CO132

Predictors of Low Disease Activity/ Remission Amongst Rheumatoid Arthritis Patients Experiencing Inadequate Response to Biologic/ Targeted Synthetic Disease-Modifying Antirheumatic Drugs

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OBJECTIVE

- This study aimed to identify predictors of treatment response in patients who previously experienced an inadequate response to a bDMARD or tsDMARD.

CONCLUSIONS

- In this large real-world study of patients with moderate-to-severe RA and prior inadequate response to biologic/targeted synthetic DMARDs, **over two-thirds (69%) and approximately two-thirds (≈63%)** of those who started a new b/tsDMARDs failed to achieve low disease activity/remission at 6- and 12-month follow-up, respectively.
- Patients with **obesity**, comorbidities such as **COPD**, **fibromyalgia**, and **osteoporosis**, **higher baseline CDAI scores**, and **those treated with bDMARDs** (vs. tsDMARDs) at index were less likely to achieve LDA/remission after 6 months of follow-up. Similar results for obesity and comorbidities were observed at the 12-month follow-up.
- These findings highlight the **significant impact of obesity and comorbidities on the clinical management of RA**, aligning with the ACR guidelines, which recommend maintaining a healthy weight to optimize long-term RA outcomes.[5]
- Future research should explore the interaction between comorbidities and RA disease activity to enable targeted interventions that improve outcomes.

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BACKGROUND

- Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent synovial inflammation, leading to bone and cartilage erosion and eventual joint destruction.[1]
- Standard treatment includes corticosteroids alongside disease-modifying antirheumatic drugs (DMARDs).[2]

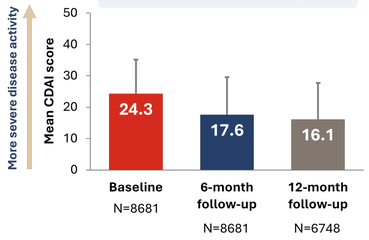
Conventional synthetic DMARDs (csDMARDs)	Biologic DMARDs (bDMARDs)	Targeted synthetic DMARDs (tsDMARDs)
Broadly suppress immune activation and inflammation.	Target specific cytokines or immune cells involved in the inflammatory process.	Selectively block key intracellular signaling pathways that drive RA inflammation.

- Despite the availability of these therapies, many patients fail to achieve low disease activity (LDA) or remission, highlighting the need for more effective treatment strategies.

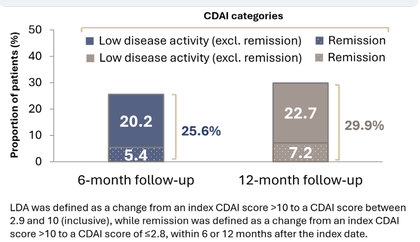
KEY RESULTS

At the 6-month follow-up, the mean CDAI decreased from 24.3 to 17.6, with 31.0% of patients achieving LDA/remission

CDAI score at different time points



Patients achieving LDA/remission at different time points



LDA was defined as a change from an index CDAI score >10 to a CDAI score between 2.9 and 10 (inclusive), while remission was defined as a change from an index CDAI score >10 to a CDAI score of ≤2.8, within 6 or 12 months after the index date.

Patients who achieved LDA/remission at 6 months were more likely to be White, have commercial insurance, reside in the Northeast, have a lower BMI, and less likely to be overweight or have a weight-related comorbidity.

