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BRIEF REPORT

Biologics Initiation in Rheumatoid Arthritis by Race and Ethnicity: Results From a Randomized Survey Study

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Objective. To investigate whether the race and ethnicity of a patient with rheumatoid arthritis (RA) influences rheumatologists' likelihood of choosing to initiate biologic disease-modifying antirheumatic drug (bDMARD) treatment.

Methods. We conducted a randomized survey experiment in which identical brief case vignettes of hypothetical patients with RA were sent to US rheumatologists (respondents). Three of the four cases included some level of treatment decision ambiguity whereas the fourth case strongly favored bDMARD initiation. Each respondent was shown the four case vignettes, with the race and ethnicity (Black, Hispanic, White) randomly assigned for each case. Each vignette offered multiple choices for next therapeutic step, which we summarized using frequencies and proportions by race and ethnicity version.

Results. Among 159 US rheumatologists, we found that for the three cases with some level of treatment decision ambiguity, there was little to no variability in the proportions of respondents who chose to start a biologic for the Black and Hispanic variants (cases 1, 2, and 3). For case 4, respondents generally agreed to start a biologic with some minimal variability across the variants (92.6% for the Black version, 98.1% for the Hispanic version, and 96.2% for the White version).

Conclusion. There are conflicting data regarding bDMARD use and initiation in patients with RA based on the sex and race of the patient. This work adds to this conversation by examining how the next therapeutic step chosen by rheumatologists varied by the race and ethnicity of the hypothetical patient.

INTRODUCTION

Up to three million adults live with rheumatoid arthritis (RA) in the US (1). Biologic disease-modifying antirheumatic drugs (bDMARDs) have transformed the management of RA over the last two decades (2). Starting with the introduction of tumor necrosis factor antagonists (anti-TNF) in the 1990s, there are now roughly 20 bDMARDs targeting a variety of immune processes for the treatment of pediatric and adult rheumatologic diseases. After nearly two decades of experience, bDMARD therapies have proven to be safe, well-tolerated, and highly effective at reducing disease activity in RA. As a result, guidelines from the current American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology recommend their use in the management of moderate to severe and refractory RA (3,4). The rapid expansion in the use of bDMARDs has come at a significant financial cost, with an average price point for bDMARDS in the US at least five times greater than for traditional disease modifying antirheumatic drugs such as methotrexate and hydroxychloroquine (5–8).

We have shown previously that racial and ethnic minorities are underrepresented in clinical trials for rheumatic diseases (9,10). Racial and ethnic disparities in the use of bDMARDs in RA have been reported, but studies are limited (11). The decision to initiate a bDMARD is likely influenced by many factors, including provider and patient attitudes, disease severity, and comorbidities. We conducted a randomized survey experiment in which identical brief case vignettes were sent to US rheumatologists to investigate whether the patient's race and ethnicity influenced

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SIGNIFICANCE & INNOVATION

- In a population of US rheumatologists, we conducted a randomized survey experiment of identical brief case vignettes to investigate whether the hypothetical patient's race and ethnicity influenced the rheumatologist's likelihood of wanting to initiate biologic disease-modifying antirheumatic drug treatment.
- Rheumatologists appeared more likely to initiate therapy in hypothetical Black and Hispanic patients (vs. hypothetical White patients) when there was some ambiguity in the vignette, but this effect was not seen in a more clearcut clinical scenario.

the rheumatologist's likelihood of wanting to initiate bDMARD treatment.

PATIENTS AND METHODS

Instrument development. Four board-certified academic rheumatologists developed four brief clinical scenarios asking about treatment for patients with RA. Each case provided basic patient demographics at the start (eg, "A 48-year-old White female with a new diagnosis of RA…") and outlined relevant symptoms, medical history, physical examination findings, and laboratory results. Each case included a single multiple-choice question at the end: "Assuming no additional information can be obtained and no absolute contraindications to any of the medication choices, what would be your next therapeutic step?" Three of the four cases were designed to leave some level of treatment decision ambiguity between choice of adjusting conventional synthetic DMARDs (csDMARDs) and initiating bDMARD answers, with bDMARD being somewhat favored based on the clinical case and current treatment guidelines. Prior studies demonstrate that implicit biases are more pronounced when clinicians are faced with a higher cognitive load, and this guided our rationale for creating intentionally ambiguous cases (12). The final case (case 4) strongly favored bDMARD initiation, serving as a contrasting control to the ambiguous cases. For each of these four cases we created three variations modifying only the single word pertaining to race and ethnicity (Black, Hispanic, and White). We then designed the instrument distribution such that each participant would receive one random race and ethnicity variant of each of the four questions. The instrument also included questions about the participants' demographics and clinical background, including years since fellowship and current practice setting. We test piloted the instrument among 13 rheumatologists and received responses that reflected the intentional ambiguity of the first three clinical questions and preference for bDMARD in the fourth question.

