Gastro Hep Advances 2024;3:190–200

ORIGINAL RESEARCH—BASIC

# Patient Preferences for Ulcerative Colitis Treatment in the Middle East Region: A Discrete-Choice Experiment

Othman AlHarbi,[1] Niazy Abu Farsakh,[2] Sameer Al-Awadhi,[3] Talal Al-Taweel,[4] Inas Mikhail,[5] Faisal Batwa,[6] Khalil Bedran,[7] Dilara Balkan,[8] Levent Mert Gunay,[9] Joseph C. Cappelleri,[10] Marco Boeri,[11,12] Colton Leach,[13] Sara Habjoka,[8,*] and Mahmoud Mosli[14]

*[1]Department of Medicine, College of Medicine, King Saud University, King Saud University Medical City, Riyadh, Saudi Arabia; [2]Gastroenterology Unit, King Abdullah University Hospital, Irbed, Jordan; [3]Rashid Hospital, Dubai, United Arab Emirates; [4]Division of Gastroenterology, Department of Internal Medicine, Jaber Al-Ahmad Hospital, Kuwait City, Kuwait; [5]Sheikh Shakhbout Medical City, Adu Dhabi, United Arab Emirates; [6]King Saud Bin Abdulaziz University of Health Sciences, Jeddah, Saudi Arabia; [7]Gastroenterology Division, Saint George Hospital University Medical Center (SGHUMC), Beirut, Lebanon; [8]Pfizer Gulf FZ LLC, Dubai, United Arab Emirates; [9]Pfizer PFE Ilaclari, Istanbul, Turkey; [10]Pfizer Inc., New York, New York; [11]RTI Health Solutions, Health Preference Assessment, Belfast, UK; [12]Queen's University of Belfast, School of Medicine, Belfast, UK; [13]RTI Health Solutions, Health Preference Assessment, Research Triangle Park, North Carolina; and [14]Department of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia*

**BACKGROUND AND AIMS:** Treatments for ulcerative colitis (UC) differ in safety, efficacy, and route of administration; patient preferences for treatment attributes should be considered in treatment decisions. No study to date has explored patient preferences for moderate-to-severe UC treatment in Middle Eastern countries. **METHODS:** A discrete-choice experiment aimed to quantify treatment preferences in patients with moderate-to-severe UC in 5 Middle Eastern countries (Saudi Arabia, Kuwait, Jordan, the United Arab Emirates, and Lebanon). Respondents chose between experimentally designed profiles for hypothetical UC treatments with varying efficacy (time until UC symptoms improve and chance of UC symptom control after 1 year), side effects (annual risk of serious infection, 5-year risk of malignancy), mode and frequency of administration, and need for occasional steroid use. A random-parameters logit model was used to estimate preference weights for these attributes, from which conditional relative importance estimates and maximum acceptable increases in risks of serious infection and malignancy were derived. **RESULTS:** Among 365 adults with moderate-to-severe UC who completed the survey (mean age, 36 years; 50% female), 5-year risk of malignancy and symptom control after 1 year had the greatest conditional relative importance. Respondents were generally willing to accept statistically significant increases in annual risk of serious infection and 5-year risk of malignancy in exchange for better efficacy, changes in mode of administration and dosing schedule, and avoiding occasional steroid use. **CONCLUSION:** Of the attributes evaluated, individuals with UC in Middle Eastern countries most value avoiding 5-year risk of malignancy and a higher probability of symptom control, on average.

*Keywords:* Discrete Choice; Preference; Ulcerative Colitis; Middle East

## Introduction

Ulcerative colitis (UC), a chronic and debilitating inflammatory bowel disease affecting nearly 7 million people globally, is increasing in prevalence in Middle Eastern countries.[1,2] In UC, treatment often begins in a "step-up" fashion with mesalamine (5-ASA) therapy, a relatively safe and effective therapy for mild-to-moderate UC. However, 5-ASA fails to induce a clinical remission in 50% or more of UC patients.[3–8] Corticosteroids are often the preferred second-line treatment in patients whose UC is not adequately controlled by 5-ASA therapy. Unfortunately, more than 50% of patients will either suffer disease recurrence upon discontinuation of corticosteroids or fail to taper off corticosteroids at all due to recurrent disease activity once lower doses of the drug are reached.[9] Due to the significant number of potential adverse side effects associated with short-term and long-term corticosteroid use, alternatives to corticosteroid therapy have been developed. These include potent classes of immunosuppressant medications such as thiopurines and biologic therapies. Cyclosporine

*At the time this research was conducted.

***Abbreviations used in this paper:*** **5-ASA, mesalamine; AE, adverse event; CI, confidence interval; CRI, conditional relative importance; DCE, discrete-choice experiment; HRQOL, health-related quality of life; IV, intravenous; KSA, Saudi Arabia; MAR, maximum acceptable risk; RPL, random-parameters logit; SC, subcutaneous; SD, standard deviation; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; UAE, United Arab Emirates; UC, ulcerative colitis; US, United States.**

Most current article



2772-5723
https://doi.org/10.1016/j.gastha.2023.10.002

and tacrolimus have also been used as a bridge to thiopurines for refractory UC, particularly in patients who have failed to respond to intravenous (IV) corticosteroids.[10,11] These treatments differ in various aspects (efficacy, side effects, route of administration, need for occasional use of steroids), making treatment choices in UC a patient preference–sensitive decision.[12]

Little is known about patients' preferences for different UC therapies. A previous United States (US) study explored physician and patient preferences in a discrete-choice experiment (DCE) involving 200 patients with moderate-to-severe UC and 200 gastroenterologists.[13] Patients considered symptom control 2.5 times as important as time to symptom improvement, and 5-year risk of malignancy was considered almost as important as long-term symptom control (conditional relative importance [CRI], 0.79 vs 0.96 for long-term symptom control). Patients preferred oral to subcutaneous (SC) or IV administration (relative importance, 0.47 vs 0.11 and 0.18, respectively). A latent-class analysis of treatment preferences among US patients with Crohn's disease indicated substantial preference heterogeneity, with some patients prioritizing symptom control, some prioritizing avoidance of steroids, and some prioritizing avoidance of treatment-related risks.[14] However, no study to date has explored patient preferences for moderate-to-severe UC treatment in Middle Eastern countries. Patient preferences vary across different regions, cultures, and healthcare systems, and a better understanding of patients' priorities for treating UC, a disease that is both burdensome and increasingly prevalent in the region,[2] is warranted.

