9)
Self-employed	4 (3.5)
Retired	19 (16.7)
<b>Monthly household income, CNY</b>	
3000–6000	2 (1.8)
6000–10,000	13 (11.4)
10,000–15,000	38 (33.3)
15,000–20,000	29 (25.4)
More than 20,000	32 (28.1)
<b>Time since being diagnosed as RA</b>	
< 2 years	38 (33.3)
2–<4 years	31 (27.2)
4–<10 years	34 (29.8)
≥ 10 years	11 (9.6)
<b>Biologics received currently</b>	
Recombinant Human TNF- $\alpha$ Receptor II: IgG Fc Fusion Protein	53 (46.5)
Adalimumab	47 (41.2)
Etanercept	9 (7.9)
Certolizumab	4 (3.5)
Golimumab	1 (0.9)
<b>Current injection mode</b>	
Only injected in hospitals by healthcare providers	57 (50.0)
Only injected out of hospitals by family caregivers or patients themselves	37 (32.5)
Both in and out of hospitals	20 (17.5)
<b>Current injection device</b>	
Only using PFS	103 (90.4)
Only using AI	10 (8.8)
Using both PFS and AI	1 (0.9)

**Note:** Data were presented as n (%) or mean (SD).

**Abbreviations:** CNY, Chinese Yuan; RA, rheumatoid arthritis; TNF, tumor necrosis factor; PFS, prefilled syringe; AI, auto-injection pen.



**Figure 2** Importance rating of attributes.

by operation steps and needle protection. The feedback indication and size were identified as less important. The results of importance rating are presented in Figure 2.

## DCE Preference Analysis

Table 3 shows the results of the main effects mixed logit model. Overall, the coefficients were significant for all seven attributes, which meant all these attributes had significant impact on patients' choice of self-injection devices. More specifically, patients presented a positive preference towards the improved level over the reference level in injection pain, operation steps, size, needle visibility, needle protection and feedback indication. As the reference level of these 6

**Table 3** Main Effects Mixed Logit Model Results (n = 114)

Attributes	Coefficient	SE <sup>a</sup>	SD	SE <sup>b</sup>
<b>Injection pain</b> (ref: slight pain) • Very slight pain	2.275***	0.309	1.854***	0.306
<b>Operation steps</b> (ref: manual injection method) • Auto-injection method	0.667**	0.233	2.078***	0.317
<b>Size</b> (ref: thinner and not easy to hold) • Thicker and easier to hold	0.614***	0.172	1.150***	0.222
<b>Needle visibility</b> (ref: visible needle) • Hidden needle	0.506*	0.216	1.752***	0.296
<b>Needle protection</b> (ref: without needle protection) • With needle protection	0.494**	0.176	1.301***	0.231
<b>Feedback indication</b> (ref: visual indication only) • Visual, audible and tactile feedback indications	0.488***	0.146	-0.633**	0.236
<b>Out-of-pocket costs</b>	-0.050***	0.009	0.055***	0.008

**Notes:** <sup>a</sup>Standard error of coefficient; <sup>b</sup>Standard error of SD. \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.

**Abbreviations:** ref, reference; SE, standard error; SD, standard deviation.



attributes represented features of PFS and AI had enhanced level of each nonmonetary attribute (very slight pain, auto-injection method, thick size, hidden needle, with needle protection and multiple feedback indications), the results could be further interpreted as patients' greater preference of AI over PFS on these attributes. The negative coefficient of the out-of-pocket costs indicated that a cheaper injection device would be preferred by patients.

All estimated standard deviations were significant, indicating the existence of preference heterogeneity. We further investigated whether age, monthly family income, reimbursement status and injection experience contributed to preference heterogeneity. Considering all subgroups did not meet the minimum sample size requirement, the results by different subgroups may have some deviations. Detailed results for subgroup analysis were provided in Supplementary materials ([Tables S1–S5](#)).

The results of the relative importance score of nonmonetary attributes are illustrated in [Figure 3](#). Patients placed the greatest preference on very slight injection pain, followed by auto-injection method, thicker size, hidden needle, with needle protection and multiple feedback indication.

## Willingness-to-Pay Analysis

Patients' marginal WTP for the improvement on each attribute was elicited by stated preference discrete choice analysis. Our analysis found that patients were willing to pay the most to improve the slight pain to very slight pain, which was estimated as 45.26 CNY (95% CI: CNY 32.01–58.51). Patients' marginal WTP for the improved level of each attribute is listed in [Table 4](#). The wide ranges of confidence interval showed that there were considerable differences in WTP, reflecting the existence of preference heterogeneity.