Baseline demographics	*Patients who achieved LDA/remission at 6 months (N=2691)*	*Patients who did not achieve LDA/remission at 6 months (N=5990)*
Mean age, years (SD)	58.4 (13.0)	58.4 (12.7)
Female, n (%)	2155 (80.1)	4952 (82.7)
Race, n (%)		
White	2115 (78.6)	4459 (74.4)
Black	203 (7.5)	551 (9.2)
Other/Unknown	373 (13.9)	980 (16.4)
Ethnicity, n (%)		
Non-Hispanic	2300 (85.5)	5022 (83.8)
Hispanic	150 (5.6)	380 (6.3)
Unknown	241 (9.0)	588 (9.8)
Insurance, n (%)		
Commercial	1148 (42.7)	2444 (40.8)
Medicare	618 (23.0)	1514 (25.3)
Multiple	332 (12.3)	856 (14.3)
Other	77 (2.9)	210 (3.5)
Census region, n (%)		
South	1924 (71.5)	4504 (75.2)
Midwest	292 (10.9)	776 (13.0)
Northeast	333 (12.4)	452 (7.5)
West	141 (5.2)	251 (4.2)
Mean BMI (SD)	30.4 (7.1)	31.4 (7.5)
BMI <18.5	19 (0.7)	68 (1.1)
BMI 18.5–24.9	632 (23.5)	1145 (19.1)
BMI 25.0–29.9	794 (29.5)	1627 (27.2)
BMI ≥30	1226 (45.6)	3074 (51.3)
Overweight + 1 weight-related comorbidity, n (%)[a]	834 (31.0)	2040 (34.1)

[a]Defined as BMI ≥ 27 kg/m^2 (overweight) with at least one weight-related comorbidity, including hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea, or cardiovascular disease (myocardial infarction, stroke, or peripheral arterial disease). This definition is in accordance with the FDA's *Obesity and Overweight: Guidance for Industry*.[4]

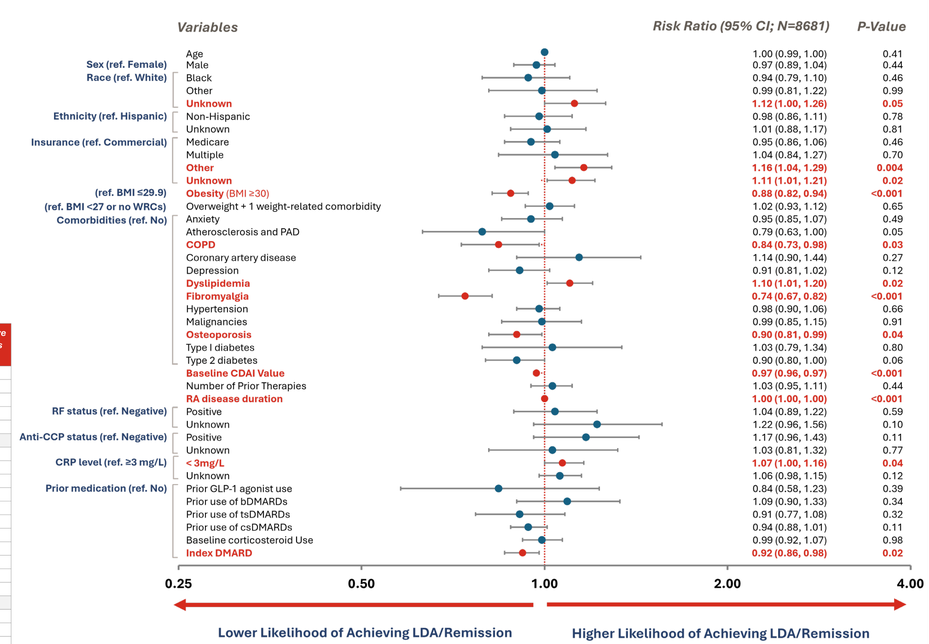
Patients who achieved LDA/remission at 6 months were more likely to have moderate disease activity, have RA for ≥2 years, and less likely to have comorbidities, including fibromyalgia.