The objectives of this study, the first of its kind to have been conducted in Middle Eastern countries, were (1) to quantify preferences for outcomes associated with UC treatments in Saudi Arabia, Kuwait, Jordan, the United Arab Emirates (UAE), and Lebanon; (2) to estimate the CRI of treatment outcomes to patients when choosing a UC treatment; (3) to calculate the maximum acceptable percentage-point increase in annual risk of serious infection and 5-year risk of malignancy to obtain an increase in efficacy, to change the mode and dosing schedule, and to avoid the need for the occasional use of steroids; and (4) to explore heterogeneity in the patient-preference data.

# Methods

## Study Design

For this study, a DCE previously conducted in the US[13] was adapted for use in clinical sites in 5 Middle Eastern countries: Saudi Arabia, Kuwait, Jordan, the UAE, and Lebanon. The DCE survey instrument was translated and adapted for the Middle East to quantify patient preferences for the same attributes identified in the original study; it also included the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) to measure respondent health-related quality of life (HRQOL).[15] The survey was completed by patients on an electronic device at participating sites. The RTI International Institutional Review Board reviewed the study and deemed it exempt from full review. In addition to the RTI International Institutional Review Board review, each site obtained local ethic committee approval to conduct the study. All survey respondents provided written informed consent to a staff member at each participating site.

The DCE, which was chosen as the primary stated-preference method for this study, is a widely used survey method that allows researchers to elicit preferences for health treatments or services described by multiple attributes and explore the tradeoffs that respondents are willing to make.[16] In a DCE, respondents are presented with a series of choice questions in which they are asked to select their preferred alternative among treatment profiles defined by a set of attributes with levels that vary experimentally. Each hypothetical treatment profile consists of combinations of attribute levels.[17] The DCE survey instrument and experimental design were developed following good research practice guidelines published by The International Society for Health Economics and Outcomes Research (ISPOR)[18,19] and followed those used in the prior US study.[13]

## Study Population

Patients were recruited at clinical sites and completed the survey in person. Eligible patients were aged 18–75 years, reported receiving a clinical diagnosis of UC at least 6 months before screening, were able to read and understand English and/or Arabic, and reported current or past use of any of the following treatments for UC: immunosuppressant medication (eg, 6-mercaptopurine, azathioprine, cyclosporine), biologic therapy (eg, adalimumab, golimumab, infliximab, vedolizumab, ustekinumab), a targeted synthetic molecule (tofacitinib), or a corticosteroid (eg, prednisone, budesonide). Treatment-naïve patients were ineligible.

## Survey Instrument

The original survey instrument used in the US study[13] was translated into Arabic, and questions specific to this study (ie, the SIBDQ) were added. When completing the survey, patients had the option to use either the English or the Arabic version. In the DCE, respondents were presented with a series of 12 choice questions that each asked them to choose between 2 experimentally designed hypothetical UC treatment profiles.[13] A sample choice question is shown in Figure 1. Each hypothetical UC treatment profile was described using 7 attributes characterized by varying levels: (1) time until symptoms begin to improve, (2) probability that UC symptoms are under control after 1 year, (3) annual risk of a serious infection, (4) 5-year risk of malignancy, (5) mode of administration, (6) dosing schedule, and (7) need for occasional use of steroids (attributes and levels are presented in Table 1). The experimental design included in this study was the same used in the US study, which included 48 choice questions split in 4 blocks of 12 choice questions each. To ensure that the combinations of attributes and levels were realistic, the design was constrained to include only certain combinations of mode of administration and dosing schedule.

The SIBDQ was also included in the survey to characterize respondents' HRQOL. The SIBDQ includes 10 items scored on a 7-point Likert scale from 1 (severe problem) to 7 (no problems at all). Total scores range from 10 to 70, with lower scores indicating poor HRQOL and higher scores indicating better HRQOL.[15]

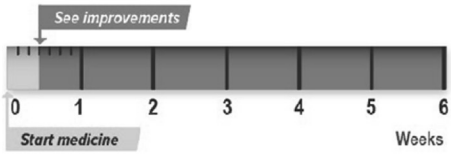
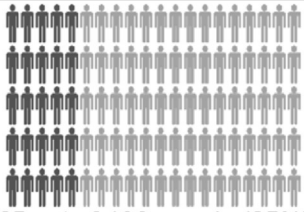
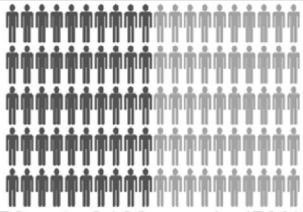
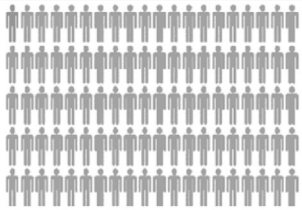
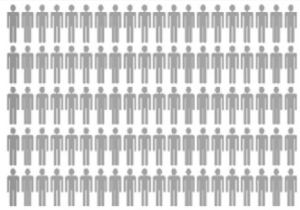
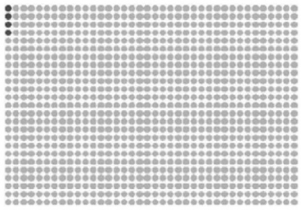
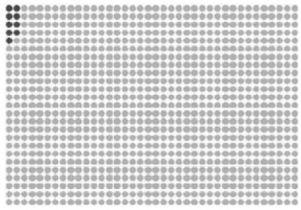
| Medicine Feature (Attribute) | Medicine A | Medicine B |
|---|---|---|
| How long it takes until you see some improvement in your UC symptoms |  3 days |  2 weeks |
| Chance that your UC symptoms will continue to be under control after 1 year |  25 out of 100 people (25%) |  50 out of 100 people (50%) |
| Risk of having a serious infection each year while you are taking the medicine |  1 out of 100 people (1%) |  5 out of 100 people (5%) |
| Risk of developing cancer in the next 5 years because you used the medicine |  4 out of 1,000 people (0.4%) |  9 out of 1,000 people (0.9%) |
| How you take the medicine |  Oral pills or tablet at home |  Self-injection at home |
| How often you take the medicine | Once a day | Every 2 weeks (twice a month) |
| You will need occasional use of steroids to keep your UC symptoms under control |  |  |
| Which medicine would you choose? |  |  |

Figure 1. Example of a discrete-choice experiment question. UC, ulcerative colitis.