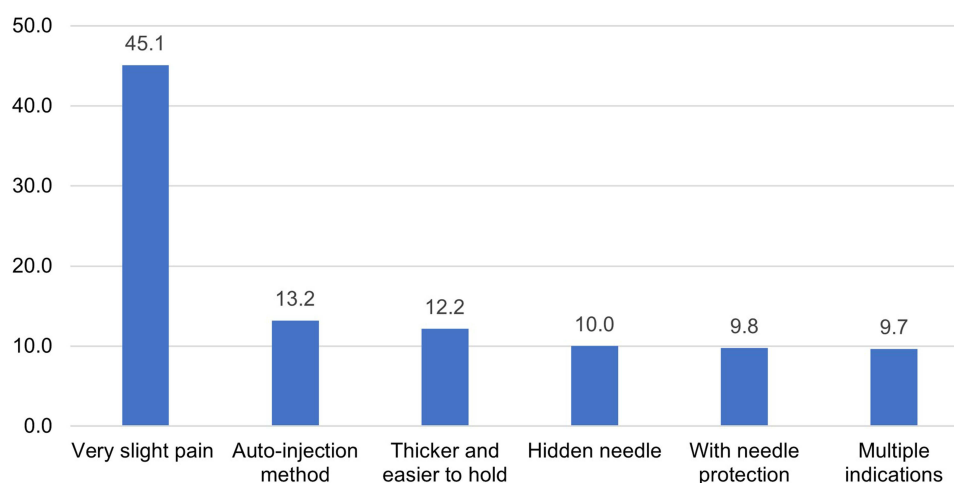
When all attributes were considered together, the analysis found that patients were willing to pay CNY 100.3 additionally for AI with all enhanced attributes. While the WTP of AI was obtained via an open-ended question, it was CNY 61.1.

## Selection Probability

[Figure 4](#) shows the change in the selection probability of patients for the two self-injection devices when the additional out-of-pocket cost of AI was changed. When the out-of-pocket costs of both AI and PFS were CNY 0, the probability of selecting AI is 99%, while the probability of selecting PFS is 1%. When the additional out-of-pocket costs of AI was increased to CNY 100.3, the probability of selecting AI and PFS was the same (both 50%).

## Discussion

This study employed the DCE method to estimate RA patients' preferences for different attributes of self-injection devices. Individual data from 114 patients were analyzed to explore how different features (operation steps, injection pain, feedback indication, needle visibility, needle protection, size, out-of-pocket costs) influence their choice of injection



**Figure 3** Relative importance score.



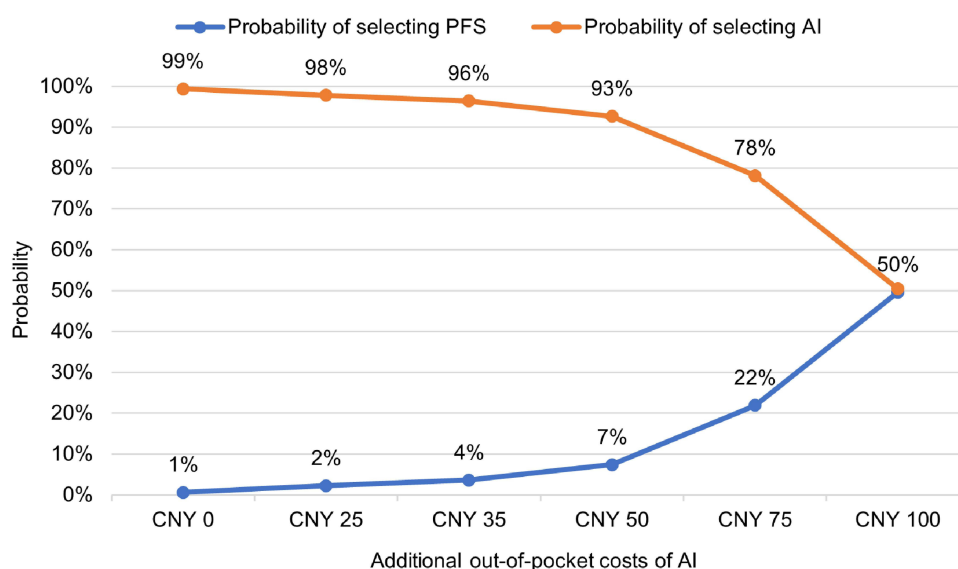
**Table 4** Patients' Marginal WTP for Each Attribute Level

Attributes	WTP (CNY)	95% CI
<b>Injection pain</b> (ref: slight pain) • Very slight pain	45.26	(32.01, 58.51)
<b>Operation steps</b> (ref: manual injection method) • Auto-injection method	13.26	(4.5, 22.03)
<b>Size</b> (ref: thinner and not easy to hold) • Thicker and easier to hold	12.22	(4.62, 19.81)
<b>Needle visibility</b> (ref: visible needle) • Hidden needle	10.06	(1.88, 18.24)
<b>Needle protection</b> (ref: without needle protection) • With needle protection	9.82	(2.88, 16.75)
<b>Feedback indication</b> (ref: visual indication only) • Visual, audible and tactile feedback indications	9.70	(3.86, 15.54)

**Abbreviations:** ref, reference; WTP, willingness-to-pay; CNY, Chinese Yuan; CI, confidence interval.

device. The results suggested that RA patients had strong and positive preference towards all the enhanced attributes of AI compared with PFS. Injection pain mattered most to patients and had the highest marginal WTP. To our knowledge, this is the first study to evaluate patient preferences and WTPs for self-injection device in RA patients in China. Our study provided an understanding of RA patients' preferences and their WTP for the main attributes considered in auto-injectors and could inform clinical decision-making in China.