Baseline clinical characteristics	*Patients who achieved LDA/remission at 6 months (N=2691)*	*Patients who did not achieve LDA/remission at 6 months (N=5990)*
RA disease duration, ≥2 Years, **n (%)**	1861 (69.2)	3812 (63.6)
CDAI score, n (%)		
Moderate activity: 10.1-22.0	1773 (65.9)	2809 (46.9)
High activity: 22.1-76.0	918 (34.1)	3181 (53.1)
Charlson comorbidity index, Mean (SD)	1.9 (1.6)	2.1 (1.7)
Comorbidities, n (%)		
Hypertension	852 (31.7)	2067 (34.5)
Dyslipidemia	606 (22.5)	1363 (22.8)
Fibromyalgia	314 (11.7)	1128 (18.8)
Osteoporosis	347 (12.9)	875 (14.6)
Type II diabetes	314 (11.7)	876 (14.6)
Depression	249 (9.3)	744 (12.4)
Anxiety	236 (8.8)	646 (10.8)
Rheumatoid factor, n (%)		
Positive	110 (4.1)	267 (4.5)
Negative	62 (2.3)	120 (2.0)
Unknown	2519 (93.6)	5603 (93.5)
Anti-citrullinated peptide antibody, n (%)		
Positive	76 (2.8)	223 (3.7)
Negative	129 (4.8)	374 (6.2)
Unknown	2487 (92.4)	5398 (90.1)
C-reactive protein	n=1869	n=4075
Mean (SD)	8.1 (17.5)	7.7 (16.3)

Comorbidities reported in >10% of patients who did not achieve LDA/remission at 6 months are shown in this table; other comorbidities are presented in the supplementary.

Multivariable associations of baseline characteristics on achieving LDA/remission at 6-month follow-up

Patients with obesity, osteoporosis, COPD, fibromyalgia, higher baseline CDAI scores, or those who initiated bDMARDs (vs. tsDMARDs) were less likely to achieve LDA/remission at 6 months.



*Statistical significance is denoted by values in **bold red***
C-Statistic=0.65 (A measure of the model's ability to classify subjects achieving LDA at 6 months)

Note: The statistical significance observed for the 'Unknown' race category and CRP levels <3 mg/L may be influenced by missing data. Similarly, key laboratory variables such as RF status and anti-CCP status also had missing data. As a result, interpretation of findings related to these variables is limited and warrants caution.

METHODS

STUDY DESIGN
- New-user retrospective cohort study

DATA SOURCE
- OM1 PremiOM™ RA (OM1, Boston, MA), a multisource real-world dataset with linked claims and EHR data on patients with RA in the US

STUDY POPULATION
- Adult patients with moderate-to-severe RA who initiated a b/tsDMARD between January 2013 to June 2024 and had used a different b/tsDMARD in the previous year.
  - Patients had at least 365 days of baseline data available prior to and including the index date
  - Patients had at least one CDAI score >10 in the 90 days prior to and including the index date (baseline), and at least one CDAI score in the 180 days following the index date (follow-up)
  - Initiation of pre-specified b/tsDMARDs of interest: bDMARDs (abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab) and tsDMARDs (baricitinib, tofacitinib, upadacitinib)

DATA ANALYSIS
- Primary outcome was LDA (CDAI ≤10.0) or remission (CDAI ≤2.8) measured at 6 months post treatment initiation.
- Risk ratios and 95% CI were estimated using log-binomial regression to model the probability of achieving LDA/remission with baseline characteristics as predictors at 6- and 12-months follow-up.
- Predictors included age, sex, race, ethnicity, insurance type, obesity, overweight AND weight-related comorbidity, fibromyalgia, depression, anxiety, COPD, cardiovascular disease, history of type 1 or 2 diabetes, RA disease duration, RF status, anti-CCP status, CRP level, baseline CDAI score, number of prior RA therapies used, prior use of GLP-1 agonist, corticosteroids, bDMARDs, tsDMARDs, csDMARDs and whether the index treatment was a bDMARD vs. a tsDMARD.
- Estimated CDAI (eCDAI), a validated machine learning algorithm that estimates a patient's CDAI score using clinical notes,[3] was used to supplement missing CDAI scores at follow-up.

STRENGTH

- Given an adequately sized sample with baseline characteristics representative of the US population, the study results are widely generalizable to US patients with moderate-to-severe RA initiating b/tsDMARDs after an inadequate response to prior b/tsDMARDs therapy in routine clinical practice.

LIMITATIONS

- Due to the open nature of claims in the OM1 PremiOM™ RA dataset, patients may have had incomplete data from certain sources (e.g., pharmacy claims) during specific time periods.
- To address the limitation of potential missing data on medications, prescription orders from the EMR were included to provide a more complete picture of treatment patterns.
- At the 12-month follow-up timepoint, CDAI values were missing for 20–30% of patients, which limits the interpretation of the analyses. However, results from augmenting missing CDAI values with the eCDAI were similar.