**Table 1.** Attributes and Levels for the Discrete-Choice Experiment

| Attribute | Label used in the patient survey instrument | Levels used in the choice questions |
|---|---|---|
| Time until symptoms begin to improve | How long it takes until you see some improvement in your UC symptoms | 3 d<br>2 wk<br>6 wk |
| Probability that UC symptoms are under control after 1 y | Chance that your UC symptoms will continue to be under control after 1 y | 9 of 100 people (9%)<br>25 of 100 people (25%)<br>50 of 100 people (50%) |
| Annual risk of a serious infection | Risk of having a serious infection each year while you are taking the medicine | 1 of 100 people (1%)<br>3 of 100 people (3%)<br>5 of 100 people (5%) |
| 5-y risk of malignancy | Risk of developing cancer in the next 5 y because you used the medicine | 1 of 1000 people (0.1%)<br>4 of 1000 people (0.4%)<br>9 of 1000 people (0.9%) |
| Mode of administration | How you take the medicine | Oral pill or tablet at home<br>Subcutaneous injection at home<br>IV infusion at a doctor's office, hospital, or clinic |
| Dosing schedule | How often you take the medicine | Twice a day<br>Once a day<br>Every 2 wk<br>Every 8 wk |
| Need for occasional use of steroids | You will need occasional use of steroids to keep your UC symptoms under control | Yes<br>No |

IV, intravenous; UC, ulcerative colitis.
Subcutaneous injection at home was presented to respondents as "Self-injection at home."

## Statistical Analysis

The analysis of data from a DCE is based on the conventional random utility theory framework,[20,21] which asserts that utility is derived from the characteristics of the option chosen and that, when facing a choice, respondents select the option that maximizes their utility. The data from this DCE were analyzed using a random-parameters logit (RPL) model to estimate preference weights for the attributes.[22] Preference weights can be interpreted as weights indicating the relative strength of preference for each attribute level included in the survey. More-preferred outcomes are associated with higher preference weights. With the model output, it is possible to determine whether the mean estimates are statistically significantly different from one another at the 5% level of significance by using a simple *t*-test on the difference. Graphically, if the 95% confidence interval of 1 level does not overlap the mean estimate associated with another level, on average preferences for the 2 levels are statistically significantly different from one another at the 5% level of significance.

The estimated preference weights were used to calculate the CRI of each attribute as well as the maximum acceptable percentage-point increase in the risk of serious infection and malignancy that patients would accept for each of the changes in each of the other attributes (time until symptoms begin to improve, probability that UC symptoms are under control after 1 year, need for occasional use of steroids, changes in frequency for the same mode of administration, and changes in mode of administration for each frequency). The CRI of each attribute was calculated as the difference between the preference weight for the most-preferred and least-preferred of its levels. The results were rescaled so that the sum of the attribute CRIs was set to 100, making the CRI of each attribute a percentage of this total. In this way, the CRI can be interpreted as the percentage of utility that can be gained by moving from the least-preferred to the most-preferred level for an attribute relative to the maximum utility that can be gained by having all attributes moving from the least-preferred to the most-preferred level. The standard errors (and 95% confidence intervals) for these differences were calculated using the delta method.[23,24]

The maximum acceptable percentage-point increase in the risk of serious infection and malignancy was defined as the negative of the ratio between the marginal utility for the change in 2 levels of an attribute and the disutility of a unit increase in the risk of serious infection and malignancy. Since all attribute levels (including risks) were modelled as categorical variables in the RPL model, the disutility on an increase in risk was assumed to be linear between each pair of effects-coded risk levels included in the survey instrument. The disutility of a unit increase in each risk for each segment of risk (ie, between each consecutive level) was therefore derived by dividing the disutility generated by going from a lower to a higher level of a risk by the difference between the 2 risk levels considered.[25]

Since preference heterogeneity is emerging as an important topic in health preference assessment,[26] 5 prespecified, mutually exclusive subgroups were explored in our subgroup analysis. Subgroups were defined by age, country, gender, SIBDQ score, and time since diagnosis. Systematic differences in preferences were tested using a Wald test. A *P* value less than .05 indicates that subgroups presented systematic differences across all DCE attributes that were statistically significant at the 95% confidence level.

## Results

### Respondent Characteristics

A total of 365 adults with moderate-to-severe UC completed the survey. Most respondents completed the survey in Saudi Arabia (44%), followed by the UAE (23%), Jordan (20%), Kuwait (9%), and Lebanon (3%); approximately 86% of the sample completed the survey in Arabic (Table 2). Average patient age was 36 years, and approximately 50% of respondents were females (Table 2). Respondents had generally good HRQOL: the average SIBDQ score across the full sample was 47.3 (standard deviation, 12.8) and ranged from 12 to 70. Respondents' scores averaged approximately 79% of the maximum SIBDQ score (Table 2).

### Preference Weights and Conditional Relative Attribute Importance

Figure 2 presents preference-weight estimates for each attribute level. Within a particular attribute, levels associated with higher preference weights are preferred to levels associated with lower preference weights. The vertical distance between 2 attribute levels indicates the utility the average respondent would get moving from a less-preferred to a more-preferred level of a given attribute. Better efficacy and lower risk were preferred, as expected. On average, reducing the 5-year risk of malignancy from 0.9% to 0.1%, and increasing the probability that UC symptoms are under control after 1 year from 9% to 50%, had the greatest impact on respondents' utility. Respondents also preferred the oral routes of administration at the lowest frequency tested (once every 2 weeks) over other frequencies of administration, preferred an IV infusion once every 8 weeks to IV infusion every 2 weeks, and preferred avoiding the occasional use of steroids.

Figure 3A shows the scaled CRI estimate for each attribute. The 5-year risk of malignancy and the probability that UC symptoms are under control after 1 year are the most important attributes (greatest CRIs), although the CRI of the probability that symptoms are under control after 1 year was not statistically significantly different from the CRI of pill administration by dosing schedule ($P = .11$). Both improving the probability that UC symptoms are under control and reducing the 5-year risk of malignancy from the least-preferred to the most-preferred level generate almost half the utility that can be generated by improving all the attributes. For comparison, improving from their least-preferred to most-preferred attribute level for (1) annual risk of serious infection, (2) pill or IV by dosing schedule, and (3) need for occasional steroid use each generated approximately 10% of the total utility improvement achievable. Finally, the CRI of SC injection by dosing schedule was not statistically significantly different from 0, indicating that, on average, the attribute combining dosing frequency by SC injection did not have a significant influence on respondents' utility (and on their choices).