The findings of this study are consistent with several previous studies<sup>19,26–30</sup> in patients with rheumatic diseases about their preferred attributes in self-injection devices. For instance, Boeri et al found that injection speed control and injection reminders were preferred features for RA patients when selecting self-injection devices.<sup>26</sup> Shingler et al conducted a DCE and the results revealed that reducing the discomfort associated with device use, the addition of feedback indications, and improved needlestick injury prevention were highly valued features for patients.<sup>34</sup> Scalone et al employed a DCE in Italian patients with rheumatic diseases. The results showed that patients and rheumatologists

**Figure 4** Selection probability of two self-injection devices under different additional costs of AI.

**Abbreviations:** CNY, Chinese Yuan; PFS, prefilled syringe; AI, auto-injection pen.

preferred subcutaneous self-injection with AI, and the reduced frequency of reactions at the site of drug administration was the most important consideration.<sup>29</sup> Another study conducted by Rho et al in Poland enrolled RA patients who received at least one self-injection both via the PFS and the AI. They found that the AI was more preferred considering its characteristics in less pain, convenience, ease of use and safety.<sup>30</sup>

In addition to the DCE analysis, an open-ended question to ask the WTP of AI compared with PFS was also included in the questionnaire, which aimed to help estimate the differences in the monetary values of AI between the analyzed result from DCE and the open-ended question. The WTP of AI calculated in DCE was higher than that obtained via an open-ended question, which is consistent with several previous studies.<sup>35,36</sup> Ryan et al found that the WTP value for chlamydia screening elicited using DCE approach was higher than the value obtained via an open-ended method (payment card).<sup>35</sup> Marjor et al tested a convergent validity by comparing the WTP estimates between the DCE and an open-ended method. The results showed that the mean WTP produced by the open-ended question was substantially lower than that derived from the DCE.<sup>36</sup> The reason could be that the DCE survey may be more likely to elicit patients' implicit preferences and the WTP estimates were closely related to the levels that are chosen for the cost attributes.<sup>37</sup> Besides, PFS and AI are sold with biologics as whole packages in China. For the same kind of biologics, there is no difference in patients' out-of-pocket costs no matter using PFS or AI. The WTP of AI derived from the open-ended method might be correspondingly lower.

There are several strengths of this study. First, all attributes and levels applied in this DCE were collected from the literature review and then further validated in pilot physician interviews. To avoid misunderstandings and lack of comprehension for patients which may lead to unclear interpretations of the data, we also conducted pilot patient interviews. The results of the pilot interviews indicated that this DCE survey was easily understood by study subjects. Second, to ensure the authenticity and accuracy of patients' answers, we reviewed each patient's record and conducted follow-up validation with them via phone call. Besides, a consistency test was performed on two choice sets, which could help ensure the reliability of our study results. Third, we not only included DCE survey but also asked patients to rank the attributes directly. We found that the results of importance rating were directly relatively consistent with DCE result. Both results indicated patients mattered more on injection pain and injection steps.

Some limitations of this study should be noted. One limitation is that the sample size of patients might be small, which could in turn pose a challenge when conducting a subgroup analysis. Although the current sample size met the minimum sample size required for DCE statistical analyses according to the thumb rule, further researches with larger sample sizes may be helpful to reflect patients' preference in specified subgroups.<sup>25</sup> Second, considering biologics were currently more common in tertiary hospitals in urban areas, our patients were mainly recruited from tertiary hospitals in the first- and second-tier cities in China, where the economy is more developed than the national average. Additionally, the proportion of patients with junior college and above education in our study is much higher than the national average (76% vs 17%).<sup>38</sup> The well-educated population with good economic level might be more likely to accept new technologies. Therefore, the results of this study may not comprehensively reflect the patient preferences in rural areas or low-income regions and may limit the generalizability of the results. With the increased use of biologics across the country, the preferences of patients in other regions can be further explored. Finally, most patients in this study had considerable experience treating with PFS, while only limited patients had experience or knowledge of AI. Our study combined pictures with texts when presenting DCE questionnaires to help improve patients' understanding about AIs, but it may still be difficult for them to understand the differences in different attribute levels, especially the pain sensation.

## Conclusion

The results indicated that all six enhanced attributes would significantly influence RA patients' preference on self-injection devices, and patients were willing to pay CNY 100.3 additionally for the improved attributes of AI compared with PFS. The findings of this study provided useful evidence to understand patients' preference on injection devices, which may further help promote patient-centered care in autoimmune diseases, improve treatment adherence and even drive better treatment outcomes.

## Ethics Statement

Ethical approval was approved by the Medical Ethics Committee of the School of Public Health, Fudan University (No. IRB2021080914). All of the procedures in the study complied with the Declaration of Helsinki.

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## Author Contributions

Yan Wei and Jin Zhao should be regarded as co-first authors. Xuewu Zhang and Yingyao Chen are regarded as co-correspondence.

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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