ABBREVIATIONS: ACR, American College of Rheumatology; bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CCP, cyclic citrullinated peptide; CDAI, Clinical Disease Activity Index; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease; CRP, C-reactive protein; eCDAI, Estimated Clinical Disease Activity Index; EHR, electronic health records; EMR, electronic medical record; GLP1, glucagon-like peptide-1; LDA, low disease activity; N, total number of patients; PAD, Peripheral Artery Disease; RA, rheumatoid arthritis; RF status, Rheumatoid factor status; Rh, Rheumatoid; tsDMARD, targeted synthetic disease-modifying antirheumatic drug; SD, standard deviation; US, United States; WRCs, weight-related comorbidities.

DISCLOSURES

Chandrasekar Gopalakrishnan, Kathryn Starzyk, and Luis Rangel: Employee of OM1, Inc.;
Eric Hanson, Michael Behling, Andrea Cohee, Beth Mitchell, and Russel Burge: Employee and/or stockholder of Lilly.

ACKNOWLEDGMENT: Pranshu Roy, an employee of Eli Lilly Services India Pvt. Ltd, provided medical writing support.

SUPPLEMENTAL MATERIALS

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2. Deson S., *Int. J. Clin. Rheumatol.* 2024;19(6):208–210.
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SUPPLEMENTARY INFORMATION

Predictors of Low Disease Activity/ Remission Amongst Rheumatoid Arthritis Patients Experiencing Inadequate Response to Biologic/ Targeted Synthetic Disease-Modifying Antirheumatic Drugs

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RESULTS

Baseline comorbidities

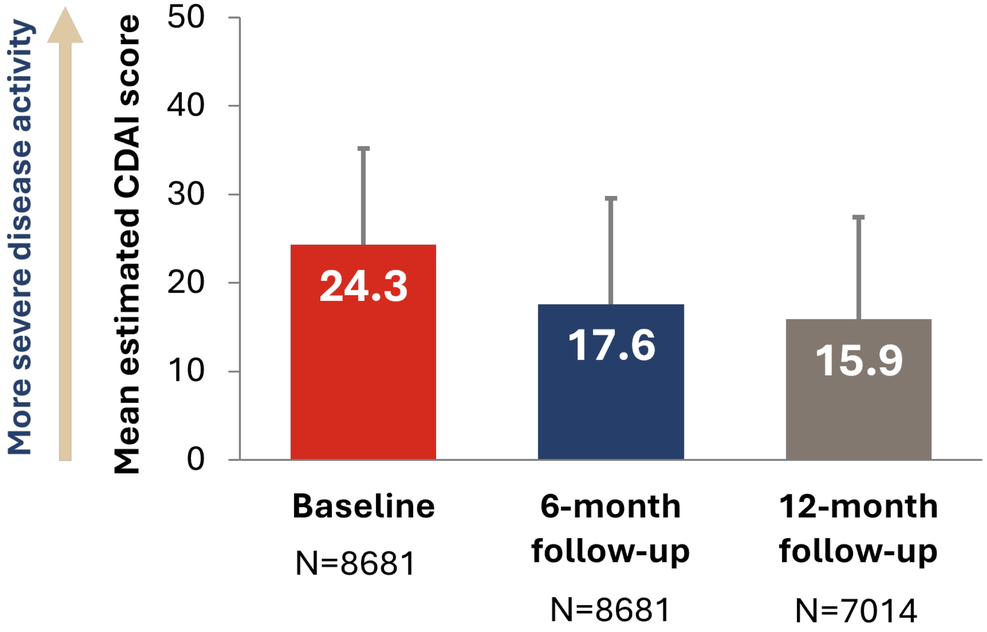
Baseline clinical characteristics	*Patients who achieved LDA/remission at 6 months (N=2691)*	*Patients who did not achieve LDA/remission at 6 months (N=5990)*
Comorbidities, n (%)		
Hypertension	852 (31.7)	2067 (34.5)
Dyslipidemia	606 (22.5)	1363 (22.8)
Fibromyalgia	314 (11.7)	1128 (18.8)
Osteoporosis	347 (12.9)	875 (14.6)
Type II diabetes	314 (11.7)	876 (14.6)
Depression	249 (9.3)	744 (12.4)
Anxiety	236 (8.8)	646 (10.8)
Atherosclerosis and PAD	162 (6.0)	451 (7.5)
COPD	142 (5.3)	437 (7.3)
Coronary artery disease	146 (5.4)	377 (6.3)
Malignancies	115 (4.3)	275 (4.6)
Type I diabetes	34 (1.3)	84 (1.4)
Charlson comorbidity index, categorical, n (%)		
0-1	1556 (57.8)	3143 (52.5)
2-3	800 (29.7)	1940 (32.4)
4-5	220 (8.2)	568 (9.5)
6+	115 (4.3)	339 (5.7)