**Table 2.** Summary of Patient Characteristics and Results of SIBDQ

| Variable | N = 365 |
|---|---|
| Gender, n (%) | |
| Male | 181 (49.7%) |
| Female | 183 (50.3%) |
| Missing | 1 |
| Age (mean), y (SD) | 35.6 (12.3) |
| Age (mean) when diagnosed with UC, y (SD) | 27.2 (11.4) |
| Country in which respondents completed survey, n (%) | |
| Saudi Arabia | 160 (43.8%) |
| Kuwait | 34 (9.3%) |
| Jordan | 74 (20.3%) |
| United Arab Emirates | 85 (23.3%) |
| Lebanon | 12 (3.3%) |
| Surveys completed in Arabic or English, n (%) | |
| Arabic | 313 (85.8%) |
| English | 52 (14.2%) |
| Current treatment, n (%)[a] | |
| Immunosuppressants | 169 (46.3%) |
| Biologics | 214 (58.6%) |
| Targeted synthetic molecule | 11 (3.0%) |
| 5-ASAs | 201 (55.1%) |
| Corticosteroids | 85 (23.3%) |
| Other | 7 (1.9%) |
| No medicine | 6 (1.6%) |
| Experience with serious infection, n (%) | 46 (12.6%) |
| Frequency of steroid use in previous year, n (%) | |
| Never | 158 (43.3%) |
| 1–5 times | 164 (44.9) |
| More than 5 times | 27 (7.4%) |
| Other/Don't know or not sure | 16 (4.4%) |
| Mode of administration experience, n (%)[a] | |
| By mouth (oral pills or tablets) | 340 (93.2%) |
| By injection (either at home or in doctor's office) | 97 (26.6%) |
| By intravenous infusion | 257 (70.4%) |
| Suppository | 197 (54.0%) |
| Other | 10 (2.7%) |
| SIBDQ[b] | |
| Mean (SD) | 47.3 (12.8) |
| Median | 48.0 |
| Range | 12.0–70.0 |
| Missing | 2 |

SD, standard deviation; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; UC, ulcerative colitis.
[a]Respondents could select more than one response option, so percentages may not total 100%.
[b]The SIBDQ provides a score ranging from 10 to 70, where higher scores represent higher health-related quality of life. Respondents' scores averaged approximately 79% of the maximum score ([47.3/(70−10)] × 100%). Two respondents did not complete the full questionnaire and were excluded from the calculations on the SIBDQ.

### Maximum Acceptable Increase in Risk of Adverse Events

Table 3 presents the maximum percentage-point increases in annual risk of serious infection and 5-year risk of