Study participants and data collection. We obtained an email list of 3389 rheumatologists in the US from Span Global Services. We initially sent the instrument to this entire email list on March 1, 2022, and provided a $20 incentive through an online incentive manager, Tango Rewards, which we increased to $75 at the final email reminder on April 26, 2022. Respondents were blinded to the purpose of the study and the randomization of case race and ethnicity. After the initial mailing, 1397 emails were returned as undeliverable, leaving 1992 valid contacts. Nearly ten percent of these valid contacts (n = 183) opened the email and started the survey. We excluded five individuals who self-reported that they were not rheumatologists, two individuals who did not answer whether they were rheumatologists, and

Table 1. Characteristics of the 159 rheumatologist survey respondents

Characteristic	Value
Gender, n (%)	
Woman	78 (49.1%)
Man	80 (50.3%)
Other specified	1 (0.6%)
Age, in years, median [IQR]	54 [42-69]
Race, n (%)	
Asian	46 (28.9%)
Black or African American	2 (1.3%)
White	102 (64.2%)
Other[a]	9 (5.7%)
Ethnicity, n (%)	
Hispanic or Latino/a	6 (3.8%)
Not Hispanic or Latino/a	153 (96.2%)
Years since fellowship, n (%)	
Currently in fellowship	1 (0.6%)
<5 y ago	20 (12.6%)
5-10 y ago	24 (15.1%)
11-19 y ago	35 (22.0%)
>20 y ago	79 (49.7%)
Setting, n (%)	
Rural	6 (3.8%)
Suburban	53 (33.3%)
Urban	100 (62.9%)
Practice setting, n (%)	
Academic	77 (48.4%)
City or county public hospital	4 (2.5%)
Other[b]	9 (5.7%)
Private solo or group practice	51 (32.1%)
Retired	10 (6.3%)
VA	2 (1.3%)
HMO	3 (1.9%)
Working but not practicing clinically	3 (1.9%)
What majority of time is spent on, n (%)	
Administrative	4 (2.5%)
Education	10 (6.3%)
Patient care	126 (79.2%)
Research	19 (11.9%)

Abbreviations: HMO, health maintenance organization; IQR, interquartile range; VA, Veterans Affairs.
[a]Other race was predominantly individuals reporting multiple race categories as well as one individual who identified as American Indian or Alaska Native.
[b]Other current practice setting responses include psychiatric hospital, multispecialty group practice, and community teaching hospital.

17 who did not complete the entire survey, leaving 159 respondents. Our study was approved by the Stanford University Institutional Review Board (IRB-59395).

Statistical analysis. We summarized the respondent characteristics with frequencies and proportions to characterize our study population. Next, we calculated the distribution of responses for each case, stratified by case race and ethnicity.

RESULTS

Nearly half of respondents were women, and the median age of the 159 rheumatologists who completed the full survey was 54 years. Approximately 28% reported that they obtained their medical degree outside of the US. Respondents were from 34 different US states, plus the District of Columbia and Puerto Rico. The majority reported practicing in urban areas (63%), and most either worked in academics (48%) or worked in private practice (32%). Nearly 80% of respondents reported spending most of their working time on patient care, and an additional 12% specified research as their primary focus (Table 1).

In this descriptive work, little variability was observed for cases 1, 2, and 3, which may be due to chance. For example, 61.4% and 61.5% for Black and Hispanic variants of case 2, compared with 52% for the White version. For case 4, respondents generally agreed to start a biologic with some minimal variability across the variants (92.6% for the Black version, 98.1% for the Hispanic version, and 96.2% for the White version). Variability in the alternative therapeutic strategies selected are summarized in Table 2.

DISCUSSION

Overall, respondents chose to initiate a bDMARD as the next therapeutic step in most cases regardless of whether the case was presented as a Black, Hispanic, or White patient, holding all other factors constant. There was some variability by race and ethnicity presentation—for example, case 1 presented a patient with borderline findings of ongoing RA disease activity, hinting at possible incomplete response to triple therapy with methotrexate, sulfasalazine, and hydroxychloroquine. In this case, respondents chose bDMARD initiation nearly 76% of the time when presented as Black, 70% when Hispanic, and 65% when presented as White. Cases 2 and 3 were also nuanced, with therapeutic dilemmas including medication side effects (case 2) and reluctance to take medications (case 3). In these cases, starting a bDMARD also appeared to be slightly less favored. This contrasts with the clinical scenario in case 4, which presented clear evidence of treatment failure, ongoing disease activity, and radiographic progression on csDMARD and no additional complicating factors, strongly favoring bDMARD initiation. In this case, most participants chose bDMARD initiation, and there was little variability by case race and ethnicity. Given the small sample size and lack of power, we refrained from statistical testing. If these observed small differences are real, we can only theorize as to why race and ethnicity was less variable in the more clearcut case,

Table 2. Distribution of the next therapeutic steps by case race and ethnicity among 159 respondents