Abbreviations: COPD, chronic obstructive pulmonary disease; LDA, low disease activity; N, total number of patients; PAD, peripheral arterial disease;

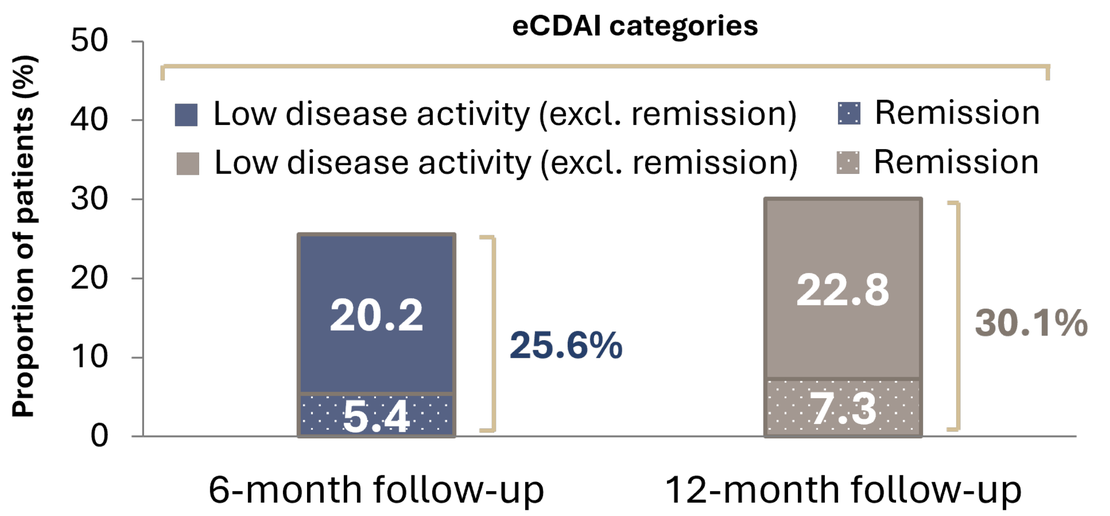
RESULTS

At the 6-month follow-up, the mean eCDAI decreased from 24.3 to 17.6, with 31.0% of patients achieving LDA/remission.

eCDAI score at different time points



Patients achieving LDA/remission at different time points



A machine learning-based algorithm was used to derive the eCDAI, a validated measure that estimates a patient's CDAI score based on information derived from clinical notes.[3]