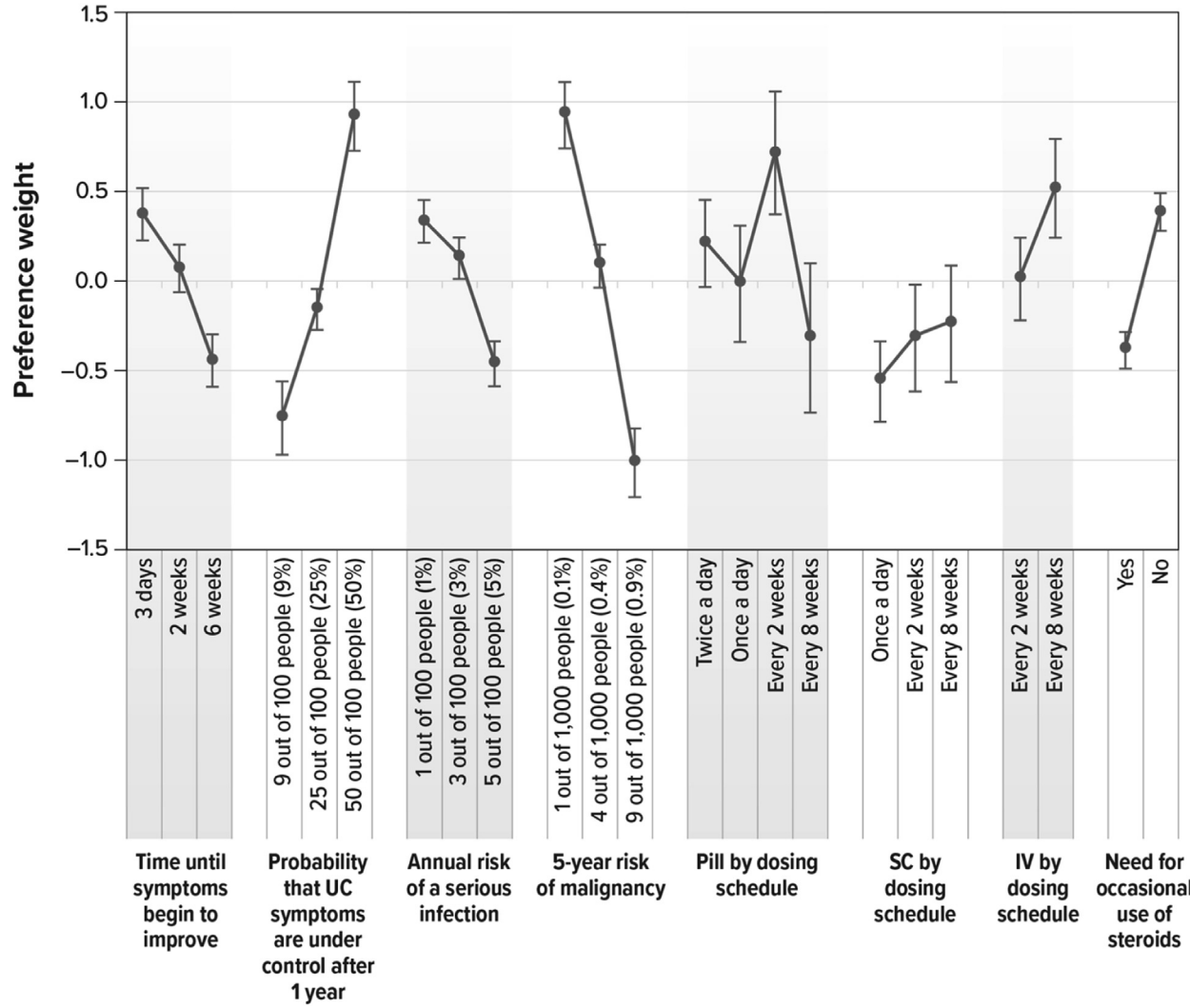



**Figure 2.** Preference weights (N = 365). IV, intravenous infusion; SC, subcutaneous injection; UC, ulcerative colitis. The vertical bars surrounding each mean preference weight denote the 95% confidence interval (computed by the delta method). Preference weights are relative to each other and do not have an absolute interpretation. The attribute levels with larger preference weights are preferred to attribute levels with smaller preference weights. The utility variation caused by a change in the levels of each attribute is represented by the vertical distance between the preference weights for any 2 levels of that attribute. Larger differences between preference weights indicate that respondents viewed the change as relatively more important. For example, the figure shows that an increase in the probability that UC symptoms are under control after one year from 9% to 50% was about 2.1 times more important than a reduction in the time until symptoms begin to improve (fastest onset of action) from 6 weeks to 3 days (ie, 2.1–2.061 = [0.916 − {−0.762}]/[0.372 − {−0.442}]).

malignancy that would be acceptable to respondents to reduce the time until symptoms begin to improve, to increase the probability that UC symptoms are under control after 1 year, to avoid the need for steroids, and to vary mode of administration and dosing schedule. In general, respondents were willing to accept statistically significant increases in the annual risk of serious infection to obtain an increase in efficacy, to change the mode and dosing schedule, and to avoid the need for the occasional use of steroids. On average, respondents would be willing to accept an increase in annual risk of infection more than 4% (the maximum increase included in the DCE design) to improve the time until symptoms begin to improve from 6 weeks to 3 days and to improve the probability that UC symptoms are under control after 1 year from 9% to 50% and from 25% to 50%.

In general, respondents were also willing to accept an increase in the 5-year risk of malignancy to obtain faster onset of action, to increase the probability of symptom control, to change the mode and dosing schedule, and to avoid the need for the occasional use of steroids. Respondents were willing to accept approximately a 0.3% increase in the 5-year risk of malignancy to improve onset of action from 6 weeks to 3 days and approximately a 0.7%