	Black case	Hispanic case	White case
Case 1	N = 54	N = 53	N = 52
Add low-dose prednisone	1 (1.9%)	3 (5.7%)	1 (1.9%)
Continue current therapy and monitoring for now	6 (11.1%)	3 (5.7%)	5 (9.6%)
Increase dose of oral methotrexate	6 (11.1%)	7 (13.2%)	10 (19.2%)
Start a biologic therapy	41 (75.9%)	37 (69.8%)	34 (65.4%)
Switch methotrexate to leflunomide	0 (0%)	3 (5.7%)	2 (3.8%)
Case 2	N = 57	N = 52	N = 50
Continue current therapy and prescribe antidiarrheal medication	8 (14.0%)	11 (21.2%)	10 (20.0%)
Continue current therapy and reassess in 3 mo	6 (10.5%)	5 (9.6%)	10 (20.0%)
Start combination leflunomide and methotrexate at lower doses and stop sulfasalazine	5 (8.8%)	2 (3.8%)	3 (6.0%)
Stop sulfasalazine and start a biologic therapy	35 (61.4%)	32 (61.5%)	26 (52.0%)
Switch from leflunomide back to methotrexate at a lower dose and stop sulfasalazine	3 (5.3%)	2 (3.8%)	1 (2.0%)
Case 3	N = 53	N = 53	N = 53
Add hydroxychloroquine	15 (28.3%)	10 (18.9%)	12 (22.6%)
Add low-dose prednisone	1 (1.9%)	1 (1.9%)	3 (5.7%)
Start a biologic therapy	35 (66.0%)	36 (67.9%)	32 (60.4%)
Switch methotrexate to leflunomide	0 (0%)	4 (7.5%)	3 (5.7%)
Continue current therapy and monitoring for now	2 (3.8%)	2 (3.8%)	3 (5.7%)
Case 4	N = 54	N = 53	N = 52
Add prednisone	3 (5.6%)	1 (1.9%)	1 (1.9%)
Start a biologic therapy	50 (92.6%)	52 (98.1%)	50 (96.2%)
Increase dose of methotrexate	0 (0%)	0 (0%)	1 (1.9%)
Switch methotrexate to leflunomide	1 (1.9%)	0 (0%)	0 (0%)

but it is possible that subconscious consideration of race and ethnicity in clinical decision making may play less of a role in situations of lower cognitive loading (12,13).

We had a diverse population of respondents, although lower than expected participation, which limited additional analyses such as examining racial concordance. Compared with the 2015 ACR Workforce Study population, we had more women participants, and a higher proportion self-reported being of Asian race (14). We cannot exclude the possibility that there may be some respondent bias in this survey study, and due to small numbers, we did not conduct hypothesis testing. To simplify the survey, we collected minimal background information on participants and cannot report on details of their clinical practice, such as the proportion of patients on csDMARDs or bDMARDs or the proportion uninsured. Additional strengths include the randomized design and broad distribution to a national mailing list of rheumatologists, an approach we and others have previously used (15). We confirmed that the randomization was successful as only three individuals (1.9%) got the same race and ethnicity for all four RA cases. These were retained in the analysis.

There is mixed evidence regarding bDMARD use and initiation in patients with RA on the basis of sex and race (11,16,17). These studies differed not only in whether they evaluated new versus ongoing bDMARD use but also in the populations they studied. A recent review noted that patients' decisions to accept recommendations to initiate a bDMARD were influenced by structural nonbiological, social, and biological factors, and it highlighted multiple solutions, including increasing representation in clinical trials and increasing access to medications (18).

The present work adds to this conversation by examining how the next therapeutic step chosen by rheumatologists varied by the race and ethnicity of the patient. We found that rheumatologists demonstrated little to no difference across the cases. This contrasts with our initial hypothesis, which was that non-White cases would be less likely to receive bDMARDs. This may be explained a few ways. First, given the current awareness of the pernicious impact of structural racism on health outcomes, we cannot rule out social desirability bias (19,20). Second, these findings could reflect a shift in awareness of the impact of racism, and respondents may be "over-correcting" for these effects. Third, bDMARDs require less laboratory monitoring and are potentially simpler to adhere to than csDMARDs. Triple therapy can require up to seven or more pills per day, with laboratory surveillance every 3 months, whereas bDMARD injection or infusion occurs every 1 to 8 weeks, typically with laboratory surveillance every 6 months. Thus, perceptions regarding how patients of different races and ethnicities adhere to medications and interact with health care may also be at play. We did not specify insurance status in our case vignettes and therefore cannot determine how assumptions by participants about insurance may influence these results.

The goal of equity is one in which treatment and treatment response is uniform across subgroups. We recognize that case vignettes are not the same as treating individuals; however, in this randomized vignette-based survey, we observed generally similar bDMARD initiation by the race and ethnicity of the hypothetical RA cases. It will be important to extend these survey data to real world data, and in particular pay attention to how trends have changed over time. Additionally, studies investigating the role of patient-provider racial and ethnic concordance in bDMARD initiation are needed to understand the impact that minority underrepresentation in the rheumatology workforce may be having on RA management and outcomes.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article and revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Simard and Dr. Lu had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Simard, Falasinnu, Baker, Deluna, Horomanski, Fairchild.

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Analysis and interpretation of data. Simard, Lu, Falasinnu, Baker, Hawa, Deluna, Horomanski, Fairchild.

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