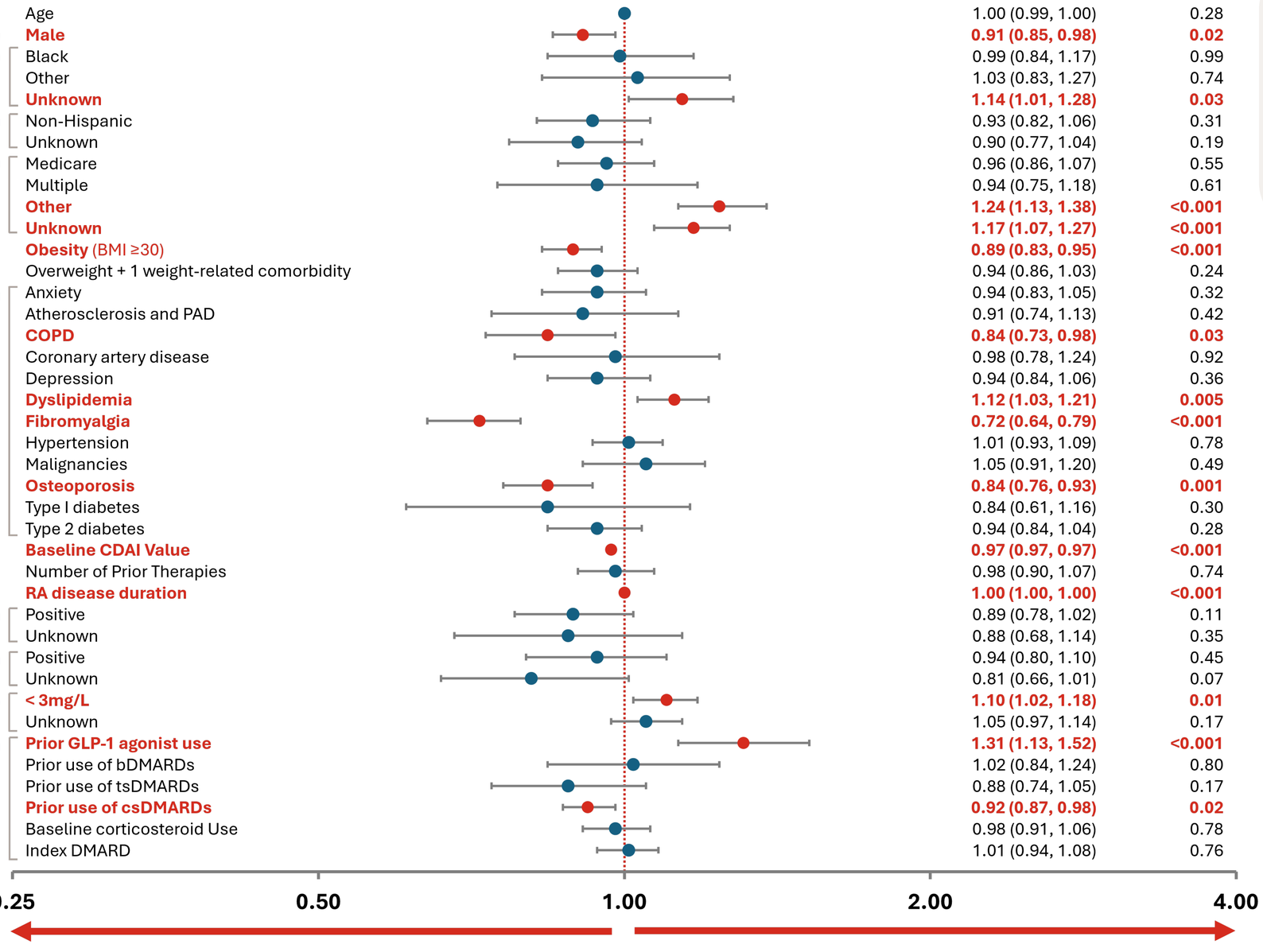
LDA was defined as a change from an index eCDAI score >10 to an eCDAI score between 2.9 and 10 (inclusive), while remission was defined as a change from an index eCDAI score >10 to an eCDAI score of ≤2.8, within 6 or 12 months after the index date.

3. Spencer AK, et al. *RMD Open.* 2021;7(3):e001781.
Abbreviations: eCDAI, Estimated Clinical Disease Activity Index; N, total number of patients

RESULTS

Multivariable associations of baseline characteristics on achieving LDA/remission at 12-month follow-up