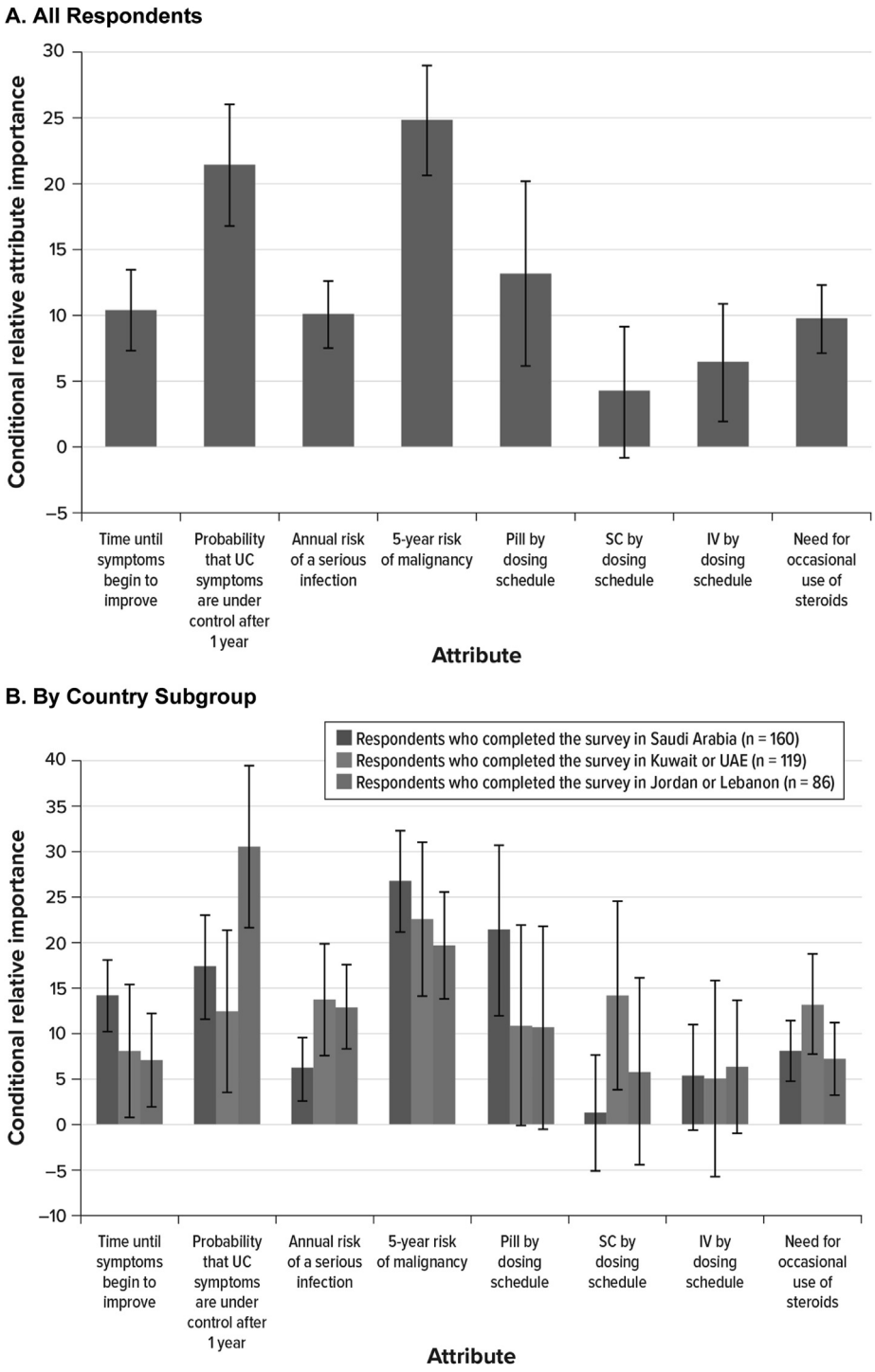



**Figure 3.** Scaled conditional relative importance of the attributes (N = 365). (A) All respondents. (B) By country subgroup. CI, confidence interval; CRI, conditional relative importance; DCE, discrete-choice experiment; IV, intravenous infusion; SC, subcutaneous injection; UC, ulcerative colitis. The vertical bars surrounding each relative importance denote the 95% CI (computed by the delta method). Attributes are presented in the order in which they appeared in the DCE questions. The CRI is the difference between the preference weights on the most-influential attribute level and the least-influential attribute level. These differences are summed across attributes, and the sum is scaled to 100. The conditional importance of each attribute is a percentage of this total. The standard errors and the 95% CIs for these differences were calculated using the delta method. The 95% CI around the point estimate is represented by the black vertical bars on top of the blue bars. The range of dosing frequencies was different for each mode of administration, and the CRI for each mode of administration was computed over the range of dosing frequencies presented to the respondents. Intravenous infusion was only presented with dosing schedules of every 8 weeks and every 2 weeks; SC injection was only presented with dosing schedules of every 8 weeks, every 2 weeks, and once a day; and oral pill was presented with all 4 possible dosing schedules.

increase in the 5-year risk of malignancy to increase the probability that UC symptoms are under control after 1 year from 9% to 50%.

## Subgroup Analysis

The analysis of preferences among the 5 prespecified subgroups of interest is summarized in Table S1 (Supplemental Material). Only 1 of the subgroups explored (ie, the country in which respondents completed the survey) resulted in systematically different preferences. For respondents who completed the survey in Jordan or Lebanon, the probability that UC symptoms are under control after 1 year had the greatest CRI (Figure 3B). The 5-year risk of malignancy had the next greatest CRI; however, this estimate was not statistically significantly different from the CRI of annual risk of serious infection ($P = .07$) or the CRI of pill administration by dosing schedule ($P = .21$). The CRI of

any mode of administration (pill, SC injection, or IV infusion) by dosing schedule was not statistically significantly different from 0. For respondents who completed the survey in Saudi Arabia, the 5-year risk of malignancy had the greatest CRI; however, this estimate was not statistically significantly different from the CRI of pill administration by dosing schedule ($P = .40$) (Figure 3B). The CRI of any SC injection or IV infusion by dosing schedule was not statistically significantly different from 0. For respondents who completed the survey in Kuwait or the UAE, the 5-year risk of malignancy had the greatest CRI; however, this estimate was not statistically significantly different from the CRI of the probability that UC symptoms are under control after 1 year ($P = .10$), the risk of serious infection ($P = .10$), the CRI of pill administration by dosing schedule ($P = .11$), or the CRI of SC injection by dosing schedule ($P = .26$) (Figure 3B). The CRI of any pill or IV infusion by dosing schedule was not statistically significantly different from 0.

The results of the subgroup analysis were used to calculate the maximum percentage-point increase in annual risk of serious infection and 5-year risk of malignancy that would be acceptable to respondents from each group for changes in other treatment attributes (Tables S2 and S3, Supplemental Material).

## Discussion

This is the first DCE study exploring patient preferences for moderate-to-severe UC treatment in Middle Eastern countries. Results of this study revealed that 5-year risk of malignancy and the probability that UC symptoms are under control after 1 year had the greatest CRIs, although the CRI of probability that symptoms are under control after 1 year was not statistically significantly different from the CRI of pill administration by dosing schedule ($P = .11$). In general, respondents were willing to accept statistically significant increases in the annual risk of serious infection and the 5-year risk of malignancy to obtain an increase in efficacy, to change the mode of administration and dosing schedule, and to avoid the need for occasional steroid use.

Subgroup analysis revealed statistically significant differences in preferences across respondents who completed the survey in different countries. Respondents who completed the survey in Jordan or Lebanon prioritized UC symptom control, whereas respondents who completed the survey in Saudi Arabia prioritized avoiding risk of malignancy (although the CRI estimate for this attribute was not statistically significantly different from the CRI of pill administration by dosing schedule). Respondents who completed the survey in Kuwait or the UAE considered all attributes as statistically equivalent, on average, except for any pill or IV infusion by dosing schedule, which did not have an impact on their preferences.

Taken together, our findings indicate that, on average, respondents preferred a quicker onset of symptom control, a higher probability of long-term symptom control at 1 year, and a lower risk of both adverse events (AEs) to a longer time until onset of symptom control, a lower probability that symptoms are under control after 1 year, and a higher risk of both AEs. The 5-year risk of malignancy and the probability that UC symptoms are under control after 1 year were the most important attributes to respondents, on average. From these results, it is evident that patients prioritize a quick onset of action. This priority may be primarily attributable to the disease and symptom burden of UC and patients' desire to regain a sense of normalcy and an ability to maintain their daily routines.

An understanding of patients' preferences for attributes of treatments for moderate-to-severe UC can facilitate communication between physicians prescribing these treatments in Middle Eastern countries and their patients,[28] in turn supporting shared decision-making and patient-centered care. Furthermore, because treatment attributes related to efficacy, safety, and administration features play a role in patients' adherence to therapy, improving physician–patient communications about patients' preferences among these attributes may help to improve adherence.[29] In addition, as patients are key stakeholders in healthcare decision-making and delivery and are the ultimate consumers of treatments, their views are likely to be important to policy makers and payers.

Results of the previously conducted US study evaluating patient preferences for UC treatments were broadly similar to our results.[13] In the US study, long-term symptom control was 2.5 times as important to respondents as time to symptom improvement, and 5-year malignancy risk was nearly as important as long-term symptom control. US respondents preferred oral to SC or IV administration, but the occasional need for steroids did not impact their preferences. While findings from both studies indicate that patients in both the US and Middle Eastern countries value long-term symptom control, avoiding serious risks, and a quick onset of symptom control, subtle differences in preferences between the 2 study populations emerged. Specifically, respondents in Middle Eastern countries placed greater priority on avoiding malignancy and on quick onset of action than did US respondents, and they were more steroid averse. US respondents, in comparison, were more focused on long-term symptom control than the respondents in Middle Eastern countries and considered this the most important attribute. While the drivers of these different preferences are not known, they may be attributable to cultural or economic differences in the study populations, as well as to differences in clinical practice between the 2 regions. When considered in aggregate, findings from both of these studies indicate heterogeneity in preferences across Middle Eastern countries and subtle qualitative differences in preferences between patients in Middle Eastern countries and US patients. These differences emphasize the importance of evaluating patient preferences locally, as preference data may not necessarily be transferable among populations in different regions.[30]

Limitations of this study are acknowledged. Respondents who chose to complete the survey may have preferences that differ from those who chose not to participate in the survey. Furthermore, the coronavirus disease 2019

**Table 3.** Random-Parameters Logit Model Estimates: Maximum Acceptable Percentage-Point Increase in Risk of Serious Infection (N = 365)

| Benefit | From | To | Maximum acceptable increase in annual risk (95% CI), (percentage points) |
|---|---|---|---|
| Maximum acceptable increase in annual risk of serious infection | | | |
| Time until symptoms begin to improve | 6 wk | 2 wk | 3.05 (2.08–4.03) |
| | 2 wk | 3 d | 2.34 (1.27–3.4) |
| | 6 wk | 3 d | 4.08 (2.92–5.24)[a] |
| Probability that UC symptoms are under control after 1 y | 9% | 25% | 3.38 (2.33–4.42) |
| | 25% | 50% | 4.95 (3.73–6.18)[a] |
| | 9% | 50% | 7.02 (4.99–9.05)[a] |
| Change in mode of administration and dosing schedule | SC once a day | IV every 2 wk | 3.26 (2.13–4.38) |
| | SC once a day | Pill twice a day | 3.91 (2.68–5.14) |
| | SC every 2 wk | IV every 8 wk | 4.15 (2.71–5.60)[a] |
| | SC every 2 wk | IV every 2 wk | 2.44 (0.95–3.93) |
| Need for occasional use of steroids | Yes | No | 3.91 (2.97–4.84) |
| Maximum acceptable increase in 5-y risk of malignancy[b] | | | |
| Time until symptoms begin to improve | 6 wk | 2 wk | 0.18 (0.08–0.28) |
| | 2 wk | 3 d | 0.11 (0.03–0.19) |
| | 6 wk | 3 d | 0.29 (0.17–0.40) |
| Probability that UC symptoms are under control after 1 y | 9% | 25% | 0.22 (0.11–0.32) |
| | 25% | 50% | 0.40 (0.26–0.54) |
| | 9% | 50% | 0.68 (0.50–0.86) |
| Change in mode of administration and dosing schedule | SC once a day | IV every 2 wk | 0.20 (0.07–0.33) |
| | SC once a day | Pill twice a day | 0.27 (0.13–0.41) |
| | SC every 2 wk | IV every 8 wk | 0.30 (0.12–0.47) |
| | SC every 2 wk | IV every 2 wk | 0.12 (−0.05 to 0.29) |
| Need for occasional use of steroids | Yes | No | 0.27 (0.18–0.36) |

CI, confidence interval; DCE, discrete-choice experiment; IV, intravenous infusion; MAR, maximum acceptable risk; SC, subcutaneous injection; UC, ulcerative colitis.
If the 95% CIs for any MAR estimate include 0, the MAR is not statistically significantly different from 0. The delta method was used to calculate standard errors for the preference weight for each omitted attribute level (Hensher et al., 2005).[27]
[a]This maximum acceptable percentage-point increase in annual risk of serious infection lies outside the risk range used in the DCE experimental design (ie, it is more than a 4% annual increase in risk of serious infection). The slope computed for the 2 highest risk levels was used in a linear extrapolation to calculate this maximum acceptable increase in risk.
[b]The maximum acceptable percentage-point increase in 5-y risk of malignancy is presented in risk per 1000 people (1/10 percentage points). The level included in the survey ranged from 1 to 9 in 1000 people.

pandemic may have caused selection bias, as some patients may have avoided going to clinical sites, or may have influenced preferences, as respondents might have acted and responded differently during this period as compared with other times. Although respondents were recruited at clinical sites by referral, responses to questions about experience with UC and treatments for UC were self-reported and not confirmed by a physician. However, physician referral of patients who fit the profile of eligible criteria further supported identification of respondents. An additional limitation of this study, and all voluntary surveys, is potential volunteer bias, which may have led to an underestimate or overestimate of respondent preferences. Potential information and selection bias introduced by the study design may limit the generalizability of the results.

Despite these limitations, this DCE study is characterized by a number of strengths derived from the use of best practices.[18] In particular, the survey was adapted from a previously published study,[13] was carefully designed, and used an experimental design developed using good research practices.[19] The treatment-choice data were analyzed using advanced RPL methods following good research practices[22,31] that avoid (1) estimation bias from unobserved variation in preferences across the sample and (2) within-sample correlation in the choice sequence for each respondent. Furthermore, observable preference heterogeneity was explored through a predefined subgroup analysis.

## Conclusion

Respondents with UC in the Middle East value a quicker onset of symptom control, a higher probability that symptoms are under control after 1 year, and a lower risk of both AEs. The 5-year risk of malignancy and the probability of

long-term UC symptom control at 1 year were among the most important attributes to respondents, on average. The strength of preferences for these attributes and the willingness to make tradeoffs among treatment features varied across respondent characteristics, suggesting that stakeholders should consider patient preferences as well as other factors such as geographic location, age, and lifestyle when discussing treatment options with their patients. Understanding patient preferences for attributes of treatments for moderate-to-severe UC can contribute to patient–physician shared decision-making, facilitating the improvement of patient care.

## Supplementary Materials

Material associated with this article can be found in the online version at https://doi.org/10.1016/j.gastha.2023.10.002.