Variables		Risk Ratio (95% CI; N=6748)	P-Value
	Age	1.00 (0.99, 1.00)	0.28
Sex (ref. Female)	**Male**	**0.91 (0.85, 0.98)**	**0.02**
Race (ref. White)	Black	0.99 (0.84, 1.17)	0.99
	Other	1.03 (0.83, 1.27)	0.74
	Unknown	**1.14 (1.01, 1.28)**	**0.03**
Ethnicity (ref. Hispanic)	Non-Hispanic	0.93 (0.82, 1.06)	0.31
	Unknown	0.90 (0.77, 1.04)	0.19
Insurance (ref. Commercial)	Medicare	0.96 (0.86, 1.07)	0.55
	Multiple	0.94 (0.75, 1.18)	0.61
	Other	**1.24 (1.13, 1.38)**	**<0.001**
	Unknown	**1.17 (1.07, 1.27)**	**<0.001**
(ref. BMI ≤29.9)	**Obesity** (BMI ≥30)	**0.89 (0.83, 0.95)**	**<0.001**
(ref. BMI <27 or no WRCs)	Overweight + 1 weight-related comorbidity	0.94 (0.86, 1.03)	0.24
Comorbidities (ref. No)	Anxiety	0.94 (0.83, 1.05)	0.32
	Atherosclerosis and PAD	0.91 (0.74, 1.13)	0.42
	COPD	**0.84 (0.73, 0.98)**	**0.03**
	Coronary artery disease	0.98 (0.78, 1.24)	0.92
	Depression	0.94 (0.84, 1.06)	0.36
	Dyslipidemia	**1.12 (1.03, 1.21)**	**0.005**
	Fibromyalgia	**0.72 (0.64, 0.79)**	**<0.001**
	Hypertension	1.01 (0.93, 1.09)	0.78
	Malignancies	1.05 (0.91, 1.20)	0.49
	Osteoporosis	**0.84 (0.76, 0.93)**	**0.001**
	Type I diabetes	0.84 (0.61, 1.16)	0.30
	Type 2 diabetes	0.94 (0.84, 1.04)	0.28
	Baseline CDAI Value	**0.97 (0.97, 0.97)**	**<0.001**
	Number of Prior Therapies	0.98 (0.90, 1.07)	0.74
	RA disease duration	**1.00 (1.00, 1.00)**	**<0.001**
RF status (ref. Negative)	Positive	0.89 (0.78, 1.02)	0.11
	Unknown	0.88 (0.68, 1.14)	0.35
Anti-CCP status (ref. Negative)	Positive	0.94 (0.80, 1.10)	0.45
	Unknown	0.81 (0.66, 1.01)	0.07
CRP level (ref. ≥3 mg/L)	**< 3mg/L**	**1.10 (1.02, 1.18)**	**0.01**
	Unknown	1.05 (0.97, 1.14)	0.17
Prior medication (ref. No)	**Prior GLP-1 agonist use**	**1.31 (1.13, 1.52)**	**<0.001**
	Prior use of bDMARDs	1.02 (0.84, 1.24)	0.80
	Prior use of tsDMARDs	0.88 (0.74, 1.05)	0.17
	Prior use of csDMARDs	**0.92 (0.87, 0.98)**	**0.02**
	Baseline corticosteroid Use	0.98 (0.91, 1.06)	0.78
	Index DMARD	1.01 (0.94, 1.08)	0.76



Patients who were male, had obesity, osteoporosis, COPD, fibromyalgia, higher baseline CDAI scores, or prior use of csDMARDs were less likely to achieve LDA/remission at 12 months.

*Statistical significance is denoted by values in **bold red***
C-Statistic=0.66 (A measure of the model's ability to classify subjects achieving LDA at 12 months)

Multivariable analyses were conducted among patients with non-missing CDAI data at 12 months (N=6,748). Risk ratios and 95% CIs were estimated using log-binomial regression to model the probability of achieving LDA/remission based on baseline patient characteristics as predictors.

Abbreviations: bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CCP, cyclic citrullinated peptide; CDAI, Clinical Disease Activity Index; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; CI, confidence interval; COPD, Chronic Obstructive Pulmonary Disease; CRP, C-reactive protein; GLP1, glucagon-like peptide-1; LDA, low disease activity; PAD, Peripheral Artery Disease; RA, rheumatoid arthritis; RF status, Rheumatoid factor status; tsDMARD, targeted synthetic disease-modifying antirheumatic drug; US, United States; WRCs, weight-related comorbidities.