## References


1. G. B. D. Inflammatory Bowel Disease Collaborators. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol 2020;5:17–30.
2. Alharbi OR, Azzam NA, Almalki AS, et al. Clinical epidemiology of ulcerative colitis in Arabs based on the Montreal classification. World J Gastroenterol 2014; 20:17525–17531.
3. Hanauer S, Schwartz J, Robinson M, et al. Mesalamine capsules for treatment of active ulcerative colitis: results of a controlled trial. Pentasa Study Group. Am J Gastroenterol 1993;88:1188–1197.
4. Hanauer SB, Sandborn WJ, Kornbluth A, et al. Delayed-release oral mesalamine at 4.8 g/day (800 mg tablet) for the treatment of moderately active ulcerative colitis: the ASCEND II trial. Am J Gastroenterol 2005;100:2478–2485.
5. Hanauer SB, Sninsky CA, Robinson M, et al. An oral preparation of mesalamine as long-term maintenance therapy for ulcerative colitis. A randomized, placebo-controlled trial. The Mesalamine Study Group. Ann Intern Med 1996;124:204–211.
6. Harrell LE, Hanauer SB. Mesalamine derivatives in the treatment of Crohn's disease. Gastroenterol Clin North Am 2004;33:303–317, ix-x.
7. Levine DS, Riff DS, Pruitt R, et al. A randomized, double blind, dose-response comparison of balsalazide (6.75 g), balsalazide (2.25 g), and mesalamine (2.4 g) in the treatment of active, mild-to-moderate ulcerative colitis. Am J Gastroenterol 2002;97:1398–1407.
8. Sninsky CA, Cort DH, Shanahan F, et al. Oral mesalamine (Asacol) for mildly to moderately active ulcerative colitis. A multicenter study. Ann Intern Med 1991; 115:350–355.
9. Faubion WA Jr, Loftus EV Jr, Harmsen WS, et al. The natural history of corticosteroid therapy for inflammatory bowel disease: a population-based study. Gastroenterology 2001;121:255–260.
10. Actis GC, Fadda M, David E, et al. Colectomy rate in steroid-refractory colitis initially responsive to cyclosporin: a long-term retrospective cohort study. BMC Gastroenterol 2007;7:13.
11. Gonzalez-Lama Y, Gisbert JP, Mate J. The role of tacrolimus in inflammatory bowel disease: a systematic review. Dig Dis Sci 2006;51:1833–1840.
12. Elwyn G, Frosch D, Rollnick S. Dual equipoise shared decision making: definitions for decision and behaviour support interventions. Implement Sci 2009;4:75.
13. Boeri M, Myers K, Ervin C, et al. Patient and physician preferences for ulcerative colitis treatments in the United States. Clin Exp Gastroenterol 2019;12:263–278.
14. Bewtra M, Reed SD, Johnson FR, et al. Variation among patients with Crohn's disease in benefit vs risk preferences and remission time equivalents. Clin Gastroenterol Hepatol 2020;18:406–414 e407.
15. Irvine E, Zhou Q, Thompson A. The short inflammatory bowel disease questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT investigators. Canadian Crohn's Relapse Prevention Trial. Am J Gastroenterol 1996; 91:1571–1578.
16. Soekhai V, de Bekker-Grob EW, Ellis AR, et al. Discrete choice experiments in health economics: past, present and future. Pharmacoeconomics 2019;37:201–226.
17. Louviere JJ, Hensher DA, Swait JD. Stated choice methods: analysis and applications. Cambridge, UK: Cambridge University Press, 2000.
18. Bridges JF, Hauber AB, Marshall D, et al. Conjoint analysis applications in health—a checklist: a report of the ISPOR good research practices for Conjoint analysis task force. Value Health 2011;14:403–413.
19. Johnson FR, Lancsar E, Marshall D, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint analysis experimental design good research practices task force. Value Health 2013;16:3–13.
20. Manski CF. The structure of random utility models. Theory Decis 1977;8:229–254.
21. Thurstone LL. A law of comparative judgment. Psychol Rev 1927;34:273.
22. Hauber AB, González JM, Groothuis-Oudshoorn CG, et al. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR Conjoint analysis good research practices task force. Value Health 2016;19:300–315.
23. Hole AR. A comparison of approaches to estimating confidence intervals for willingness to pay measures. Health Econ 2007;16:827–840.
24. Greene WH. Econometric analysis. 7th ed. New York: Pearson, 2012.
25. Gonzalez JM, Boeri M. The impact of the risk functional form assumptions on maximum acceptable risk measures. Patient 2021;14:827–836.
26. Vass C, Boeri M, Karim S, et al. Accounting for preference heterogeneity in discrete-choice experiments: an ISPOR special interest group report. Value Health 2022; 25:685–694.
27. Hensher DA, Rose JM, Greene WH. Applied choice analysis. 2nd ed. Cambridge, UK: Cambridge University Press, 2005.

28. Webair HH. Patient-centered care in the Middle East. In: Laher I, ed. Handbook of healthcare in the Arab world. Cham: Springer, 2020.
29. Sharara AI, Al Awadhi S, Alharbi O, et al. Epidemiology, disease burden, and treatment challenges of ulcerative colitis in Africa and the Middle East. Expert Rev Gastroenterol Hepatol 2018;12:883–897.
30. ISPOR Health Preference Research Special Interest Group. When and how can health-preference measures be transferred between Contexts? 2021. https://www.ispor.org/docs/default-source/euro2021/europe-2021-marsh-forum.pdf?sfvrsn=86139f31_0. Accessed April 28, 2023.
31. Ho MP, Gonzalez JM, Lerner HP, et al. Incorporating patient-preference evidence into regulatory decision making. Surg Endosc 2015;29:2984–2993.

**Received January 27, 2023. Accepted October 3, 2023.**

**Correspondence:**
Address correspondence to: Marco Boeri, PhD, RTI Health Solutions, 123B Forsyth House, Cromac Square, Belfast BT2 8LA, UK. e-mail: mboeri@rti.org.

**Acknowledgments:**
Kimberly Moon of RTI Health Solutions provided overall project management for this study. Kate Lothman of RTI Health Solutions provided medical writing services, which were funded by Pfizer Gulf.

**Authors' Contributions:**
Othman AlHarbi, Niazy Abu Farsakh, Sameer Al-Awadhi, Talal Al-Taweel, Inas Mikhail, Faisal Batwa, Khalil Bedran, Dilara Balkan, Levent Mert Gunay, Joseph C. Cappelleri, Marco Boeri, Colton Leach, Sara Habjoka, and Mahmoud Mosli declare that they have made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; have substantially revised or critically reviewed the article; have approved the final article; and agree to take responsibility and be accountable for the contents of the article.

**Conflicts of Interest:**
These authors disclose the following: Dilara Balkan, Joseph C. Cappelleri, and Levent Mert Gunay are employees of Pfizer Inc and may hold stocks or stock options; Sara Habjoka was an employee of Pfizer Inc when this research was conducted. Marco Boeri and Colton Leach are employees of RTI Health Solutions which was a contracted vendor to Pfizer in connection with the development of this manuscript, study design, and data management. The remaining authors disclose no conflicts.

**Funding:**
This study was sponsored by Pfizer Gulf.

**Ethical Statement:**
The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

**Data Transparency Statement:**
The study sponsor will share the data upon reasonable request.

**Reporting Guidelines:**
None. No EQUATOR guidelines have been developed for discrete-choice experiment studies.